
An Analysis of Potassium Iodide (KI) Prophylaxis for the General Public in the Event of a Nuclear Accident

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Prepared by
H. Behling, K. Behling, S. Cohen & Associates, Inc.
H. Amarasooriya, J. Kotsch, Scientech, Inc.

S. Cohen & Associates, Inc.
1355 Beverly Road, Suite 250
McLean, VA 22101

Scientech, Inc.
11821 Parklawn Drive
Rockville, MD 20852

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ABSTRACT

A generic difficulty encountered in cost-benefit analyses is the quantification of major elements that define the costs and the benefits in commensurate units. In this study, the costs of making KI available for public use, and the avoidance of thyroidal health effects predicted to be realized from the availability of that KI (i.e., the benefits), are defined in the commensurate units of dollars.

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PREFACE

Commercial nuclear power is a relatively new technology that was introduced in the 1960's. Today, more than 100 licensed power reactors in the United States provide nearly 20 percent of the country's electricity. Most of these facilities are sufficiently close to major population centers that in the event of a major accident, human exposure to airborne radiation would be inevitable. Exposure to radioactive isotopes of iodine, in particular iodine-131, possibly presents the most serious radiological risk from the accidental release of fission products into the atmosphere.

The early and dominant hazard would arise from population exposure to a passing plume containing radioiodines and other radioactive fission products. There is unanimous scientific consensus that the administration of stable iodine can prevent thyroidal uptake of radioiodine with nearly 100 percent efficiency. In spite of the effective remedial action of stable iodine, there are, however, some limitations on its use in protecting the public.

This report provides a comprehensive overview of all topics relevant to arriving at a national policy regarding potassium iodide for general public use in the event of a nuclear accident. For a policy decision, relevant topics include not only the scientific basis for iodide prophylaxis, but also an assessment of the economic costs and the economic benefits to society. Intangible factors such as public perception and potential logistical problems, which cannot be defined in scientific or economic terms, must also be considered.

Content and Organization of the Report

Because of the complexity of relevant subject topics and the potentially diverse background of individuals involved in a policy decision, sufficient background information is provided to assist those who may have expertise in some but not all pertinent subject areas.

Chapters are sequenced in a manner that allows for a logical expansion and transformation of data needed for a final evaluation of the cost-effectiveness of KI prophylaxis.

The assignment of monetary values to human health effects in determining a cost-benefit ratio is far from an established science. For this report, experts in various disciplines were consulted to provide guidance in assigning monetary equivalent values for radiation-induced thyroid effects. Because a cost-benefit evaluation of KI prophylaxis is a central objective of this report and unprecedented methodologies were used to assign monetary values to thyroid health effects, the reader is encouraged not to skip to the final cost-benefit section of the report. A fair evaluation of KI prophylaxis cannot be limited to an assessment of cost-benefit ratio values, but must include a thorough understanding of how these ratio values were derived. Lastly, the text identifies many important subjective factors that could not be incorporated in the cost-benefit ratio. For these reasons, the inclusion of an executive summary containing "bottom-line" cost-benefit values was considered inappropriate for this report.

Following an introduction, which defines existing policy and recent recommendations by Federal and non-governmental agencies, the main body of the report begins with background information relating to thyroid function and disease (Chapter 2). This chapter provides a basic understanding of iodide metabolism in health and disease, the mechanism of thyroid blockade by stable iodine, our present knowledge about radiation-induced thyroid effects and their medical treatments, and the potential adverse reactions to iodide when administered in pharmacological doses equal to those recommended for prophylaxis. Chapter 3 derives the lifetime age- and sex-dependent risk coefficient for several population subgroups in terms of thyroid nodules, thyroid cancers, and hypothyroidism. Chapter 4 provides an overview of the exposure pathways and the thyroid dose model used in this report for estimating population thyroid exposure. Potential population thyroid doses are defined for specific severe accident scenarios using 1990 census data and empirical population data obtained from existing nuclear facilities. By means of previously derived risk coefficients and thyroid doses, population thyroid health effects are defined for the major reactor accident scenarios with and without KI. The economic cost of providing KI and the economic equivalence of each thyroid health effect are quantitatively derived in Chapter 5. In Chapter 6, the programmatic cost of providing KI is weighed against the total number of expected thyroid health effects multiplied by their respective monetary value for a cost-benefit ratio. The significance of the derived cost-benefit ratios to a policy decision is discussed in Chapter 7. The final chapter summarizes the findings and attempts to define the limitations of quantitative values assumed and derived in this report.

Additional data and information used to support Chapters 1 through 8 are provided in several appendices. The sequence of appendices follows the order in which they are referenced in the text. Principal appendices include (1) a detailed description of the methodology used for the valuation of thyroid effects (Appendix D), (2) the experience gained from the Three Mile Island accident, the Soviet accident at Chernobyl, and a pilot project at a nuclear facility in Tennessee (Appendix E), and (3) the derivation of an adverse reaction incidence rate to stable iodide from empirical data obtained from pharmaceutical firms and an FDA computer database (Appendix C).

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CHAPTER 1

INTRODUCTION

1.1 Past Policy and Recommendations

The option to use potassium iodide for thyroidal blocking to protect the general public resides with State and, in some cases, local health authorities. Guidance in these matters, however, is provided by the Federal Emergency Management Agency (FEMA) and the U.S. Nuclear Regulatory Commission (NRC). The NRC and FEMA have issued guidance to State and local authorities as well as licensees of operating commercial nuclear power plants in 50 FR 30258, July 24, 1985. The guidance suggests that any decision by State and local authorities to use potassium iodide should be based on the site environment and conditions at the time of an emergency for the specific operating commercial nuclear power plant and should include detailed plans for distribution, administration, and medical assistance.

The recommendation for stockpiling and distribution of KI during emergencies for thyroidal blocking is currently limited to emergency workers and institutionalized individuals. The Federal position regarding the predistribution or stockpiling of potassium iodide for use by the general public is that it should not be required.

Thyroid blocking for emergency workers and institutionalized individuals was recommended because:

- (1) These individuals would be more likely to be exposed to the radioiodine in an airborne radioactive release in the event of a nuclear emergency.
- (2) The number of individuals involved at any site is relatively small and requires a limited supply of KI that can be readily distributed.
- (3) The storage, distribution, and administration of KI can be readily controlled.
- (4) The known sensitivity to iodide of this limited number of individuals can be reviewed.
- (5) These individuals can be readily monitored for adverse side effects by medical personnel.

In the past, the recommendation to exclude the stockpiling and predistribution of KI for the general public was based on the ability to evacuate the general population, logistical and practical problems, and the low cost-effectiveness of a nationwide program (NUREG/CR-1433).

The Food and Drug Administration (FDA) issued its own recommendation on the use of potassium iodide as a thyroid-blocking agent (47 FR 28158, June 29, 1982). The FDA's recommendations were based on the benefits of using KI and the radiation risks to the thyroid

from I-131. Neither costs nor practical and logistical problems associated with stockpiling and distribution were considered. Based on the ability of KI under optimal conditions to eliminate nearly all internal thyroid exposure and the assumed minimal number of expected adverse reactions to KI, the FDA concluded that the risk/benefit ratio favors the use of the drug when the projected internal dose to the thyroid is equal to or greater than 25 rads. The FDA recommends potassium iodide in doses of 130 mg per day for adults and children over one year of age and 65 mg per day for infants under one year of age. The FDA's projected thyroid dose for pharmacologic intervention equals the upper intervention level of the Environmental Protection Agency (EPA).

Protective Action Guides (PAGs) promulgated by the EPA for projected thyroid dose range from 5 to 25 rem (EPA 1980). Protective action is recommended at the lower level for sensitive populations (pregnant women and children), or if there are no local constraints to providing protection at that level. Protective actions are recommended regardless of local constraints if the projected dose exceeds 25 rem. However, the EPA does not identify the use of KI as a protective measure for public use. Only evacuation and controlled area access are cited as protective measures.

In 1977, the National Council of Radiation Protection and Measurements (NCRP) issued a report (NCRP 1977) that comprehensively reviewed pertinent scientific information regarding iodine metabolism, physiology, and pathology of the thyroid gland. The report, however, did not attempt to evaluate the cost-effectiveness of a program of KI prophylaxis. Practical and logistical problems regarding the distribution of KI to the general population were identified and discussed along with alternative options for public protection. In the report's "Summary and Recommendations," the NCRP recommended daily doses of 130 mg for the duration of potential exposure for projected inhalation thyroid doses of 10 rads or more, but issued a stark warning that:

"The short- and long-term consequences of inhalation of radioactive iodine are far less than the possible injury that might result from individual and mass panic arising from efforts to obtain the blocking agent . . . "

Based on an earlier study conducted by the EPA (EPA 1974), the NCRP paradoxically also concluded that mass evacuation of urban and rural populations can be achieved promptly and safely without loss of life.

1.2 Events Leading to a Reevaluation of the Federal Policy and the Writing of this Report

The American Thyroid Association's Environmental Hazards Committee issued a report in 1984 that assessed the use of iodine as a thyroidal blocking agent in the event of a reactor accident (Becker 1984). This committee of clinical and scientific experts on matters relating to the thyroid gland stated that:

"The development of an appropriate strategy for proper protection against radioiodine contamination requires risk-benefit (risk-ratio of radioiodine hazards to stable iodine hazards) and cost-benefit evaluations, but adequate data are not now available for either the numerator or the denominator."

On the basis of existing but incomplete risk-benefit information, the American Thyroid Association (ATA) concluded the following:

- (1) Potassium iodide in 130 mg scored tablet form should be manufactured in quantities sufficient to fill anticipated needs if its use is required.
- (2) The projected threshold intervention dose of 10 rads recommended by the National Commission on Radiation Protection and Measurement for iodine blockade is overly conservative.
- (3) It is unlikely that clinically significant thyroid disease would result from individual thyroid exposures of less than 100 rads. Iodide prophylaxis is, therefore, recommended for projected doses of 100 rads or greater.
- (4) To provide an added measure of protection for sensitive population groups which include children and pregnant women, a radiation dose of 50 rads to the thyroid is suggested as a threshold for iodine blockade.
- (5) Due to the complexity of the problems, predistribution of potassium iodide is not recommended. (The committee recommended the development of emergency plans for the prompt and efficient distribution in the event of a nuclear emergency.)

The ATA's recommendations urged more vigorous attempts to obtain additional data through clinical studies and a central registry. Clinical studies involving the use of radioiodine as well as potassium iodide would improve our estimates of radiation thyroid risks and adverse reactions to stable iodide. Additionally, the establishment of a central registry for iodide side-effects would provide a more credible means for estimating population risks related to stable iodine.

Following the 1986 Chernobyl accident and the release of information regarding the use of KI by Soviet and Polish officials, the American Thyroid Association in September 1989 submitted a letter to the chairman of the Federal Radiological Preparedness Coordinating Committee (FRPCC). The letter stated ATA's support of KI and requested that the committee reconsider its position on stockpiling KI for general public use. On the basis of the ATA's letter, the FRPCC petitioned the Department of Health and Human Services (HHS) through the Centers for Disease Control (CDC) to review the medical and clinical status of the general use of KI. A workshop chaired by the CDC convened in July 1990 to assess the testimony of various experts. The workshop committee concluded that although no new scientific data were presented that contradicted the scientific basis for the 1985 FRPCC guidance, there was sufficient reason

to establish an ad hoc Subcommittee on Potassium Iodide. The Subcommittee's principal charter was to monitor the activities of the following groups:

- The Conference of Radiation Control Program Directors (CRCPD)
- International Agencies: The World Health Organization (WHO) and the Commission of the European Communities (CEC)
- Nuclear Regulatory Commission (NRC)

The CRCPD. The Conference of Radiation Control Program Directors' study (as requested by the FRPCC and conducted by the CRCPD's E-6 Committee) recently assessed the emergency programs of individual States. By means of a survey, the E-6 Committee obtained data from States with commercial nuclear power plants. Survey data pertain to the distribution of KI within the 10-mile emergency planning zone (EPZ). The information received from responding States is summarized in Appendix A of this report.

The WHO and the CEC. Following the Chernobyl accident, the World Health Organization (WHO) and the Commission of the European Communities (CEC) organized a joint workshop in July 1988 to assess current knowledge and to make recommendations for national contingency plans involving nuclear emergencies. Eminent experts in public health, endocrinology, and radiation protection attended the workshop. The conclusion and recommendations of the workshop provided the basis for guidelines on iodide prophylaxis that were subsequently issued by the WHO Regional Office for Europe (WHO 1989).

The major scientific issues addressed by the workshop committee included the efficacy and limitations of stable iodide prophylaxis and all pertinent factors, which modify the benefit as well as the potential adverse reactions to KI. The major variables considered included dietary intake levels of iodide, age, gender, and underlying thyroid pathologies. The WHO/CEC's formal conclusions regarding the impact of these modifying factors reflect the scientific consensus of the workshop participants, who are referenced throughout this report.

The workshop committee submitted recommendations for iodine prophylaxis, which were subsequently adopted as WHO guidelines, in behalf of the following population groups:

- pregnant women
- lactating mothers
- infants
- children and adolescents
- adults

Appendix B defines the WHO/CEC recommendations for KI use among the five sub-populations identified and provides supportive rationale.

The NRC. Concurrently, but independently of the activities of other agencies, the NRC concluded that because of new information regarding KI, there is a need to reevaluate the existing Federal policy (55 FR 39768, September 28, 1990). New information related to (1) revision in estimates of the release fraction in iodine during reactor accidents, (2) revision in thyroid risk coefficients that are age and sex specific, (3) reduction in the efficacy of I-131 to impart thyroid damage, (4) increased shelf-life of KI, (5) experiences gained from the Chernobyl accident and the pilot projects conducted by the State of Tennessee, (6) improved understanding of potential adverse reactions to stable iodide, and (7) a recommendation by the American Thyroid Association to increase the threshold of the projected thyroid dose for pharmacologic intervention (i.e., KI prophylaxis).

As part of the reevaluation, the Commission contracted this report in order to update the original 1980 analysis (NUREG/CR-1433, "Examination of the Use of Potassium Iodide (KI) as an Emergency Protective Measure for Nuclear Reactor Accidents") with the most current technical information and to expand the cost-benefit analysis to include a more comprehensive evaluation of the monetary value assigned to thyroid health effects.

A comprehensive evaluation of KI prophylaxis and a defensible cost-benefit analysis are complicated tasks made difficult by the need to draw upon multiple disciplines for a complete understanding of the benefits, risks, and economic costs of iodide prophylaxis. Essential to an objective assessment is a basic understanding of (1) thyroid histology, physiology, and iodide metabolism, (2) radiation thyroid pathologies and their treatments, (3) internal dosimetry relating to radioiodine, (4) epidemiological risk assessment methods, and (5) economic methods used to assign monetary values to human illness and associated health care.

CHAPTER 2

BACKGROUND INFORMATION

2.1 Thyroid Function

A basic knowledge of thyroid physiology and metabolism of iodide will help the reader understand the basis for iodide prophylaxis, the potential for adverse reactions to stable iodide, and the evaluation of specific modifying factors relating to internal thyroid dose. Also included in this chapter is a brief overview of the major thyroid pathologies and their treatments; the intent is to promote a better understanding of radiation-induced thyroid injury and specific cost factors. Principal cost factors are represented by direct medical costs, indirect costs associated with loss of economic opportunity, and psychological cost estimates, which reflect a reduction in the quality of life.

The Thyroid Gland. The normal thyroid gland is butterfly shaped and consists of two elongated lobes positioned on either side of the trachea. In the adult, the average weight of the thyroid is between 15 and 20 grams. The dominant microscopic structural feature of the thyroid is its composition of numerous follicles. Each spherically shaped follicle of about 200 microns is lined by columnar epithelial cells (15 μ high) that surround a colloid-filled luminal space (Figure 2-1). The colloid is a mixture of proteins of which thyroglobulins comprise about 80 percent. The flow of blood through the thyroid, per unit weight of tissue, is high and exceeds that of the kidney. The normal thyroid is able to remove iodide from the blood at a rate of 5-12 ml per minute. It is important to note that iodide is concurrently removed from the plasma and excreted by the kidneys at a rate of about 20-30 ml per minute. For a given dietary intake of stable iodide, the kinetics of these two competing removal mechanisms of iodide from the blood form the basis of the iodide uptake fraction from the blood by the thyroid. In instances of radioactive iodine, the uptake fraction (i.e., f_2' value) proportionately determines the dose to the thyroid.

The iodide concentrating mechanism by thyroid cells is frequently referred to as the iodide pump and involves an active energy-dependent membrane transport mechanism. Cell-sequestered iodide becomes a critical constituent of thyroid hormones. In its endocrine role, the thyroid gland exhibits three characteristic functions: (1) trapping of iodide, (2) synthesis of organically bound iodide, and (3) storage and secretion of iodothyronine hormones (Figure 2-2). The thyroid cells actively transport iodide across the cell membrane and maintain a concentration gradient of 25:1 over the level in the blood plasma. Iodination of the amino acid tyrosine is accomplished first at the third position and then at the fifth position to form monoiodotyrosine (MIT). The subsequent synthesis of diiodotyrosine (DIT) and formation of the thyroid hormones triiodothyronine (T_3) and tetraiodothyronine (T_4) occur within the cells of the follicle before being secreted into the follicular lumen to become part of the colloid (Figure 2-2).

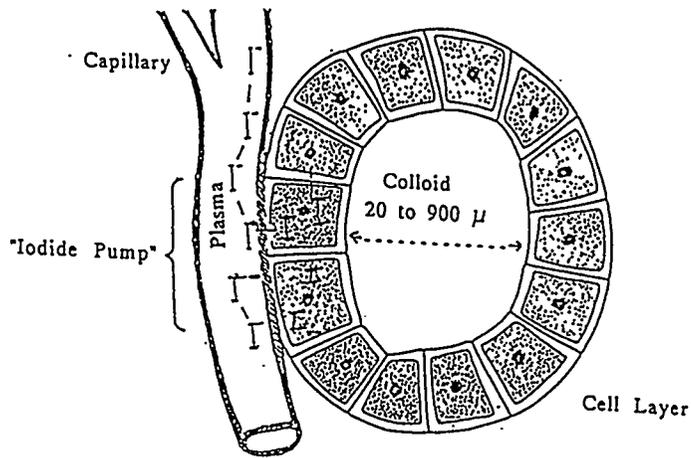


Figure 2-1. Anatomical Features of the Thyroid Follicle

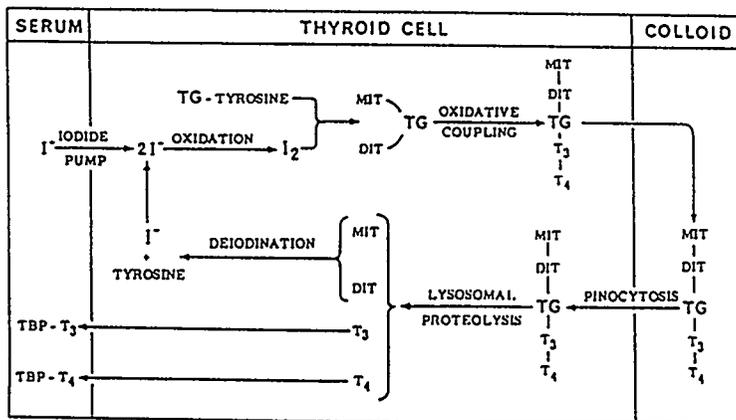
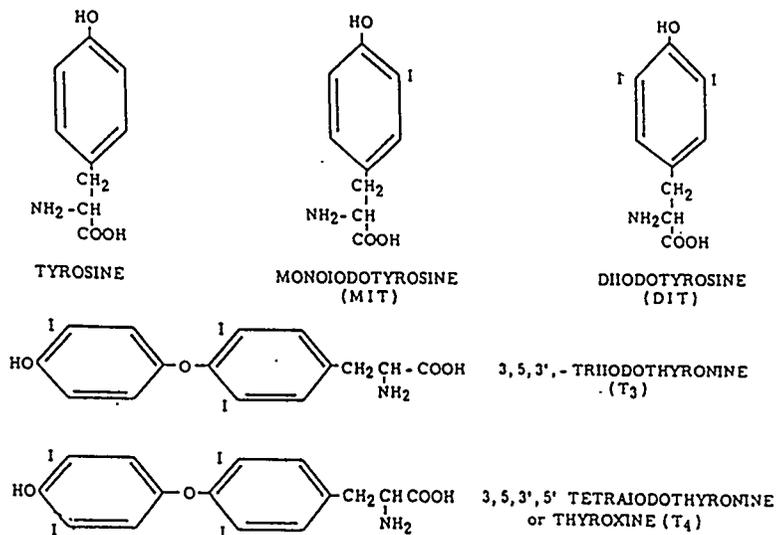


Figure 2-2. Compounds and Pathways of Thyroid Hormone Production

Each day the thyroid releases approximately 60 to 100 μg of hormonal iodide, of which 90% is thyroxine (T_4) and 10% is triiodothyronine (T_3). Although the usual ratio of T_4 to T_3 secreted by the thyroid is 10 to 1, the ratio of T_4 to T_3 in plasma is normally about 40 to 1 due to metabolism differences and the enhanced affinity of T_4 to bind plasma proteins.

Both the synthesis and release of iodothyronines into the blood stream are regulated processes that are primarily under the control of the pituitary gland. Pituitary-secreted thyroid stimulating hormone (TSH) is the main regulator of thyroid function. TSH increases the rate of iodide uptake, organification, and release. The TSH homeostatic feedback control system is designed to maintain a constant level of serum T_4 and T_3 . To achieve this, the gland must accumulate a constant amount of iodide each day. Variations in dietary iodide intake must be countered by reciprocal changes in thyroid uptake and organification of serum iodide. Thus, a lowering of dietary intake of iodide produces correspondingly low serum levels of free iodide that is "sensed" by the pituitary gland. The increased release of pituitary TSH stimulates thyroid cell proliferation, which is aimed to increase the efficiency of the thyroid to capture a limited supply of available serum iodide. A marked and prolonged dietary deficiency of iodide results in thyroid enlargement (simple goiter). On the basis of this homeostatic regulatory mechanism, it is obvious that the fraction of ingested iodide that is accumulated by the thyroid is heavily dependent on the dietary content of iodide. For normal (euthyroid) individuals in the United States with an average daily dietary intake of about 225 μg of iodide, the daily thyroidal uptake of 50 to 60 μg of iodide represents a 25% fractional uptake (i.e., f_2' value). For lower dietary intakes of iodide, the fraction of iodide retained by the thyroid can be considerably higher and may reach levels in excess of 90% (WHO 1989).

The primary significance of dietary iodide levels is that for a common exposure to radioiodide (i.e., inhalation or ingestion), individuals with a lower dietary intake of stable iodide will have a higher thyroid uptake of radioiodide resulting in a proportionately higher thyroid exposure. Daily intake levels of stable iodide may also influence adverse reactions to stable iodide when administered in doses that greatly exceed dietary levels.

2.2 Thyroid Pathology

2.2.1 Hormone Imbalance

The thyroid gland is not indispensable to life, but its presence is necessary for normal growth and development, heat production, and the well-being of the individual. The most prominent effect of the thyroid hormones is their regulatory control of respiratory exchange and basal metabolic rate (BMR). The thyroid gland serves as the body's metabolic thermostat by controlling the rate of oxidative metabolism of individual cells, which collectively provide heat and maintain body temperature.

Under conditions of hyperthyroidism (i.e., increased production or administration of the thyroid hormone), there is increased oxygen consumption, heat production, food metabolism, cardiac output and plasma volume. This clinical state is also referred to as thyrotoxicosis.

Hyperthyroidism is most commonly associated with Graves' Disease. Graves' Disease is an autoimmune disease in which the body's own immune system is directed against cellular and secretory products of the thyroid gland. Hyperthyroidism can also be caused by excessive production of hormones by a single "toxic" nodule, by thyroid carcinomas, and by medications inclusive of potassium iodide. Clinical manifestations of hyperthyroidism range from very mild to severe and may include weakness, increased fatigue, weight loss, changes in skin and hair texture, intolerance to heat, perspiration, blurred vision, heart arrhythmias, and feelings of emotional anxiety.

Hypothyroidism (thyroiditis) is marked by a depression of thyroid hormone production that leads to a progressive slowing down of all bodily activities. Three types of thyroiditis are recognized: chronic, acute, and subacute. Chronic thyroiditis (or Hashimoto's Disease) is not an infection or, in the usual sense, an inflammation, but like Graves Disease is thought to involve an autoimmune reaction. Acute and subacute thyroiditis are normally associated with bacterial and viral infections of the thyroid and are, therefore, self-limiting. Prominent clinical manifestations of hypothyroidism include cold intolerance, dry skin and sometimes thickening of the skin, hoarse voice, constipation, slow speech, weight gain, fatigue, and emotional changes often confused with depression. In adults, thyroid hormones also participate in the organization of cells. When thyroid function is reduced or eliminated, certain cellular functions become disorganized. Two typical examples of this are the epiphyseal dysgenesis and the myxedema. The epiphyseal dysgenesis is manifested by the spotty and irregular calcification of skeletal tissues. The myxedema of hypothyroidism is characterized by the accumulation of an abnormal protein in the interstitial spaces.

During childhood and puberty, thyroid hormones have a profound effect on the rate of body growth and development. A reduced hormone level during this time causes marked reduction in skeletal maturation and prevents full-body growth to adult dimensions. Thyroid deficiency during human fetal life and the post-natal period produces a profound diminution in development and growth, including the central nervous system with a decided loss of intellect. Because radioiodide and stable iodide may uniquely affect fetal thyroid development and function, these effects are discussed separately in Section 2.5.

2.2.2 Thyroid Nodules

Single or multiple nodules of sufficient size may cause obvious enlargement of the thyroid. Usually a nodular thyroid is asymptomatic, but with progressive growth, there may be a visible enlargement in the neck, tracheal compression producing a sensation of choking or coughing, and hoarseness. A nodule(s) refers to a replacement of the normal homogeneous cytostructure of the thyroid with a histologic pattern ranging from colloid-filled cysts and colloid adenomas to follicular adenomas. Nodules are frequently associated with fibrosis and, in some cases, there is evidence of hemorrhage and lymphocytic infiltration. In some patients, enlargement and nodularity of the thyroid are found during routine physical examinations. Since the incidence is 10 to 20 times as great in women as in men, and since it develops and progressively increases

in size during life, it is most frequently found in females 50 to 70 years of age. It is not uncommon for nodules to remain undetected until a post-mortem examination.

Small nodules in euthyroid subjects require no therapy. If the gland is grossly enlarged and causes a cosmetic problem or tracheal compression, resection may be suggested along with thyroid hormone replacement therapy. The potential problems of thyrotoxicosis and malignancy are discussed below.

A small percentage of thyroid nodules tend to produce thyroid hormones uncontrollably and in excess (i.e., the nodule is not under the regulatory control of the pituitary gland and is clinically referred to as toxic nodular goiter). The presence of these autonomously functioning thyroid nodules leads to hyperthyroidism (thyrotoxicosis). Although the pathophysiological problems do not differ from that of other forms of thyrotoxicosis, congestive heart failure, atrial fibrillation, and muscle weakness tend to be more prevalent.

Toxic nodular goiter, like Graves Disease, may be treated surgically (thyroidectomy) or by therapeutic dose(s) with radioactive iodine. A frequent side effect of radioiodine therapy is the induction of hypothyroidism years later.

Although some patients with thyroid nodules are never referred for evaluation or for therapy, the sudden growth of one area of a multinodular gland, the palpation of an unusual firm area, or the development of hoarseness may raise the question of malignancy. Thus, patients for whom surgery (or radioiodine therapy) has been recommended are obviously highly selected because they have developed symptoms that brought them to a physician and that were considered significant enough for referral. Among those patients who are operated upon, the incidence of verified carcinoma (usually papillary adeno-carcinoma) varies from 2 to 20 percent. Because of this frequency, some physicians view the presence of multinodular goiter as sufficient indication for thyroidectomy.

2.2.3 Thyroid Adenomas

Adenomas are new growths of thyroid tissue having a homogeneous histologic pattern surrounded by a capsule of fibrous tissue or compressed normal cells. Pathologically, adenomas are principally of papillary and follicular forms. They may be present as a single structure in otherwise normal glands, as two or three discrete adenomas, or they may be a feature of the multinodular goiter. The most common variety is the follicular adenoma composed of large colloid-filled follicles. There is uncertainty whether these "colloid" nodules are true adenomas.

On clinical and laboratory examination, most patients with thyroid adenomas are euthyroid, and radioactive iodine uptake and scanning studies show that the nodule is "cold" with an ability to concentrate iodide that is equal to or less than normal thyroid tissue. Less frequently, thyroid adenomas produce excessive hormones leading to thyrotoxicosis. Thus, the clinical problem most often presented by the thyroid adenomas is not the management of the thyroid nodule, but the ability to differentiate such lesions from thyroid cancer. Although the probability of

malignancy is reduced for warm or hot (as compared to cold) nodules, nevertheless, 3 to 10 percent of carcinomas are warm to hot. Thus, clinical examination and isotope scanning are not conclusive in establishing whether a nodule is a benign adenoma or a malignant carcinoma.

Treatment: Nodules with strong support for a benign diagnosis can be followed with thyroid hormone suppressive therapy, and hyperfunctioning nodules can be ablated by appropriately large doses of I-131. Nodules with suggestive findings on history (e.g., previous radiation exposure), those with biopsy or cytologic study suggestive of malignancy, those that are cosmetically a problem, or nodules causing a real degree of anxiety are best surgically resected.

The operative procedure is usually subtotal lobectomy if the lesion appears benign and with no observable lymph node involvement. If the diagnosis of adenoma is confirmed upon histological tissue examination, no further procedure is required. If the lesion is malignant, a more extensive procedure is carried out. Patients who have a subtotal resection for a benign adenoma commonly require permanent thyroid hormone replacement therapy.

2.2.4 Thyroid Carcinomas

Thyroid carcinomas are generally classified on the basis of cell origin and histological profiles and include (1) papillary, (2) follicular, (3) medullary, and (4) anaplastic carcinomas. Radiation is generally considered a causative agent only for the induction of papillary and follicular carcinomas.

Papillary carcinoma. Nearly 80 percent of all thyroid carcinomas (and about 90% of radiation-induced thyroid carcinomas) are papillary tumors. Papillary lesions are frequently very small and often found as incidentally observed microscopic tumors in glands removed from some other lesion. Papillary tumors tend to metastasize early to lymph nodes in the neck at a time when the primary tumor cannot be detected by physical examination or by scanning. The tumor remains confined to cervical lymph nodes for a long time, but may invade locally into strap muscles and the larynx, and metastasize to the lungs. Tumor growth tends to be partially dependent on TSH and is less aggressive in individuals under the age of 40. The ten-year survival rate with various forms of therapy is up to about 90%.

Follicular carcinoma. Follicular thyroid carcinomas vary in histological appearance and tend to metastasize early via the bloodstream to lung and bones. The tumors are TSH responsive and tend to pick up and metabolize iodide and to form the thyroid hormone. In the absence of treatment, the unchecked biosynthesis may lead to clinical thyrotoxicosis. The ten-year survival rate with this type of thyroid carcinoma is about 50%.

Treatment of Thyroid Cancer: The selection of patients for surgery was discussed above. Patients with a neck mass thought to be cancerous, or those with a thyroid mass plus cervical nodes, should have thyroidectomy. During surgery, a diagnosis is made based on examination of the primary lesion, resection of lymph nodes, and subsequent histological tissue examination. If the lesion is differentiated papillary cancer under 1 cm in size and is confined to the thyroid,

a total lobectomy is done for the involved side, a subtotal resection is performed on the other side, and resection of the tracheo-esophageal groove is carried out. If there is evidence of multicentricity, if the tumor is over 1 cm in size, if there is a history of radiation exposure to the area, or if it has metastasized to the neck, a near total thyroidectomy is done (with preservation of the parathyroids) along with a limited neck dissection. If there is definitive evidence of lymph node involvement or metastases, patients are given one or more therapeutic doses of iodine-131 to ablate residual tissues and metastatic foci.

2.2.5 Life-Expectancy and Thyroid Cancer

Important parameters in a cost-benefit analysis include not only estimates of potential thyroid effects but also their time of occurrence and their course of outcome. An assessment of time intervals at which cancer may first be diagnosed and, subsequently, the time intervals at which death may occur yield the following two important estimates:

- (1) the collective number of years of life lived with diagnosed cancers, and
- (2) the total years of life lost due to premature death from thyroid cancers.

Both of these parameters are important in quantifying direct costs, indirect costs, and psychological costs, and are discussed further in Chapter 5 and in Appendix D.

Radiation-induced thyroid cancers are essentially confined to the papillary and follicular kind. The proportion of papillary and follicular thyroid carcinomas, when induced by radiation, are assumed to be 90% and 10%, respectively. Beach (1962) and Raventos (1964) analyzed the time of thyroid cancer occurrence among 660 cancer cases involving external radiation in childhood. Following a minimum latency period of five years, the time intervals between exposure and cancer diagnosis exhibited a log-normal distribution that reached a plateau about 15 to 25 years after exposure. The mean time of appearance of thyroid cancers was 10.5 years.

Clinical studies indicate that about 10% of thyroid cancers are fatal and, therefore, result in years of life lost. The times at which deaths from papillary and follicular thyroid cancer occur have been documented by McConahey (1981) and Cody (1976) and involve a combined population of 1,595 thyroid cancer patients treated between 1931 and 1971. The distributions for the time of death for each of the cancer types as well as their weighted means are provided in Table 2-1.

Table 2-1. Time Distribution of Deaths Due to Papillary and Follicular Carcinoma of the Thyroid

Time after Diagnosis (Years)	Papillary (%)	Follicular (%)	Average Weighted Value (%)
1 - 5	44	51	44.7
6 - 10	22	17	21.5
11 - 15	10.5	8.5	10.3
16 - 20	3.5	20.5	5.2
21 or more	20	3	18.3
TOTAL	100	100	100

Using the midpoint of time-intervals and the corresponding percentage value as a weighting factor, an overall mean survival time of 9.3 years following cancer diagnosis can be estimated.

2.3 Health Effects Associated with Radiation Exposure

Radioiodine uptakes from inhalation could result in acute, chronic, and delayed thyroid effects. For very high doses, acute effects include thyroiditis induced within two to three weeks after exposure and hypothyroidism within a period of several months. Following a latency period of years to decades, chronic and delayed thyroid effects may involve the gradual insufficiency of thyroid hormone production (i.e., hypothyroidism) or the appearance of thyroid nodules and cancer.

2.3.1 Acute Radiation Thyroiditis

Acute radiation thyroiditis generally occurs within two to three weeks after an internal exposure to radioiodine and is characterized by inflammation and necrosis of thyroid tissue (Maxon 1977). The symptoms are generally mild but in some instances may be intensely exacerbated by the rapid release of stored thyroid hormones (thyroid storm) (Shafer 1971). In most instances, this syndrome is abated within several weeks of onset.

Data from human subjects who were administered I-131 for the ablation of residual thyroid tissue after thyroidectomy for thyroid cancer suggest that acute radiation thyroiditis has a threshold dose value of about 20,000 rads. Above the apparent 20,000 rads threshold, it is estimated that about five percent of exposed individuals are likely to develop thyroiditis for each incremental dose of 10,000 rads, which yields a D_{50} or median value of 120,000 rads (Maxon 1977).

Based on these observations, the occurrence of radiation-induced thyroiditis is highly improbable even for severe accident conditions and near field populations. Moreover, if sufficiently high

thyroid doses were to occur, they would most likely be accompanied by lethal external radiation exposure doses. For this reason, acute radiation thyroiditis is not relevant to a cost-benefit analysis for iodide prophylaxis and will not be considered in this report.

2.3.2 Chronic Lymphocytic Thyroiditis

Chronic lymphocytic thyroiditis is an inflammation of the thyroid that is characterized by autoimmune reactions and occurs years after radiation exposure. An abundance of lymphocytes within the thyroid tissue and the prevalence of antimicrosomal and antithyroglobulin antibodies are strong evidence of an autoimmune reaction triggered by radiation (DeGroot 1983). While incidence rates and risk estimates have been established for populations exposed to external radiation during childhood, there is insufficient data to permit risk estimates of chronic thyroiditis for I-131 exposure (DeGroot 1977). From a practical point of view, this condition has limited clinical significance unless the inflammation is associated with hypothyroidism or thyroid nodules in which case risk estimates for hypothyroidism and thyroid nodules would encompass potential manifestations of chronic lymphocytic thyroiditis. Chronic lymphocytic thyroiditis will, therefore, not be assessed as a separate radiation-induced thyroid condition.

2.3.3 Hypothyroidism

Hypothyroidism represents a metabolic state in which the thyroid produces an insufficient quantity of the thyroid hormone for normal physiologic function. For radiation-induced hypothyroidism, it must be assumed that a substantial number of cells are either killed or rendered non-functional, because of the large reserve capacity of the normal thyroid. In recognition of this reserve capacity and the classical sigmoid dose-response relationship of somatic cell survival, a linear model with a threshold is generally assumed for hypothyroidism.

Clinical studies of patients treated with I-131 for Graves' Disease (Becker 1971) and cardiac disease (Segal 1958) convincingly show a linear correlation between the radiation dose to the thyroid and the probability of hypothyroidism above a threshold dose. Based on these and other human data, thyroid doses of 60,000 rads would be expected to result in a 100% probability of hypothyroidism.

The latency period between exposure and symptoms of hypothyroidism ranges from less than one year to several decades and increases with decreasing doses. Another important variable affecting latency is the age at exposure. As a result, hypothyroidism can be expected to occur over an ill-defined but limited time period. In this report, a mean latency period of five years is assumed for radiation-induced hypothyroidism.

2.3.4 Thyroid Neoplasms

Thyroid neoplasms include benign nodules (adenomas) and cancerous nodules (carcinomas). Thyroid neoplasms occur spontaneously in the general population and with increased frequency among populations with radiation thyroid exposure.

Estimates of spontaneous incidence of thyroid nodules and thyroid cancers for the general population are generally based on clinically evident thyroid conditions, which do not include "occult" thyroid neoplasms (i.e., thyroid neoplasms, which go undetected and are only noted incidentally). Based on the analysis of several independent studies and fitting data points with a linear regression function, Maxon (NUREG-4214) estimated the spontaneous incidence of clinically detectable thyroid nodules at 0.1% per year of life for the general population with a lifetime risk of approximately 7%. In estimating the number of expected cancers from the total incidence of thyroid nodules, Maxon assumed that 10% of the nodules were malignant, yielding an annual risk of 0.01% and a lifetime risk of about 0.7%.

2.3.5 External Radiation and Thyroid Neoplasms

The most informative human data providing a quantitative relationship between radiation exposure and the delayed formation of thyroid neoplasms involve retrospective studies on subjects exposed to doses up to 1,500 rads of external radiation in childhood for a variety of benign diseases. For a period of about 30 years (1925-1955), x-rays were commonly used in (1) scalp irradiation for ringworm (Modan 1974, Shore 1976 or later, Ron 1984); (2) neck and chest irradiation for pertussis (Webber 1975), enlarged thymus (Shore 1985), adenoids, tonsils (Crile 1975); and (3) skin irradiation for facial acne and hemangiomas (Goldschmidt 1977).

Higher doses of external irradiation in the range of 2,000 to 5,000 rads were used between 1920 and 1940 for the treatment of goiter (DeLawter 1963), hyperthyroidism in adults (Einhorn 1967), and cancer in the neck region during childhood (Kaplan 1983). Collectively, studies of individuals with external thyroid exposures in excess of 1,500 rads show that there is a reduced risk of neoplasms per unit dose than for lower doses. It is generally assumed that at external doses above 1,500 rads, cell-killing increasingly reduces the potential for neoplastic cell transformation. The incidence of thyroid neoplasms among these populations was, therefore, not considered appropriate for formulating risk estimates.

Our current estimates of thyroid risks are based on external exposures ranging from about 5 to 1,500 rads. Thyroid exposures for scalp epilation are estimated to range from 5 to 50 rads, for enlarged thymus 60 to 500 rads, enlarged tonsils and adenoids 400 to 800 rads, and 600 to 1,500 rads for facial acne.

For risk estimates, the most significant studies to date, involving childhood exposures of less than 1,500 rads, are those of Shore (1976), Maxon (1980), Frohman (1977), Hempelman (1975), DeGroot (1983), and Ron (1984). Their studies indicate a linear dose-response with no clear threshold for thyroid nodules and cancers. Additionally, these studies provide strong evidence of a minimum latency period and a variety of modifying factors involving age, gender, and ethnic origin.

2.3.6 Thyroid Neoplasia from Internal Exposures to Radioiodine

The thyroidal effects from internal deposition of radioiodines have been studied for three categories of exposed individuals: (1) patients receiving large therapeutic doses of I-131 for thyroid disorders, (2) patients receiving much smaller doses of I-131 for diagnostic purposes, and (3) fallout exposures from atomic weapons.

Therapeutic Exposures. In the treatment of hyperthyroidism associated with Graves' Disease, I-131 is administered in sufficient quantities to cause partial to full ablation of the thyroid. Depending upon patient-specific iodine metabolism and size of thyroid gland, radioiodine may be administered in millicurie quantities which yield thyroid doses from a few thousand to more than ten thousand rads.

In two independent studies involving more than 20,000 adult subjects (Dobyns 1974; Holm 1984), there was no evidence of I-131 induced thyroid cancers. In fact, the thyroid cancer incidence rate among I-131 treated patients with Graves' Disease was well below the level of patients not treated with radioiodine. It has been assumed that this apparent absence of carcinomas may be due in large part to the effects of cell-killing and/or sterilization at such high dose levels. Additionally, in both studies, the follow-up time (less than ten years) was relatively short, and the studies involved adults whose thyroids are less susceptible than those of children.

In two smaller studies with a combined population of 304 patients between 1 and 20 years of age, two thyroid cancers were observed when only 0.3 cases were expected. The difference between the observed and expected number of cancers, however, was not considered significant (Safa 1975).

Diagnostic Exposures. The most intensive follow-up studies of patients given I-131 for diagnostic purposes are the Swedish studies of Holm, et.al. (Holm 1980; 1984; 1988). The most recent study (Holm 1988) assessed the cancer incidence of 35,074 individuals who had survived at least five years following exposure to a diagnostic dose of I-131. Important statistical parameters for this study population included the following mean values: (1) thyroid dose of about 50 rads; (2) age of exposure at 44 years; and (3) a follow-up period of 20 years. A total of 50 thyroid cancers was observed among the I-131 exposed study group. Based on age and sex composition of the study group, about 39 cases were expected. The resultant standardized incidence ratio of 1.27 was not considered significant inasmuch as the observed standardized incidence ratio fell well within 95% confidence interval range of 0.94 to 1.67.

Any potential link of the observed thyroid cancers to I-131 exposure is further minimized by these facts: (1) 10 of the 50 observed thyroid cancers were medullary carcinomas that are generally regarded as non-radiogenic cancers and (2) the majority of observed cancers occurred among individuals who had received a diagnostic dose of I-131 because of suspected thyroid cancer. In summary, these studies provide no evidence that thyroid doses below 150 rads from I-131 significantly increase the risk of thyroid cancer.

In the United States, an interagency study (involving the Department of Health and Human Services' Bureau of Radiological Health, the National Cancer Institute, and the Nuclear Regulatory Commission) has been in progress since 1973. The study includes persons who during childhood were administered diagnostic levels of I-131 yielding a mean dose of 94 rads. Although no data have officially been published, to date none of the 443 treated subjects has developed thyroid cancer, and while several cases of benign thyroid nodules have been observed, their incidence is not considered significant.

Exposure to Fallout. Two population groups that have been exposed to radioiodine from weapon fallout have been extensively studied. Inhabitants of Marshall Island were exposed to fallout from the 1954 BRAVO thermonuclear test. This atmospheric nuclear test heavily contaminated the islands of Rongelap atoll and, to a lesser extent, Utrik atoll. Thyroid exposure resulted primarily from a combination of external gamma radiation and the internal exposure to a mixture of radioiodines. For the inhabitants of Rongelap and Utrik atolls, external thyroid exposures have been estimated at 175 and 14 rads, respectively. However, radioiodines contributed the largest percentage to the total thyroid doses which ranged from a low of 30 rads to greater than 1500 rads (Conard 1984). The thyroid condition of inhabitants of those two atolls included an increased prevalence of hypothyroidism, thyroid nodules, and thyroid carcinomas (Conard 1984).

In order to refine the risk of thyroid neoplasia from nuclear fallout containing radioactive iodines, studies of the Marshallese have recently been expanded to include 12 atolls previously thought to be unexposed to fallout (Hamilton 1987). As a result, the study population was expanded to 2,273 persons who were alive at the time of BRAVO test and who lived on one of the 14 atolls. On the basis of new data, a linear dose-response relationship was observed which yielded an absolute risk coefficient of 11 excess cases per one million person/rad years (Hamilton 1987). This risk estimate was 33% higher than previous estimates, which did not include the total geographical extent of the Republic of the Marshall Islands. Due to the complexity and the assumptions used in estimating thyroid doses and the uncertainty of spontaneous incidence of thyroid neoplasia, the National Research Council's Committee on the Biological Effects of Ionizing Radiation (BEIR) urges caution in interpreting data regarding the Marshall Islanders.

The second population group studied for thyroid disorders include children exposed to fallout resulting from atmospheric testing of nuclear devices at the Nevada Test Site (NTS) between 1951 and 1962. During that period, 105 tests were conducted above ground surface and 14 other tests were conducted below ground, but at a depth where containment was incomplete (Church 1990). A cohort of about 2,600 public school students, who as infants lived proximally to the Nevada Test Site in Utah and Nevada, has been studied since 1965. The prevalence of thyroid abnormalities in these children has been compared to that in a control group selected from a county in Arizona that was presumed to have received little or no fallout from the NTS. Thyroid doses were primarily the result of ingestion of radioiodine-contaminated milk, and cumulative thyroid doses among study subjects have been estimated to range from 30-700 rads (Mays 1966). The significance of milk as the primary pathway for thyroid exposure is that shorter-lived radionuclides of iodine are proportionately excluded from contributing to the

thyroid dose. Incidences of thyroid neoplasms were first reported in 1974 and 1975 (Rallison 1974 and 1975). At that time, among the 4,819 children, which included 2,140 nonexposed controls, a total of 76 nodules was detected of which 22 were diagnosed as neoplasms. (In addition to neoplastic nodules, observed palpable nodules also included colloid nodules, thyroid cysts, and solitary discrete nodules without tissue diagnosis.)

Although the rate of thyroid neoplasms among the Utah/Nevada subjects of 5.6/1,000 was higher than that of the Arizona control subjects (3.3/1,000), the difference was statistically insignificant. In a follow-up study conducted in 1985-1986, in which 3,122 of the original 4,819 subjects were reevaluated, thyroid nodules were found in 125 individuals (Rallison 1990). Of the 125 thyroid nodules detected in this later study period, 65 were considered to be neoplasms. The rate of thyroid neoplasms in Utah/Nevada subjects of 24.6/1,000 was again slightly but insignificantly higher than that of the Arizona subjects (20.2/1,000). The authors concluded that living near the NTS in the 1950s did not result in a statistically significant increase in thyroid neoplasms among exposed subjects when compared to control subjects of the same age and gender.

2.3.7 Efficacy of Radioiodides Relative to External Radiation

The studies cited above as well as others provide compelling evidence that internal exposure to I-131 is considerably less efficient in producing thyroid effects per unit absorbed dose than external X- or gamma-ray exposure. In fact, no human study in which thyroid exposure was solely due to internal exposure to radioiodine has provided causal evidence of thyroid carcinogenicity.

Among the Marshallese and Japanese A-bomb survivors where excess nodules and cancers were observed, thyroid exposure to radioiodine was accompanied by external gamma radiation. Their data are further obscured by thyroid doses that resulted in hypothyroidism. Untreated hypothyroidism resulting from partial thyroid ablation induces the excessive production and release of thyroid stimulating hormone (TSH) which is suspected to stimulate nodule formation in residual thyroid tissue. The reduced efficacy of I-131 relative to external gamma radiation is further supported by clinical data. When compared to external doses, considerably higher internal doses are needed to achieve comparable levels of thyroid ablation.

The reduced efficacy of I-131 to produce thyroidal effect per unit dose is primarily thought to be the result of differences in dose rate and dose distribution. When the efficacy of I-131 has been compared to that of external gamma radiation, the external gamma radiation dose was received in a very short period of time. Based on the effective half-life of about seven days, the internal exposure from I-131 is spread out over time, which allows for potential cellular repair. Studies assessing the differences between acute and chronic exposures have concluded that for a common dose, and depending upon the biological endpoint under investigation, a chronic exposure may be two to ten times less effective (NCRP 1980).

Potentially of greater significance are micro-dosimetric factors that result in a non-homogeneous dose distribution within the thyroid. The thyroid gland consists of spherical shaped follicles that

vary in diameter from 20 to 900 microns, with an average of 200 microns (Gillespie 1970). These structures make up about 50% to 75% of the glandular volume, the remainder being connective tissue. Each follicle consists of a single cell layer, which surrounds the colloid filled lumen (see previous Figure 2-1).

The iodide-containing thyroglobulin is synthesized within the cells and subsequently stored as a liquid colloid within the lumens of the follicles. Organically bound iodine is slowly released by the follicles into the circulating plasma as thyroid hormone. About 90% of thyroidal iodide is sequestered in the cell-free colloid. Between 90% and 95% of the energy absorbed by the thyroid from the radioactive decay of I-131 results from the absorption of beta-particles. Based on the disproportionate concentration of radioiodine within the cell-free volume of the follicle and the limited range of beta particles, it is apparent that a "calculated" thyroid dose (which assumes uniform dose distribution) overestimates the true dose received by the surrounding cellular components.

Both the National Academy of Science, BEIR V Committee (NAS 1990) and the National Council on Radiation Protection and Measurements (NCRP 1987) reviewed the wide range of values reported in the literature and concluded that for I-131, the relative effectiveness for the induction of thyroid cancer per unit dose is one-third that of external gamma radiation. For the induction of benign thyroid nodules and hypothyroidism, I-131 is considered only one-fifth as effective as external radiation (NUREG-4214).

For other fission-produced radioiodides, a relative effectiveness of 1.0 is assumed. This is based on their much shorter half-lives, higher beta energies, and a lack of human evidence suggesting otherwise.

2.4 The Basis of Potassium Iodide Prophylaxis

In the event of a nuclear accident involving the release of large amounts of radioiodines, thyroid uptakes from inhalation and ingestion could result in thyroid neoplasms and thyroid dysfunction. Under proper conditions of dosage and time, stable iodide can effectively block the thyroidal uptake of radioiodine. Thyroid blockade is primarily achieved by saturating the iodide transport mechanism at the cellular level and diluting the relatively small quantity of radioiodine with stable iodide (Wolff 1964, 1980).

A secondary mechanism for thyroid blockade involves the Wolff-Chaikoff effect. Under normal iodide intake conditions, iodide transport is the rate-limiting step in iodide accumulation in the thyroid. Over a limited range of concentrations, the ratio of iodide in the thyroid to that of the serum (i.e., T/S ratio) is constant. Thus, when serum levels of iodide increase so does the rate of uptake and organification. But when serum levels exceed 25 $\mu\text{g}/\text{dl}$, the thyroidal transport mechanism is saturated and the T/S ratio decreases which in turn triggers a reduction in the organification of iodide. This fall in iodide organification at high plasma iodide concentrations is the Wolff-Chaikoff phenomenon (Wolff 1964).

For normal individuals, the Wolff-Chaikoff effect is of limited duration. Within hours (and in spite of elevated serum levels of iodide that continue to block the iodide transport mechanism), normal organization of iodide resumes. Thus, for normal individuals, the Wolff-Chaikoff effect has limited significance in terms of its contribution to thyroid blockade.

For some individuals, however, "escape" from the Wolff-Chaikoff effect is impaired by underlying thyroidal pathologies. Unrelieved Wolff-Chaikoff suppression that leads to hypothyroidism is seen among individuals with (1) Hashimoto's thyroiditis, (2) perinatal thyroids, (3) Graves' Disease, and (4) reduced thyroid function due to partial thyroidectomy and/or I-131 treatments. The significance of the Wolff-Chaikoff effect is that a prolonged state of hypothyroidism may be induced by stable iodide among select members of a population inclusive of the fetus. This potential adverse effect of iodide is discussed in Section 2.6 of this chapter.

2.4.1 Dose Requirement for KI Prophylaxis

Both the efficacy and persistence of the thyroid blocking effect by stable iodide are dose dependent. After an oral administration, iodide is rapidly absorbed into the bloodstream from the stomach where it is progressively removed either by the thyroid or by the kidneys. This exponential clearance of iodide from the blood stream in normal subjects has been shown to have a half-period value of about five to six hours (Myant 1949). (For abnormally high and low dietary iodide intakes, there is a corresponding reduction and elevation in thyroid uptake rates that result in longer and shorter half-period values, respectively.) Given the rapid uptake of iodide (radioactive or stable), there is a limited benefit of KI administration following exposure to radioiodine. For KI to serve as an efficient blocking agent, it must be administered in sufficient quantities before or concurrently with radioiodine exposure.

The highly effective thyroid block by 100 mg of iodide or more has been demonstrated in a number of studies (Pochin 1962; Cronquist 1971). Blocking by smaller amounts of iodine was also demonstrated by Sternthal (1986). In this study, thyroid blocking was about 60 percent efficient for an iodide dose of 10 mg and asymptotically reached efficiency levels of about 95% to nearly 100% for doses of 30 mg and greater. Similar values were obtained by others as reported by the U.S. National Council on Radiation Protection and Measurements (NCRP 1977).

2.4.2 Persistence of KI Block

Although doses of about 30 mg are nearly as effective as higher doses when taken just prior or concurrently with radioiodine, the persistence of the blocking effect to subsequent exposure to radioiodine is reduced. The ability of stable iodide to maintain a thyroid block and prevent the uptake of a subsequent exposure to radioiodine is dependent on a continued elevated serum level of stable iodide. Using the value of five hours for the biological half-period serum clearance rate of iodide, one can readily determine the serum concentration level at any time following an oral administration of KI by means of the following equation:

$$C_s = Q_u e^{-\left(\frac{0.693}{t_{1/2}}\right)t_i} \quad (\text{Eq. 2-1})$$

where:

- C_s = serum level (mg) at time t_i
- Q_u = uptake quantity (mg)
- t_i = lapse time
- $t_{1/2}$ = half-period

Since a 30 mg dose confers about 95% blocking when administered just before radioiodine exposure, it would be expected that a 100 mg slug of iodide would still provide a 95% thyroid block almost nine hours after administration. This relationship is illustrated by the classical study of Il'in, et al (Il'in 1972), in which the blocking effect was assessed with time among individuals given a single 100 mg slug of stable iodide (Fig 2-3).

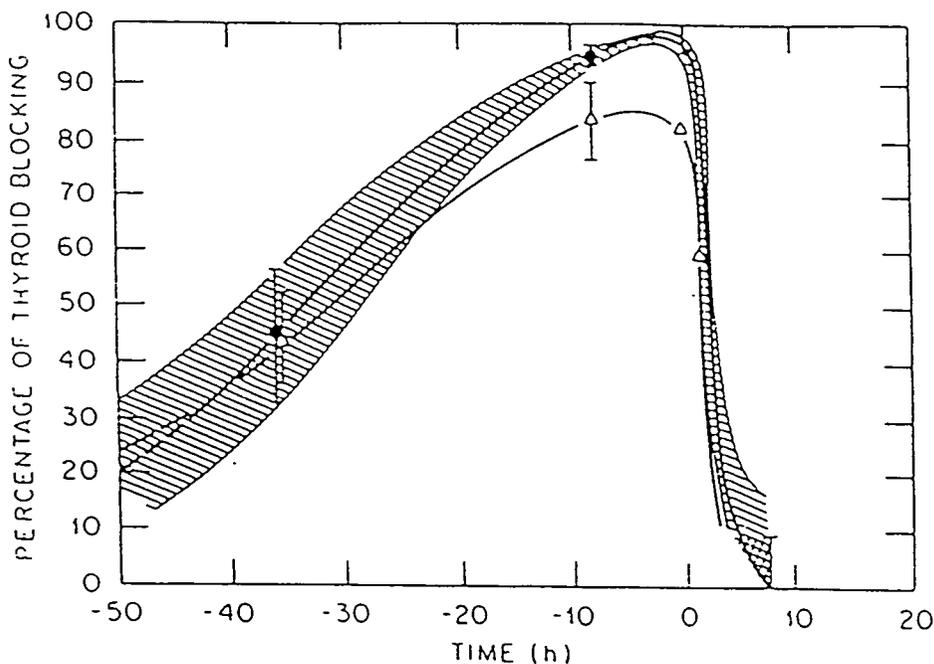


Figure 2-3. Percent of Thyroid Blocking Afforded by 130 mg of Stable KI as a Function of Time of Administration Before (-) or After (+) a Single Slug Intake of I-131.

From Figure 2-3, it is apparent that for accident conditions in which public exposure to radioiodine may last several days, there is a diminishing benefit associated with a single slug of stable iodide. For prolonged exposure conditions, Sternthal (1986) determined that a daily iodide dose of 15 mg, 30 mg, 50 mg, and 100 mg yielded blocking efficiencies of 90%, 92%, 94%, and 98.5%, respectively.

The duration of time during which KI must be taken in order to confer thyroid protection corresponds to the period of exposure or potential exposure. For a reactor emergency, this time is assumed to last from a few days to about 10 days.

2.5 Radioiodine Exposure In-Utero: A Special Case

The placenta freely passes iodide from the maternal to the fetal circulation (Roti 1983). Exposure of a pregnant female to radioiodide, therefore, has the potential for exposing the fetal thyroid. However, the capacity to concentrate iodide, as measured by the uptake of radioiodide in the fetal gland, does not start until the end of the first trimester (12 weeks). At this time, the fetal thyroid has attained a nominal weight of 5 mg but begins to increase rapidly in size to about 50 mg by 13 weeks, 100-200 mg by 20 weeks, 200-600 mg by 24 weeks (end of second trimester), and 1-3 g at term. The total iodine content of the fetal thyroid gland increases with thyroid weight and with gestational age. The fetal data indicate that the uptake per gram of thyroid tissue may be considerably greater than that of adults (Evans 1967). Studies on fetal thyroid glands do not reveal organically bound iodide until about the 19th week despite the appearance of radioiodide uptake at earlier ages (Yamanaki 1959). Labeled T_4 and T_3 have been detected in low concentrations in thyroid tissues from 20-24 week old fetuses (Sinadovic 1986; Costa 1986). The capacity to synthesize iodothyronines (e.g., T_4 , T_3) is not necessarily coincident with the onset of secreting these hormones to the fetal blood stream. Release of iodothyronines to the blood seems to require thyroid stimulation by TSH, which is not secreted by the anterior pituitary until the 28th week. Coincident with the elevation of fetal plasma TSH, there is a marked sudden increase in plasma T_4 and T_3 levels. At birth, fetal serum T_4 is as high as in the maternal serum.

2.5.1 Onset of Thyroid Hormone Secretion and Regulation

Information is limited regarding how early in fetal development the pituitary is capable of responding to changes in thyroid hormone levels. As already indicated, T_4 and TSH levels in fetal serum concurrently fluctuate sometime after mid-gestation. These findings suggest an increasing sensitivity of the fetal thyroid to TSH and of the fetal pituitary to feedback suppression by thyroid hormones (Fisher 1985; Delange 1984). The responses of the human fetal pituitary near term to thyroid hormone deficiency or excess show that the pituitary-thyroid system functions with at least a degree of autonomy from the maternal thyroid function.

The fully mature thyroid gland has the capacity to modify iodine uptake in accordance with circulating iodide levels and independently of TSH. This auto-regulatory system in the fetus is absent and develops only during the final weeks of gestation (36-40 weeks) (Delange 1984;

Delange 1985; Carswell 1970). This auto-regulatory mechanism in the mature thyroid permits the gland to overcome the suppressive effects on thyroid hormone secretion caused by excessive iodide levels (Wolff-Chaikoff blockade). A persistent maternal exposure to KI prior to the fetal development of this auto-regulatory mechanism may, therefore, impair normal fetal growth and brain development.

2.5.2 Transfer of T₄ and T₃ from Mother to Fetus

There is still considerable debate whether maternal thyroid hormones cross the placenta in amounts significant for fetal development prior to the fetus's independent ability to synthesize and secrete its own (Fisher 1981, Fisher 1985, Thilly 1978, Burrow 1975, Selenkow 1973). The reason for concern is that during the first and possibly during part of the second trimester, the human fetus would be entirely dependent on maternal thyroid function. Therefore, maternal hypothyroidism could result in a decreased availability of thyroid hormone during the initial phases of gross brain development and during the spurt in forebrain neuroblast proliferation. The outcome of pregnancies in hypothyroid women is very poor, showing a disproportionate incidence of spontaneous abortions, stillbirths, perinatal death, developmental abnormalities, and mental retardation (Greenman 1962; Man 1976). Because there is no information regarding when in the period of gestation the fetus is most vulnerable to maternal hypothyroxinemia, it is not possible to determine if maternal hypothyroxinemia of short duration would have adverse effects on the fetus.

In view of existing information and in spite of unresolved questions, a prudent policy would avoid maternal hypothyroidism or any situation in which maternal thyroid function might be impaired during the first and second trimesters. During the third trimester, the fetal pituitary-thyroid system appears to be functioning with a high degree of autonomy from the maternal thyroid. During pregnancy, iodide prophylaxis must balance the complex and time-dependent maternal and fetal risks of radioiodine with the potential adverse effects of stable iodide overload.

2.5.3 Congenital Hypothyroidism and Cretinism

Congenital hypothyroidism leading to cretinism is normally observed only in (1) endemic areas where severe iodine deficiency leads to hypothyroidism in both mother and child during fetal development and (2) individuals with congenital metabolic defects in thyroid hormone formation.

Endemic cretinism induced by iodide deficiency in-utero refers to individuals having a typical constellation of signs and symptoms which at birth include increased hair, low forehead, puffy features, umbilical hernia, enlarged tongue, and sluggish behavior. Other abnormalities may include deaf-mutism, mental retardation, and evidence of spastic paraplegia. If, after birth, a state of hypothyroidism is allowed to continue, stunted body and skeletal growth and mental retardation result. Due to the relatively high dietary iodine intakes in the United States, cretinism due to in-utero iodide deficiency is rarely encountered.

In the United States, about 1 out of 5,000 newborns suffers from hypothyroidism due to a metabolic defect in thyroid hormone formation, transport, and action. Among these individuals, the basis for congenital hypothyroidism is a genetic deficiency that impairs or prevents normal iodide trapping, iodide organification, "coupling," recycling of iodide, or resistance to the action of the thyroid hormone. These metabolic defects usually represent the expression of the homozygous recessive genetic abnormality and may, therefore, be observed in family groupings or inbred populations.

2.5.4 In-Utero Thyroid Dose

Congenital hypothyroidism may also result from the destruction of the fetal thyroid from maternal exposure to radioiodine. After the first trimester when fetal thyroid uptake starts, the fetal thyroid may be adversely affected by maternal exposure to radioiodine. Inadvertent administration of high doses of I-131 to women for treatment of thyrotoxicosis or thyroid cancer has occurred in limited numbers when their pregnancy was unknown. In most such instances, exposure occurred early in the first trimester with limited consequences. Several cases, however, have been reported where the radioiodide was administered at the end of the first or beginning of the second trimester (Lightner 1977, VanHerle 1975, Hamill 1961, Fisher 1963, Green 1971, Stoffer 1976). Considerable destruction of fetal thyroid resulting in infant hypothyroidism and other developmental abnormalities was observed in several cases. The relatively low frequency of permanent damage to the fetus is likely related to the fact that fetal uptake is very low until mid-gestation, and inadvertent administration of I-131 at such an advanced stage of gestation is infrequent.

Johnson developed a model of iodine metabolism in the human fetus from which he calculated the dose to the fetal thyroid as a function of fetal age from intake of radioiodine by the mother. Owing to the small mass of the fetal thyroid, Johnson calculated that the fetal thyroid dose per unit of maternal intake varies with time but on the average is about a factor of two above those to the mother's thyroid (Johnson 1982).

2.5.5 Pregnant Females and Stable Iodide Prophylaxis

From the previous discussion, it is apparent that the pregnant female and her fetus are at special risk in case of environmental contamination with radioiodine. Paradoxically, KI administration also poses some potentially unique adverse effects during pregnancy, which may result from iodide overloads to the maternal and/or fetal thyroids. Unfortunately, insufficient data exist regarding the incidence rates of these effects after single or short-term administration of iodide. When exposure to radioiodine yielding high doses is either probable or inevitable, the benefits of KI prophylaxis far outweigh potential adverse effects regardless of the stage of pregnancy. Specific recommendations by the World Health Organization regarding KI prophylaxis during pregnancy are discussed in Appendix B.

To guard against the potential consequences of KI-induced congenital hypothyroid, newborns of pregnant females taking KI should be monitored for an adequate period to detect signs of reduced T_4 and/or elevation of TSH levels.

Considering the current lack of information regarding the transient consequences of maternal KI overload on early fetal development, maternal thyroid function should also be monitored/controlled following KI administration to pregnant females.

2.6 Potential Adverse Reactions to Stable Iodide

Iodine is a ubiquitous but variable constituent in the environment. Due to its solubility, iodide is readily leached out of soil by rain which ultimately carries it to the world's oceans. From ocean waters, iodide evaporates to the atmosphere where it is concentrated in rain which replenishes the soil (Koutras 1980). Iodide is essential to good health, and the main source for humans is through food. The highest natural iodine content is found in seafood, which may reach concentrations as high as 800 μg iodine per kg. Other dietary sources of iodide are eggs, meat, milk, and cereals. Additionally, many foods are artificially enhanced in the United States by additives such as iodized salt. It is estimated that the daily intake of iodide for adults in the United States ranges between 125 μg to 700 μg (Oddie 1970; Rubery 1988).

Dietary iodide levels play a key role in potential adverse reaction incidence rates. When dietary levels are high, adverse reactions are assumed to be at their lowest rate. Epidemiological and metabolic studies support a minimum daily adult requirement of 100 μg ; endemic goiter is usually not found when the dietary intake of iodine is above 100 μg per day (Stanbury 1980). However, the ATA has stated that:

" . . . [while] many anecdotal reports of isolated reactions to iodides have been published, reliable incidence data do not exist. It is reasonable to assume that obvious iodide reactions are rare in the United States where the diet is high in iodine content. . . . When reactions do occur, they may be intrathyroidal or extrathyroidal" (Becker 1984).

In instances of dietary deficiency, the synthesis of thyroid hormones is restricted and the serum concentration of T_4 is low. This stimulates the thyroid pituitary feedback mechanism with increased synthesis and secretion of TSH. Elevated serum levels of TSH increase thyroid metabolism of iodide as well as the growth of the thyroid which under prolonged conditions of iodide deficiency becomes goitrous.

Stable iodide prophylaxis is based on the prompt administration of relatively large amounts of stable potassium iodide (i.e., 130 mg per day) over a period of a few days to a potentially exposed population. This transient increased intake of iodide may produce detrimental changes in iodide metabolism, thyroid function, and immune reactions among subjects with low dietary iodide intakes. Also at risk for adverse reactions are individuals with existing thyroid disorders and pathologies. Lastly, the fetal thyroid is potentially at risk from pharmacological levels of

iodide. Table 2-2 identifies the most common adverse reactions known to be associated with iodide. Adverse reactions to iodide may be categorized as intrathyroidal and extrathyroidal.

Table 2-2. Adverse Reactions to Iodide

<p><u>Intrathyroidal Effects</u> - Excess or insufficient production of thyroid hormones.</p> <ul style="list-style-type: none">• Iodide-induced thyrotoxicosis (hyperthyroidism)• Iodide-induced hypothyroidism <p><u>Extrathyroidal Effects</u> - non-thyroid related reactions and hypersensitivity reactions.</p> <ul style="list-style-type: none">• Erythema nodosum; ioderma; urticaria; bullous eruptions; acne; dermatitis herpetiformis; etc.• Swelling of salivary glands, rhinitis, iodism• Vasculitis; serum sickness; anaphylactoid reactions
--

2.6.1 Intrathyroidal Adverse Reactions

Individuals with normal thyroid function are not at risk for intrathyroidal effects leading to conditions of hyperthyroidism (thyrotoxicosis) and hypothyroidism. Hyperthyroidism, when induced by exogenous administration of iodide, is termed "Jod-Basedow" phenomenon and involves an overproduction of the thyroid hormone. This phenomenon is common to individuals whose thyroid is no longer under the regulatory control of the pituitary gland's secretion of TSH. The underlying pathologies for autonomously functioning thyroids were previously discussed and include thyroid nodules/cancer, and Graves Disease (Alexander 1965; Vagenakis 1972; Tunbridge 1977).

Iodine supplementation has also been recognized to increase the incidence of hyperthyroidism among individuals in previously iodine-deficient areas following the introduction of iodized salt. This Jod-Basedow phenomenon in previously iodide-deficient areas is also thought to involve individuals with autonomously functioning thyroids. Apparently, the thyroid in these individuals was functioning autonomously at a hyperactive level before supplemental administration of iodide, but was unable to manifest hyperthyroidism owing to the limitation of hormone synthesis imposed by the low dietary intake (Connolly 1970; Fradkin 1983).

For select individuals, the administration of iodide may have the reverse effect of induced hypothyroidism. The antithyroid action of acute iodide overload resulting in a state of hypothyroidism is well documented (Wolff 1969; Nagataki 1974). In normal subjects, an iodide overload causes a transient block of iodide organification (i.e., thyroid hormone synthesis)

known as the "Wolff-Chaikoff effect" (Wolff 1980; 1969). Even with continued administration and elevated serum levels of iodide, healthy subjects escape from this transient and subclinical hypothyroid state within hours and resume normal thyroid hormone production. In some individuals, the induction of the Wolff-Chaikoff effect by exogenous iodide is not followed by a prompt escape of its inhibitory effect of iodide organification, so that a state of prolonged hypothyroidism and possible goiter develops. Continuing and unrelieved Wolff-Chaikoff thyroid suppression is seen among individuals with Hashimoto's thyroiditis, Graves' Disease, and after surgical thyroidectomy or I-131 treatments (Wolff 1969; Braverman 1971).

Sub-Populations Likely to Manifest Intrathyroidal Effects from KI Prophylaxis. It is well established that Hashimoto's thyroiditis, Graves' Disease, and idiopathic myxedema are organ-specific autoimmune disorders of the thyroid. These and other autoimmune disorders probably develop because of the consequences of an abnormal function or reaction of the immune system that is genetically predisposed. The concept that excess iodine might indirectly influence thyroid function by triggering thyroid autoimmune reactions is based on clinical studies that suggest an association between increased consumption of dietary iodine and autoimmune thyroid disorders. Studies have shown a greatly reduced incidence rate of lymphocytic infiltration of thyroid tissue, Hashimoto's thyroiditis, and Graves' Disease in iodine-deficient and goiter-endemic areas when compared to areas of iodine sufficiency (Bouki 1983; Hall 1996; McGregor 1985). Although the precise mechanisms responsible for the initiation of autoimmune phenomena against the thyroid gland in genetically predisposed individuals are highly speculative, there is evidence that iodine can play a role in the initiation and expression of these autoimmune thyroid disorders.

The quantity of exogenous iodide capable of inducing thyroid suppression is not easily defined since it will depend on external factors, such as dietary intake of iodide, and the inter-relationship of internal factors such as the intra-glandular pool of iodide, the efficiency of the autoregulatory mechanism which protects against thyroid overloading, and the underlying thyroid disorder. The American Thyroid Association estimates that daily doses of between 50 and 500 mg of iodide may induce prolonged hypothyroidism among these predisposed individuals (Becker 1984).

A second susceptible target population which may be regarded as normal/healthy includes fetuses in the second and third trimester. The partially developed fetal thyroid during this time has the ability to concentrate iodide, but does not yet possess the autoregulatory mechanism needed to escape the Wolff-Chaikoff effect (Delange 1985; Sherwin 1982).

Chronic consumption of iodide-containing medications such as cough medicine and antiasthmatic drugs has been shown to induce fetal hypothyroidism and fetal goiter (Walfish 1983; Mehta 1983). Fetal and neonatal iodine overload has also been observed following the use of iodinated x-ray contrast media during pregnancy (Rodesh 1976) and the cutaneous application of iodinated skin disinfectants (Povidone-iodine) at the time of delivery (Chanoine 1986). The concentration of maternal iodide required to induce a fetal Wolff-Chaikoff effect has not been properly quantified but is thought to be relatively high (Delange 1988).

2.6.2 Extrathyroidal Adverse Reactions

Numerous non-thyroidal effects have been linked to the pharmacological use of iodide. Persons potentially at risk for non-thyroidal adverse reactions are individuals with a known sensitivity to iodide. A particularly sensitive target population comprises individuals with hypocomplementemic vasculitis (Curd 1979). The most common reactions involve swelling of the salivary glands (sialadentitis or iodide mumps), a host of skin reactions (erythema nodosum, ioderma with necrotic skin lesions, urticaria, bullous eruptions, acne-form skin eruptions, etc.), iodide fever, rhinitis, and iodism (Becker 1987; Rubery 1988; Yalow 1983). These reactions are generally observed with large doses of iodide, are self-limiting, and are readily reversed by cessation of drug use. Rare, but of greater significance, are certain hypersensitive or allergic reactions which produce symptoms such as fever, pain in joints, edema of the face and glottis, angitis, vasculitis, and anaphylactoid/anaphylaxis reactions.

2.6.3 Adverse Reaction Incidence Rate

Potential adverse reactions to iodide when taken orally in daily doses of 130 mg can be assumed to be very few for the general United States population. This assumption is based on the extrapolation of data reported to the Food and Drug Administration (FDA). The FDA's Division of Epidemiology and Surveillance maintains a computerized data base of adverse drug reactions known as the Adverse Reaction Reporting System (ARRS).

The primary purpose of the ARRS is to serve as an early warning system for adverse reactions to drugs subject to FDA regulations. Approximately 90% of adverse reaction reports received by the FDA are submitted by drug manufacturers who by law must report all adverse events that become known to them. The remaining 10% of reports are submitted directly by health care professionals in response to suspected adverse reactions among their patients.

An estimate of the potential adverse reaction incidence rate to iodide is best derived from data involving cough syrups and expectorants. Potassium iodide is a major ingredient in these oral medications and results in average daily doses of several hundred milligrams of KI. Among the few adverse reactions that have been reported, the reactions are not life-threatening. In most instances, the reactions are self-limiting or quickly abate with discontinued medication.

A second major class of pharmaceuticals for which adverse reactions have been reported is iodinated x-ray contrast media. The high attenuation of diagnostic x-rays by organified iodine is the basis for its use in routine medical procedures. However, extrapolation of an adverse reaction incidence rate from iodinated contrast data is subject to numerous uncertainties.

Appendix C contains summary data of adverse reactions to iodide which have been reported to the FDA. Also included are basic assumptions and quantitative methods used to derive a best estimate of the adverse reaction incidence rate.

<p>The most current data suggest an adverse reaction incidence rate to a daily oral dose of 130 mg of KI at 1×10^{-7} or less.</p>
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CHAPTER 3

RISKS OF RADIATION THYROID EFFECTS

3.1 Risk of Thyroid Cancer

Susceptibility to radiation-induced thyroid cancer is greater early in childhood and coincides with the period of thyroid growth. Between birth and early adulthood (approximately 18 years), the thyroid mass increases from a neonatal weight of 1-3 g to an adult weight of 17-20 g. Since cell sensitivity is affected by cell differentiation and mitotic activity, it is generally assumed that there is a two-fold increase in sensitivity to radiation carcinogenesis for thyroid glands in children and adolescents (18 years of age or less), compared to adults.

Studies of both children and adults consistently indicate that females show a much higher spontaneous thyroid cancer incidence as well as greater effect of radiation carcinogenesis of the thyroid than males exposed under similar conditions. Based on these empirical observations, risk estimates generally assume that females are subject to at least twice the risk of thyroid neoplasia as males under similar conditions. Both the NCRP and BEIR V Committee have adopted the following generic formula to estimate the age, sex, and radiation source specific risk of thyroid cancer (NCRP 1985, NAS 1990):

$$\text{Specific Risk Estimate} = R \cdot F \cdot S \cdot A \cdot Y \cdot L \quad (\text{Eq. 3-1})$$

where:

R = Absolute risk estimate of 2.5 excess cases per 10^6 persons per rad per year for consigned (both sexes), ethnically similar, populations of children exposed to external X irradiation and corrected for a minimum induction period for thyroid cancer of 5 years,

F = Dose effectiveness reduction factor (1 for external radiation, I-132, I-133, and I-135; 1/3 for I-131),

S = Sex factor (4/3 for women and 2/3 for men, assuming that women are twice as susceptible as men and that the R was derived from a population comprised of equal numbers of both sexes),

A = Age factor (1 for populations age 18 or less at exposure and 1/2 for populations over age 18 at exposure),

Y = Anticipated average number of years at risk for the population in question,

L = Lethality (assumes a maximum lifetime lethality of 1/10). Use this factor only when calculating the specific risk estimate for lifetime deaths to thyroid cancer.

Table 3-1 provides the age, sex, and source-adjusted annual risk estimates applicable to the population of the United States.

To convert the annual risk coefficients defined in Table 3-1 to lifetime risks for the current U.S. population, the number of years at risk for each of the four population subgroups has to be defined. Table 3-2 provides the most current U.S. census data by age and sex. From these data, the median ages for the four subgroups were determined by linear interpolation (Table 3-3). Mean life expectancies for the median age in each subgroup are specified by parameter #4. To determine the mean years at risk (parameter #5) for thyroid cancer and thyroid nodules, the respective minimum latency periods of five and ten years were subtracted from the mean life expectancy for each subgroup.

The lifetime risk of thyroid cancer for each of the four subgroups is shown in Table 3-4 and represents the product of the annual risk and the mean years at risk for thyroid cancer. The last column of Table 3-4 also defines the lifetime cancer risk for the general U.S. population.

This collective population risk value represents a weighted average of the four subgroups based on their percentage of the total population. Thus, for the current U.S. population, exposure to 1 million person-thyroid-rads from I-131 would be expected to yield about 23 excess thyroid cancers.

Table 3-1. Annual Risk of Total and Lethal Excess Thyroid Cancers per Million Persons per Rad of Thyroid Dose for Doses from 6 to 1,500 Rads (U.S. population)*

Source of Irradiation	Persons over age 18 years at time of exposure				Persons age 18 or less at time of exposure			
	TOTAL		LETHAL		TOTAL		LETHAL	
	Male	Female	Male	Female	Male	Female	Male	Female
I-131	0.28	0.56	0.028	0.056	0.56	1.12	0.056	0.112
External X or gamma rays and I-132, -133, -134, -135	0.84	1.68	0.084	0.168	1.68	3.36	0.168	0.336

Based on an absolute risk estimate of 2.5 cases per 10⁶ persons per rad per year in people exposed to external irradiation in childhood.

Table 3-2. 1990 Population Distribution in the United States by Age and Sex*

Age (years)	1990 Population (x 1000)					
	Male	(%)**	Female	(%)**	Total	(%)**
Under 5	9,426	(3.78)	8,982	(3.60)	18,408	(7.38)
5-17	23,377	(9.38)	22,253	(8.93)	45,630	(18.30)
18-24	13,216	(5.30)	12,824	(5.14)	26,040	(10.45)
25-34	22,078	(8.85)	21,845	(8.76)	43,923	(17.62)
35-44	18,785	(7.54)	18,112	(7.26)	36,897	(14.80)
45-54	12,406	(4.98)	13,061	(5.24)	25,467	(10.22)
55-64	10,103	(4.05)	11,260	(4.52)	21,363	(8.57)
65-74	8,171	(3.28)	10,207	(4.09)	18,378	(7.37)
75 and older	4,681	(1.88)	8,505	(3.41)	13,186	(5.29)
TOTAL	122,243	(49.04)	127,049	(50.96)	249,292	(100)

* Source: U.S. Bureau of the Census, Current Population Report Series

** Percent of total population.

Table 3-3. Years at Risk for Age and Sex Groups of the General Population of the United States for 1990

Parameter	Age Group (x 1000)			
	Greater than 18		Less than or equal to 18	
	Male	Female	Male	Female
1. No. of Individuals	89,440	95,814	32,803	31,235
2. % of Total U.S. Population	35.88	38.43	13.16	12.53
3. Median Age (Years)	38.4	41.4	9.2	9.3
4. Mean Life Expectancy for Median Age Group (Years)	34.4	38.1	61.3	68.8
5. Mean Years at Risk*				
• Thyroid Cancer	29.4	33.1	56.3	63.8
• Thyroid Nodules	24.4	28.1	51.3	58.8

* Assumes a 5 and 10 year latency period for thyroid cancer and nodules, respectively.

**Table 3-4. Lifetime Risk of Total and Lethal Excess Thyroid Cancers
per 10⁶ Persons per Rad**

Source of Irradiation	Person over age 18 at time of exposure				Persons age 18 or less at time of exposure				U.S. Population for 1990	
	Total		Lethal		Total		Lethal		Total	Lethal
	Male	Female	Male	Female	Male	Female	Male	Female		
I-131	8.23	18.5	0.82	1.85	31.5	71.5	3.15	7.15	23.2	2.32
External X or gamma; I-132, -133, -134, -135	24.7	55.6	2.47	5.56	94.6	214	9.46	21.4	69.5	6.95

3.2 Risk of Benign Thyroid Nodules

The absolute risk of benign thyroid nodules following external radiation therapy in childhood is considered to be 9.3 per 10⁶ PY per rad (NUREG-4214). Females are considered twice as susceptible as males, and persons over the age of 18 are considered one-half as susceptible as those under the age of 18 at the time of exposure. I-131 is considered only 1/5 as effective as external radiation or internal exposure from I-132, I-133, I-134, and I-135. For benign thyroid nodules, a latency period of ten years is assumed. The general formula used to calculate age, sex, and radiation source specific risks is given by the following formula (NUREG-4214):

$$\text{Specific Risk Estimate} = R \cdot F \cdot S \cdot A \cdot Y$$

where:

R = Absolute risk estimate of 9.3 x 10⁻⁶ PY per rad for benign thyroid nodules.

F = Dose effectiveness reduction factor (1.0 for external radiation, I-132, I-133, I-134, and I-135; a value of 1/5 for I-131).

S = Sex factor (4/3 for females and 2/3 for males).

A = Age factor (1 for populations age 18 and under at time of exposure and 1/2 for population over age 18).

Y = Anticipated average number of years at risk for the population. The minimum induction period for thyroid nodules is assumed to be ten years.

Table 3-5 provides annual risk estimates for the four population subgroups.

Table 3-5. Annual Risk of Excess Benign Thyroid Nodules per 10⁶ Persons per Rad of Thyroid Dose for Doses from 6 to 1,500 Rads

Source of Irradiation	Persons Over Age 18 Years at Exposure		Persons Age 18 or Less at Exposure	
	Male	Female	Male	Female
I-131	0.6	1.2	1.2	2.5
External X or gamma rays; I-132, -133, -134, -135	3.1	6.2	6.2	12.4

The lifetime risks for benign thyroid nodules are provided in Table 3-6. These were determined by means for the appropriate mean-years-at-risk values from Table 3-3 as previously described.

Table 3-6. Lifetime Risk of Excess Benign Thyroid Nodules per 106 Persons per Rad of Thyroid Dose

Source of Irradiation	Persons over age 18 at time of exposure		Persons age 18 or less at time of exposure		U.S. Population for 1990
	Male	Female	Male	Female	
I-131	14.6	33.7	61.6	147	44.7
External X or gamma; I-132, -133, -134, -135	75.6	174	318	729	227

3.3 Risk of Hypothyroidism

Due to the excess capacity of the thyroid gland to produce the thyroid hormone, radiation-induced hypothyroidism exhibits a threshold. For external radiation, a threshold of 200 rads is assumed. Iodine-131, with an efficiency factor of 1/5, is assumed to have a threshold of 1,000 rads. For external doses of 12,000 rads or greater and I-131 doses of 60,000 rads, a 100% probability of hypothyroidism has been assumed. Within this range of exposure, the induction period is highly variable and decreases with increase in dose. Due to the uncertainty and variability of the induction period for hypothyroidism, annual risk coefficients are difficult to define. Instead, the risk of hypothyroidism is defined as a lifetime risk (Table 3-7).

Table 3-7. Lifetime Risk of Hypothyroidism*

Source of Irradiation	Applicable Range of Dose (Rads)		Lifetime Risk: Cases per 10 ⁶ Persons Per Rad
	Threshold	Upper Limit	
I-131	1,000	60,000	17
External radiation, I-132, I-133, I-134, I-135	200	12,000	83

* Reference: NUREG-4214

3.4 Risk to the Unborn

Within the first trimester, the fetal thyroid is insufficiently developed to concentrate iodine. Maternal exposure to radioiodine during this period, therefore, poses minimal thyroid risk to the fetus. Data indicate that maternal exposure to radioiodine during the second and third trimester results in a fetal thyroid dose that is about twice that of the maternal thyroid dose (Johnson 1982).

Human data involving in-utero thyroidal exposure to radioiodine are sparse at best. The only documented effect of radioiodine in the human fetus is that of hypothyroidism. In isolated instances, the mothers had been treated with I-131 doses ranging from about 12 to 225 mCi (Russell 1957; Fisher 1963; Hamill 1961; Green 1971). The children in these reported instances of fetal exposure manifested the characteristic symptoms and signs of cretinism. Due to limited data, however, a dose-response relationship and risk estimate for fetal hypothyroidism are not possible. Among this small group of individuals, there was one case of thyroid adenomas having a latency of 19 years (Conard 1975).

In the absence of human data providing a scientific basis for estimating fetal thyroid risks, it is reasonable to assume that the fetal thyroid is at least as sensitive to radiation as the thyroids of individuals less than 18 years of age.

For quantifying potential thyroid effects, this report assumes the fetal risk coefficients for benign nodules, cancer, and hypothyroidism are equal to annual risk values for males and females under the age of 18. For fetal exposure, the lifetime risk, however, will be based on a 75-year life span (i.e., years at risk). The lifetime risks of thyroid cancer and nodules for individuals exposed in-utero are presented in Table 3-8.

The potential number of fetal exposures resulting from a nuclear emergency can be estimated from the 4.07 million live births for 1990 for a total U.S. population of about 250 million. This corresponds to a birth rate of 16.3 per 1,000 population per year (National Center for Health Statistics, U.S. Dept. of Health and Human Services). Adjusting for the fact that the fetal

thyroid is sensitive only during the second and third trimester, the potential number of fetuses subject to radioiodine injury at any moment in time is reduced to about 8 per 1,000 exposed population.

Table 3-8. Lifetime Risks per 10⁶ Fetal Thyroid Rads

Source of Irradiation	Thyroid Effects						
	Nodules		Cancer				Congenital Hypothyroidism
			Total		Fatal		
	Male	Female	Male	Female	Male	Female	Male or Female
I-131	90	188	42	84	4.2	8.4	17
External X or gamma; I-132, -133, -134, -135	465	930	126	252	12.6	25.2	83

CHAPTER 4

THE COMPUTER MODEL USED TO ESTIMATE THYROID EXPOSURES AND RISKS

The calculation of population exposure doses from an airborne release is complex and requires the use of a computer model. For this report, population thyroid doses were assessed with the MELCOR Accident Consequence Code System (MACCS) computer code (Chanin 1990; Rollstin 1990). MACCS is a state-of-the-art computer code used for consequence analysis. It is significantly improved from the computer code used previously in NUREG/CR-1433. This chapter presents an overview of the critical pathways analyzed, major parameters that affect the computer modeling of integrated air concentrations, and age- and sex-specific variables by which integrated air concentrations are converted to thyroid doses.

4.1 Exposure Pathways Considered

In the event of a nuclear accident in which radioiodines are released into the atmosphere, thyroid exposure may be the result of external and internal exposure. It is useful to distinguish four independent pathways in which external and internal exposures contribute to the total thyroid dose:

- Plume immersion and cloud-shine - an external dose caused by exposure to radiation emitted by radionuclides in the effluent cloud. The cloud dose that an individual at ground level receives as a result of the radionuclides in the effluent cloud is the sum of the contributions of direct radiation from all sources distributed in the air around that individual. For a passing cloud, the dose rate would begin when the cloud approaches, reach a maximum when the cloud is overhead, and falls off as the cloud recedes. The dose is estimated as a time integral of the contributions of the radionuclides in each volume element as the cloud passes through (or above) the position concerned. If the radionuclide release (radioiodine as well as other gamma emitting nuclides) is of short duration compared with the longitudinal dispersion divided by the wind speed, so is the plume immersion dose.
- Ground deposition - an external dose caused by radionuclides that have deposited by gravitation and contaminated ground and surface areas. The ground dose depends on the persistence of the contaminant, on the quantity and distribution of source material deposited at ground level, and on the subsequent time that the individual remains in the contaminated region. Since the ground-level deposit results from the fallout of aerosols, the surface source strength also depends on the radionuclide concentration in the cloud at ground level integrated over time.

- Inhalation - an internal exposure resulting from the inhalation of airborne radioactivity of a passing plume. The magnitude of the thyroid dose is primarily affected by the air concentration of radioiodines and the duration of exposure to the passing plume.
- Food pathway - an internal exposure resulting from the ingestion of food and drink that have been contaminated by radionuclides in the environment.

The uncensored ingestion of contaminated food products has the potential for high thyroid doses. However, regional populations in the United States are not critically dependent on local food sources, and the protective measures imposed by local health authorities following a nuclear accident would limit the availability and intake of contaminated food sources. Therefore, it is assumed that thyroid doses from the food pathway can readily be avoided or trivialized. External exposure doses from plume immersion and ground contamination are considered significant and have been incorporated in the computer code for thyroid dose estimates. By far the largest source of thyroid exposure, however, is the prompt inhalation of contaminated air from a passing plume. Moreover, the benefit of stable iodide prophylaxis is confined to mitigating internal exposure that results from the plume inhalation of radioiodines.

4.2 An Overview of the MACCS Model

The MACCS computer code models the off-site consequences of a severe reactor accident in which a plume of radioactive materials is released to the atmosphere. For such an accidental release, the radioactive gases and aerosols in the plume are dispersed in the atmosphere and transported by the prevailing winds. The environment is contaminated by radioactive materials deposited from the plume, and the population is exposed to radiation. The fundamental purposes of computer models for off-site consequence estimates are to track the dispersal of radioactive material away from the accident site, to account for its eventual disposition in the environment, and to estimate potential exposure doses to the surrounding population. Given information on the characteristics of the radioactive release, the local and regional weather, and population distribution, such models calculate the downwind transport, airborne dispersion and ground deposition of the radioactive material, and the radiation doses received by exposed populations from all relevant pathways.

4.2.1 Core Inventory and Source Term

Core Inventory - The radioactive inventory of the core at accident initiation (e.g., reactor scram) is required as an input. The core inventory is a function of the type and the operating power of the reactor and the duration of operation after loading fuel. The MACCS code models 60 radionuclides.

The core inventory of a pressurized water reactor (PWR) of thermal power of 3,050 MW at the end of a power cycle was used for the calculation. The inventory of seven radionuclides

important for the present calculation is given in Table 4-1. The isotopes Te-131m and -132 are important as they decay into I-131 and -132 respectively.

Table 4-1. Core Inventory of Pertinent Isotopes

Isotope	Inventory (Ci)
Te-131m	1.13E7
Te-132	1.12E8
I-131	7.74E7
I-132	1.14E8
I-133	1.64E8
I-134	1.80E8
I-135	1.54E8

Source Term - The atmospheric source term produced by the accident is required as an input. This involves the number of plume segments released, sensible heat content, timing, duration, height of each segment of release, and for each important radionuclide, the fraction of that radionuclide's release with each plume of release. Using similar chemical characteristics, 60 radionuclides are grouped into nine release categories. These are the groups of noble gas, iodine, cesium, tellurium, strontium, rubidium, lanthanum, cerium, and barium.

For thyroid exposures and health effects calculations, four radiological source terms were identified (Table 4-2). These four accident categories represent all the accidents postulated for the Surry nuclear power plant, which were described in detail in NUREG-1150. With the exception of source term category RSUR-2, all the other source terms consist of two discrete plume releases. The first plume is characterized by the event that caused the release. The second release results from corium (molten core) and concrete interactions (CCI).

Table 4-2. Radionuclide Release Characteristics into the Environment for Surry

Source Term	Freq. (yr ⁻¹)	Ele. (m)	Energy (MW)	Rel. Time (h)	Release Duration	Fraction of Core Inventory Released									
						NG	I	Cs	Te	Sr	Ru	La	Ce	Ba	
RSUR-1	2.9E-7	10	28	6	200 s	1	0.25	0.18	0.08	0.02	0.005	0.001	0.005	0.02	
		10	28	6.06	2 h	0	0.1	0.13	0.1	0.04	0.001	0.005	0.005	0.04	
RSUR-2	2.4E-6	0	0	12	3 h	1	0.06	0.03	0.09	0.003	0.001	4E-4	4E-4	3E-3	
RSUR-3	3.3E-5	0	0	6	10 h	2.5E-3	1.5E-5	1.2E-8	7.5E-9	2.5E-9	2E-10	3E-10	4E-10	2.5E-9	
		0	0	16	10 h	2.5E-3	1.5E-5	1.2E-8	7.5E-9	2.5E-9	2E-10	3E-10	4E-10	2.5E-9	
RSUR-4	1.6E-6	10	28	1	30 min	1	0.075	0.06	0.02	0.005	0.001	3E-4	0.001	0.005	
		10	28	1.5	2 h	0	0.04	0.06	0.05	0.02	6E-04	0.003	0.003	0.02	

The characteristics of the four accident categories, RSUR-1 through -4, are given in Table 4-3. For the first three categories, the initiating event of the accident is the loss of off-site power, while for the other category, RSUR-4, the initiating event is containment bypass resulting from a large break in a system interfacing with the primary reactor cooling system. The highest release of iodine is associated with the release category RSUR-1 in which the containment rupture coincides with the breach of the reactor pressure vessel induced by steam explosions. For the RSUR-2 category, the containment failure involves a leak and follows the occurrence of CCI. For RSUR-3, the containment functions as intended, and a release occurs through a leak that is within the design limits of the containment. The RSUR-3 source term is further mitigated by the operation of a containment spray system, which is not available for the other three categories. For RSUR-4, no containment failure occurs but two plumes release by bypassing the containment. For all four accident categories, CCI occurs, and the reactor coolant system is at low pressure (<200 psia) at the breach of the reactor pressure vessel.

Table 4-3. Accident Characteristics for Surry

Release Category	Plant Damage State	Accident Progression Characteristics						
		Containment Failure Time	Containment Failure Size	CCI	Amt. CCI	RCS Pres. (psia)	VB Mode	Sprays
RSUR-1	LOSP	CF at VB	Rupture	Prm-Dry	Medium	< 200	Alpha	No
RSUR-2	LOSP	CF after CCI	Leak	Prm-Dry	Large	< 200	Pour	No
RSUR-3	LOSP	No CF	No CF	Prm-Dry	Large	< 200	Pour	L+VL
RSUR-4	Bypass(V)	No CF	Bypass	Prm-Dry	Large	< 200	Pour	No

- Alpha Steam explosion induced failure
- Pour Pouring or corium (molten core)
- CCI Corium and concrete interactions
- CF Containment failure
- L Late period
- LOSP Loss of off-site power
- Prm-Dry CCI takes place promptly following VB. There is no overlying water pool to scrub the release.
- V Large break in a system interfacing the high pressure coolant system
- VB Vessel breach
- VL Very late period

4.2.2 Meteorological Parameters and Plume Dispersion

To assess the effect of meteorological variables, a single source term is dispersed at various times throughout a year and, for each set of conditions, consequence calculations are made. Each release is simulated for ensuing hours, often days, until the radioactive material travels out of the defined population area. The result is a distribution of consequences whose frequencies are dependent on the frequencies of various types of weather conditions throughout a year.

Using an entire year of weather data, about 150 individual consequence calculations are made for a typical risk calculation.

To reduce computational time for these extensive calculations, a processor groups weather data into similar bins. The binning, or grouping process, is called stratified importance sampling, and it is used to ensure that important weather conditions are fairly represented. For example, peak consequences arise from low wind speeds, narrow plumes, rainfall, and sudden calms, whereas the average consequence calculations can be associated with average weather conditions.

In the MACCS code, all releases (source terms) travel radially downwind, away from the site, as essentially a plane wave. The MACCS rainfall model predicts the washout of radionuclides from the atmosphere. For deposition of material out of the accident plume onto the ground during dry weather, MACCS includes provisions for particles of different sizes.

For accidents in which the radioactive releases occur over many hours, the release is treated most effectively as a series of "puffs." This time-variant capability is especially important for severe accident scenarios involving releases of such nuclides as strontium, barium, and lanthanum. These radionuclides may evolve during core-concrete interactions and are, therefore, released much later (hours) than more volatile chemical species (e.g., noble gases, iodine, cesium). In summary, MACCS accounts for radioactive decay and daughter product buildup within the plant before the various radionuclides are sequentially released to the environment.

The MACCS code simulates the dispersion of radioactive material over long distances using a Gaussian-distributed plume model. The code includes a plume liftoff criterion, which limits the rise off the ground from a heated release (source term). As the distance from the source increases, the concentration of the cloud monotonically decreases at its center. The plume may be depleted by contacting surfaces or by intercepting rainfall. Rainfall can be intercepted at various distances from the source, such that ground contamination can either increase or decrease at various distances from the source. Radiological exposures can result from plume immersion, plume shine, ground contamination, and plume inhalation.

4.2.3 Internal Thyroid Dose Parameters

The MACCS model for internal thyroid dosimetry is defined by all relevant radionuclides of iodine that enter the body and the factors governing their uptake, distribution, and retention within the thyroid. The internal dose of the thyroid from inhalation of airborne radioiodine can be derived from time-integrated air concentrations ($\mu\text{Ci-h m}^{-3}$) at fixed distances from a source term by the following equation:

$$D_{\text{inhal}} = [(C_o \times f_{\text{op}} \times V \times f_{\text{ot}}) + (C_i \times f_{\text{ip}} \times V \times f_{\text{it}})] \times \text{DCF}_{\text{inhal}} \quad (\text{Eq. 4-1})$$

where:

D_{inhal}	=	thyroid inhalation dose (rad)
C_o	=	time-integrated outdoor air radioiodine concentration ($\mu\text{Ci-h m}^{-3}$)
C_i	=	time integrated indoor air radioiodine concentration ($\mu\text{Ci-h m}^{-3}$)
f_{op}	=	fraction of outdoor air radioiodine on respirable particles
f_{ip}	=	fraction of indoor air radioiodine on respirable particles
V	=	ventilation rate ($\text{m}^3 \text{ h}^{-1}$)
f_{ot}	=	fraction of plume passage time spent outdoors
f_{it}	=	fraction of plume passage time spent indoors
$\text{DCF}_{\text{inhal}}$	=	inhalation dose conversion factor ($\text{rad } \mu\text{Ci}^{-1}_{\text{inhal}}$)

When it is conservatively assumed that an individual may be outdoors 100% of the time during plume passage, equation 4-1 is reduced to:

$$D_{\text{inhal}} = C_o \times V \times \text{DCF}_{\text{inhal}}$$

Estimates of dose for risk assessment have traditionally been based on models developed for the radiation protection of adult workers. For this reason, the basic biokinetic model represented by "Reference Man" (i.e., a subject with the anatomical and physiological characteristics of a healthy young adult male weighing 70 kg) was deemed appropriate. While the concept of Reference Man provides a degree of consistency for occupational dosimetry and risk assessment, Reference Man is clearly not intended to represent the general population and cannot be used for modeling population thyroid doses.

Basic principles of internal dosimetry dictate that the thyroid dose from an inhaled quantity of radioiodine is strongly influenced by several physiological parameters, some of which are age- and sex-dependent. Population thyroid doses in this report are based on the most currently available data defining the United States population in terms of gender and age distribution.

Ventilation Rates. Equation 4-1 shows that for a given air concentration, the thyroid dose is directly proportional to the individual's ventilation rate. Ventilation rates for male and female subjects of different age groups have been estimated by the NCRP (NCRP 1984). In general, ventilation rates increase with age from infant to adult and are significantly higher for active as opposed to resting conditions. They are also slightly greater for males than for females.

A reasonable selection of ventilation rates assumes that the average individual is active (i.e., engaged in physical activities, occupational and non-occupational) 50% of the time and is engaged in sleep or passive activities the remaining time. A weighted average, therefore, is the mean value of active and resting ventilation rates. Table 4-4 defines the age- and sex-dependent ventilation rates used in this report to generate population thyroid doses.

Table 4-4. Ventilation Rates by Age, Sex, and Activity*

Age Group	Sex	Ventilation Rate (m ³ /hr)		
		Resting	Active	Weighted Average
0 - 12 months	Male	0.090	0.26	0.175
	Female	0.090	0.26	0.175
1 - 11 years	Male	0.39	1.1	0.75
	Female	0.31	0.90	0.61
12 - 18 years	Male	0.46	1.8	1.13
	Female	0.34	1.5	0.92
> 18 years	Male	0.53	1.8	1.17
	Female	0.38	1.5	0.94

* Source: NCRP Report No. 76 (NCRP 1984).

Parameters Affecting Inhalation DCF Values. For common plume inhalation exposure conditions, variations in dose among individuals or groups of individuals arise from variations in the uptake and metabolism of radioiodide as well as from anatomical differences. For a heterogeneous population, the following factors must be considered in the assignment of dose conversion factors (DCFs) for radioiodine:

- Lung Deposition Fraction. The magnitude of a thyroid dose resulting from the inhalation of radioiodide particulates is affected by physical parameters that influence the initial deposition and distribution of activity within various compartments or regions of the respiratory tract. The ICRP Task Group Lung Model (ICRP 1966) defines the respiratory system as consisting of the nasopharyngeal (N-P), tracheo-bronchial (T-B), pulmonary (P), and lymphatic regions. In the model, the regions N-P, T-B, and P are assumed to receive fractions D_3 , D_4 , and D_5 , respectively, of the inhaled activity. When the sum of these three fractions is less than 1, it is assumed that the complementary fraction is promptly exhaled. The values of D_3 , D_4 , and D_5 primarily depend on the effective particle size defined in terms of the activity medium aerodynamic diameter (AMAD) of the inspired particles. In the absence of empirical information and for risk analysis, it is conventional to use the AMAD value of 1 micron. This value corresponds to deposition fractions of 0.30 (N-P), 0.08 (T-B), and 0.25 (P), or 63% of the total respired particulates. It is further assumed that radioiodine is rapidly and completely absorbed into the bloodstream either directly from the respiratory tract or by respiratory clearance into and absorption by the gastro-intestinal tract. In summary, thyroid inhalation dose values derived in this report assume an AMAD value of one micron for radioiodides.

- Organ uptake fraction - The fraction of iodide taken up from the blood by the thyroid varies widely among individuals because of differences in dietary iodine levels and metabolic factors that are age and sex related. The classic work of J. B. Stanbury has shown an inverse relation between the thyroid uptake of radioiodine and the supply of iodine in the daily diet (Stanbury 1954). Variations in committed dose from I-131 for Reference Man under various conditions of dietary intake of stable iodine were calculated by Johnson (Johnson 1982(a)) as shown in Table 4-5.

Table 4-5. Variations in Committed Dose for Reference Man with Stable Iodide Intake

Daily Iodide Intake (μg)	Rads/ μCi I-131
75	2.72
100	2.28
150	1.72
200	1.38
300	0.996
600	0.54
1000	0.32

In countries of the world where dietary intakes of iodide are low, glandular uptake may reach levels of up to 90%. In the United States, the daily dietary intake is high, varying between 125 μg and 700 μg with an average value of about 200 μg (Oddie 1970; Dumont 1988); for the normal adult, this range of dietary intake corresponds to a thyroid uptake fraction of between 15% and 30%.

Empirical measurements by Dunning and Schwarz found mean thyroid uptake fractions of 47% for newborns, 39% for infants, 47% for adolescents, and 19% for adults (Dunning 1981).

- Organ mass - The variability in thyroid mass is related to age and body weight. The mass increases during childhood and continues to increase until adulthood at which time the net growth of the organ ceases. Based on data reviewed by Dunning (Dunning 1981), the mass of an adult thyroid ranges from 2 g to 62 g with an average value of 18.3 g. This value is essentially identical with that given by the ICRP, which assumes a value of 17 g for females and 20 g for males (ICRP 1975).

- Effective half-life of radioiodide - The variability of the effective half-life of radioiodide is determined by the physical half-life of the isotope and its biological half-life (i.e., metabolic utilization and retention of organified iodide). Children and adolescents can be expected to exhibit higher turnover and elimination rates than adults (Rosenberg 1958; Heinrichs 1982; ICRP 1988). Dunning and Schwarz (1981) concluded that for adults, the observed range in biological half-lives was from 21 to 372 days and for young children 4 to 39 days.
- Effective energy per disintegration - The effective energy per disintegration (Mev/dis) of a radionuclide within an organ depends upon the decay energy and the effective radius of the organ (ICRP 1959). Considering differences in thyroid mass with age, there is a small corresponding increase in the effective energy per disintegration (Bryant 1969).

Taking into account these age-dependent parameters, empirically derived inhalation dose conversion factors have been cited that are consistently similar (NUREG-0172; Johnson 1981; Heinrich 1982; Dunning 1981, NUREG/CR-3955; ICRP 1988). Table 4-6 identifies the inhalation dose conversion values used in this report to estimate thyroid doses for five discrete age groups. In this report, the dose conversion factors for I-131 are based on values reported by Dunning and Schwarz (Dunning 1981); the DCF values for I-132, I-133, I-134, and I-135 are those of Killough and Eckerman (NUREG/CR-3955). All inhalation dose conversion factors assume that 63% of the inhaled iodide is absorbed into the blood and that iodide is a Class D aerosol with an AMAD of one micron.

Table 4-6. Thyroid Inhalation Dose Conversion Factors for Radioiodides

Radionuclide	Dose Conversion Factor (rad/ μ Ci)			
	0-12 mos.	1-11 yrs.	12-18 yrs.	> 18 yrs.
I-131	12.99	7.26	2.78	0.88
I-132	0.076	0.027	0.01	0.006
I-133	2.63	0.84	0.36	0.16
I-134	0.011	0.005	0.002	0.002
I-135	0.42	0.14	0.05	0.03

Fetal Thyroid Dose Factors. In the fetus, iodine accumulation begins at 10-12 weeks after conception and thereafter increases nearly linearly until birth. But due to the rapid change in fetal thyroid mass during the second and third trimesters, the fetal thyroid burden per unit mass is not linear (Dyer 1972; Evans 1967). Johnson (1982) has estimated fetal thyroid dose per unit uptake by the mother. The fetal thyroid dose per maternal unit of uptake increases over the period from 12 to 22 weeks gestation and reaches a peak value of about three rads per

microcurie in the maternal blood. This value is more than twice the dose received by the maternal thyroid. Following a steady decline in relative dose, about two percent of the iodide in the maternal blood will be accumulated by the fetal thyroid at term, which on the basis of relative mass, yields a fetal dose essentially that of the mother.

Fetal thyroid doses in this report are conservatively estimated at twice the value of the maternal thyroid. Maternal thyroid exposures are based on ventilation and dose conversion values corresponding to females greater than 18 years of age.

4.3 Reactor Accident Specific Thyroid Doses

This section provides thyroid dose estimates for population cells in the plume pathways corresponding to reactor accident categories RSUR-1, RSUR-2, RSUR-3, and RSUR-4. Thyroid risk coefficients were applied to estimate the corresponding population thyroid health effects. All exposure values were estimated for normal activity. Normal activity assumes that individuals spend approximately 75% of their time indoors and 25% outdoors. Table 4-7 provides relative dose factors for individuals (1) located outdoors, (2) engaged in normal activity, and (3) sheltered.

Table 4-7. Relative Dose Factors

Exposure Source	Outdoors	Normal Activity	Sheltering
Plume immersion/ cloud-shine	1.0	0.75	0.6
Ground deposition	1.0	0.33	0.2
Inhalation	1.0	0.41	0.33

4.3.1 Plume Centerline Thyroid Doses by Age and Sex

Tables 4-8 to 4-11 present the plume centerline thyroid doses from all exposure pathways for each of the seven population subgroups located at discrete distances from the reactor facility. Independent of reactor accident release category, a comparison of thyroid doses among the subpopulations reveals that the male child (age 1-12) receives the highest thyroid dose while the adult female receives the lowest (Figure 4-1). Subgroup differences reflect the impact of age- and sex-specific variations (i.e., ventilation rate, iodide metabolism, and thyroid mass) on the thyroid dose. The last column in each of the four tables defines the plume centerline dose to the "average person." This set of values was derived by weighting each subgroup value by its respective percentage of the total population. For near-field residents residing within a five-mile radius, thyroid exposures in the thousands of rads are estimated for RSUR-1, RSUR-2, and RSUR-4. Thyroid doses for RSUR-3 are lower by several orders of magnitude and beyond ten miles may be considered trivial.

Table 4-8. Plume Centerline Thyroid Doses* (rem) for RSUR-1 Versus Distance

Distance Range (mi)	Infant	Female Child	Male Child	Female Teenage	Male Teenage	Female Adult	Male Adult	Average Person
< 5	2.0E+04	3.4E+04	4.2E+04	2.2E+04	2.6E+04	8.1E+03	1.1E+04	2.0E+04
5-10	7.4E+03	1.3E+04	1.6E+04	8.1E+03	9.8E+03	3.0E+03	4.2E+03	7.3E+03
10-25	1.8E+03	3.1E+03	3.8E+03	1.9E+03	2.4E+03	7.3E+02	1.0E+03	1.8E+03
25-50	3.0E+02	5.2E+02	6.3E+02	3.3E+02	4.0E+02	1.2E+02	1.7E+02	3.0E+02
50-100	6.9E+01	1.2E+02	1.5E+02	7.7E+01	9.3E+01	2.9E+01	3.9E+01	7.0E+01
100-150	3.1E+01	5.5E+01	6.8E+01	3.5E+01	4.2E+01	1.3E+01	1.8E+01	3.2E+01
150-200	1.9E+01	3.4E+01	4.2E+01	2.1E+01	2.6E+01	7.9E+00	1.1E+01	1.9E+01
200-350	8.2E+00	1.5E+01	1.9E+01	9.5E+00	1.2E+01	3.5E+00	4.7E+00	8.5E+00

Table 4-9. Plume Centerline Thyroid Doses* (rem) for RSUR-2 Versus Distance

Distance Range (mi)	Infant	Female Child	Male Child	Female Teenage	Male Teenage	Female Adult	Male Adult	Average Person
< 5	5.6E+03	1.0E+04	1.2E+04	6.7E+03	8.1E+03	2.8E+03	3.9E+03	6.1E+03
5-10	7.0E+02	1.2E+03	1.5E+03	8.2E+02	9.9E+02	3.5E+02	4.8E+02	7.5E+02
10-25	1.3E+02	2.4E+02	2.9E+02	1.6E+02	1.9E+02	6.8E+01	9.2E+01	1.5E+02
25-50	2.2E+01	4.0E+01	4.9E+01	2.7E+01	3.2E+01	1.1E+01	1.6E+01	2.5E+01
50-100	5.1E+00	9.2E+00	1.1E+01	6.1E+00	7.4E+00	2.6E+00	3.6E+00	5.6E+00
100-150	2.3E+00	4.2E+00	5.1E+00	2.8E+00	3.4E+00	1.2E+00	1.6E+00	2.5E+00
150-200	1.4E+00	2.5E+00	3.1E+00	1.7E+00	2.0E+00	7.0E-01	9.6E-01	1.5E+00
200-350	6.1E-01	1.1E+00	1.4E+00	7.5E-01	9.1E-01	3.1E-01	4.3E-01	6.9E-01

Thyroid dose includes all radionuclides and pathways (i.e., inhalation, cloud-shine, plume immersion, ground deposition); exposure condition is for "normal activity."

Table 4-10. Plume Centerline Thyroid Doses* (rem) for RSUR-3 Versus Distance

Distance Range (mi)	Infant	Female Child	Male Child	Female Teenage	Male Teenage	Female Adult	Male Adult	Average Person
< 5	1.8E+00	3.0E+00	3.7E+00	1.9E+00	2.3E+00	6.8E-01	9.3E-01	1.7E+00
5-10	2.2E-01	3.8E-01	4.7E-01	2.4E-01	2.9E-01	8.8E-02	1.2E-01	2.2E-01
10-25	4.5E-02	7.7E-02	9.5E-02	4.9E-02	5.9E-02	1.8E-02	2.4E-02	4.4E-02
25-50	8.5E-03	1.5E-02	1.8E-02	9.3E-03	1.1E-02	3.3E-03	4.5E-03	8.3E-03
50-100	1.9E-03	3.4E-03	4.1E-03	2.1E-03	2.5E-03	7.4E-04	1.0E-03	1.9E-03
100-150	8.1E-04	1.4E-03	1.8E-03	8.9E-04	1.1E-03	3.1E-04	4.2E-04	7.9E-04
150-200	4.7E-04	8.5E-04	1.0E-03	5.2E-04	6.3E-04	1.8E-04	2.5E-04	4.7E-04
200-350	1.9E-04	3.5E-04	4.3E-04	2.2E-04	2.6E-04	7.6E-05	1.0E-04	1.9E-04

Table 4-11. Plume Centerline Thyroid Doses* (rem) for RSUR-4 Versus Distance

Distance Range (mi)	Infant	Female Child	Male Child	Female Teenage	Male Teenage	Female Adult	Male Adult	Average Person
< 5	5.8E+03	9.8E+03	1.2E+04	6.3E+03	7.6E+03	2.5E+03	3.4E+03	5.8E+03
5-10	2.2E+03	3.6E+03	4.5E+03	2.3E+03	2.8E+03	9.0E+02	1.2E+03	2.1E+03
10-25	5.1E+02	8.6E+02	1.1E+03	5.5E+02	6.6E+02	2.1E+02	2.9E+02	5.0E+02
25-50	8.6E+01	1.5E+02	1.8E+02	9.4E+01	1.1E+02	3.6E+01	5.0E+01	8.5E+01
50-100	2.0E+01	3.4E+01	4.2E+01	2.2E+01	2.6E+01	8.4E+00	1.1E+01	2.0E+01
100-150	8.9E+00	1.6E+01	1.9E+01	1.0E+01	1.2E+01	3.8E+00	5.2E+00	9.0E+00
150-200	5.3E+00	9.4E+00	1.2E+01	6.0E+00	7.3E+00	2.3E+00	3.1E+00	5.4E+00
200-350	2.3E+00	4.2E+00	5.2E+00	2.7E+00	3.2E+00	9.9E-01	1.4E+00	2.4E+00

Thyroid dose includes all radionuclides and pathways (i.e., inhalation, cloud-shine, plume immersion, ground deposition); exposure condition is for "normal activity."

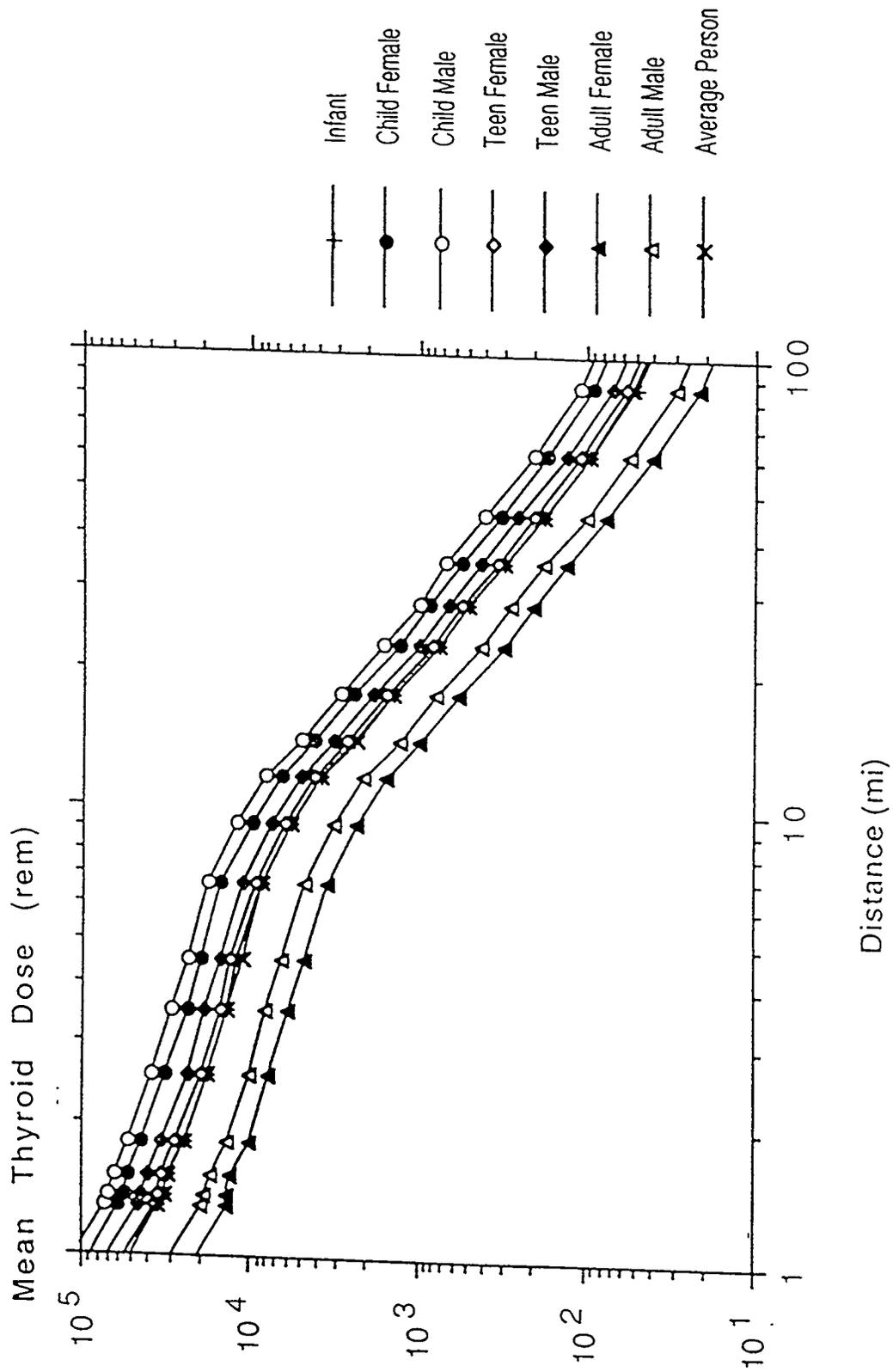


Figure 4-1. Thyroid Dose from RSUR-1 to Different Population Groups

Figure 4-2 graphically compares the mean thyroid dose to the average person for each of the four accident scenarios and demonstrates the reduction of mean thyroid doses as a function of distance. For incremental distances, the thyroid dose is reduced primarily due to the combined effects of plume dispersion, plume depletion, and radioactive decay of short-lived radioiodines.

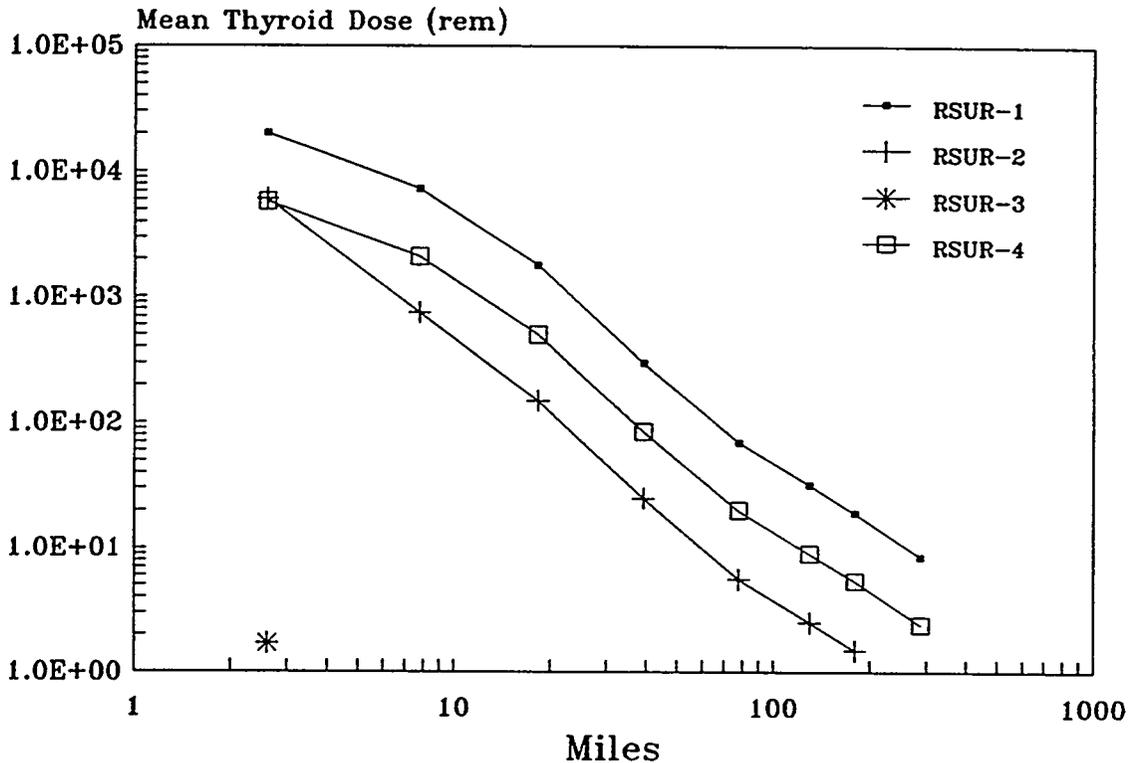


Figure 4-2. Comparison of Mean Thyroid Doses to Average Person by Distance

4.3.2 Radial Distance and Thyroid Intervention Levels

Central to the cost-benefit analysis is the need to estimate the potential population size for which KI may have to be made available. A highly conservative approach is to (1) define that distance at which the most vulnerable sub-population may exceed a pre-selected thyroid dose under the worst accident condition(s) and (2) assume that KI would be distributed to select population subgroups. A less conservative approach assumes that KI will be distributed/administered to all sub-populations. For this assumption, the population radius may be more appropriately defined by that distance at which the "average person" thyroid dose may exceed a selected intervention level. Prospective thyroid intervention levels include those of the EPA (5 - 25 rem), NCRP (10 rem), FDA (25 rem), and ATA (50 and 100 rem). Figure 4-3 is a probability plot that quantifies the radial distances corresponding to male child thyroid doses of 5, 10, 25, and 50 rem for RSUR-1 accident conditions. The conditional probability curves depict the variability

of mean thyroid values. For example, in the downwind sector, the child thyroid dose of at least 50 rem has a probability of nearly 100% for distances out to about 50 miles. Between 50 and 175 miles, the probability of exceeding 50 rem declines steadily and approaches a zero value. A 0.5 conditional probability corresponds to a radial distance of about 160 miles, which agrees closely with the mean thyroid values shown in Table 4-8. Similar plots for RSUR-1 are shown for the population average and include the ATA's upper intervention level of 100 rem (Figure 4-4). For the thyroid intervention levels of 50 and 100 rem, the 0.5 conditional probability of exceeding these levels occurs within the radial distances of about 75 miles and 50 miles, respectively. For thyroid dose intervention levels lower than those proposed by the ATA, larger radial distances would have to be considered for stockpiling.

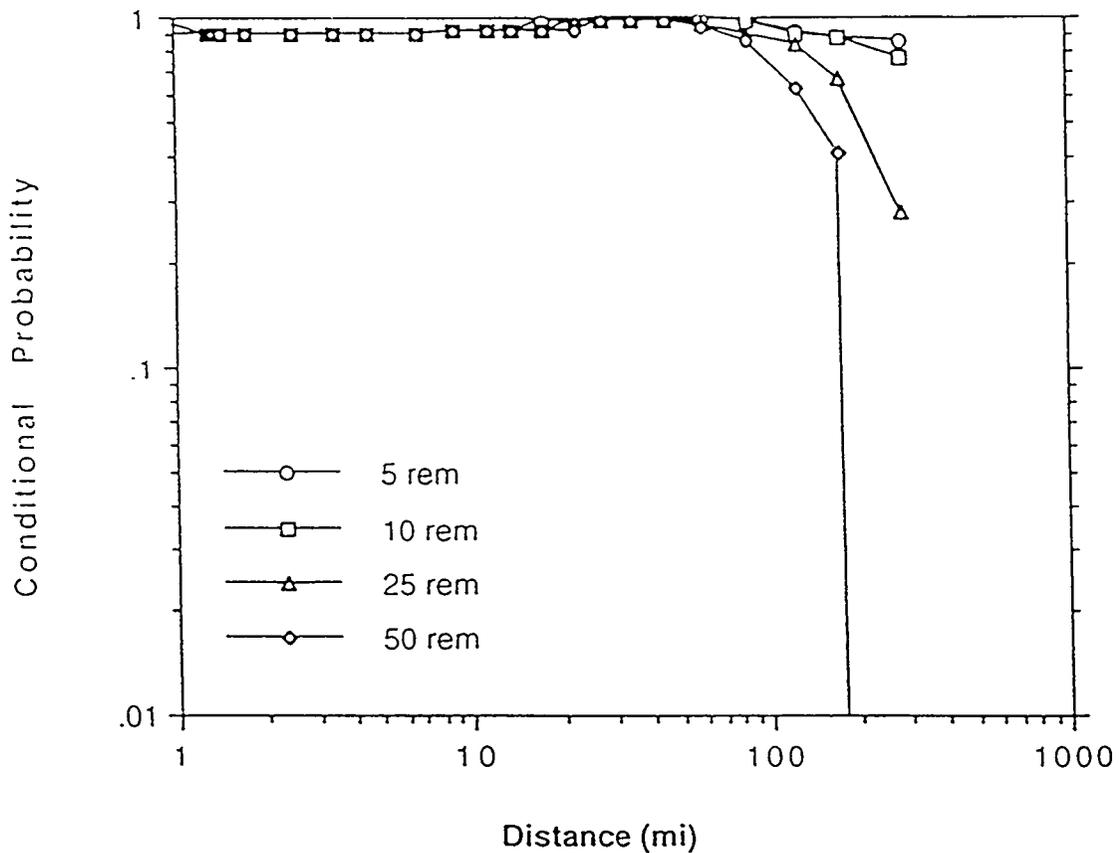


Figure 4-3. Total Thyroid Dose (RSUR-1, Child Male)

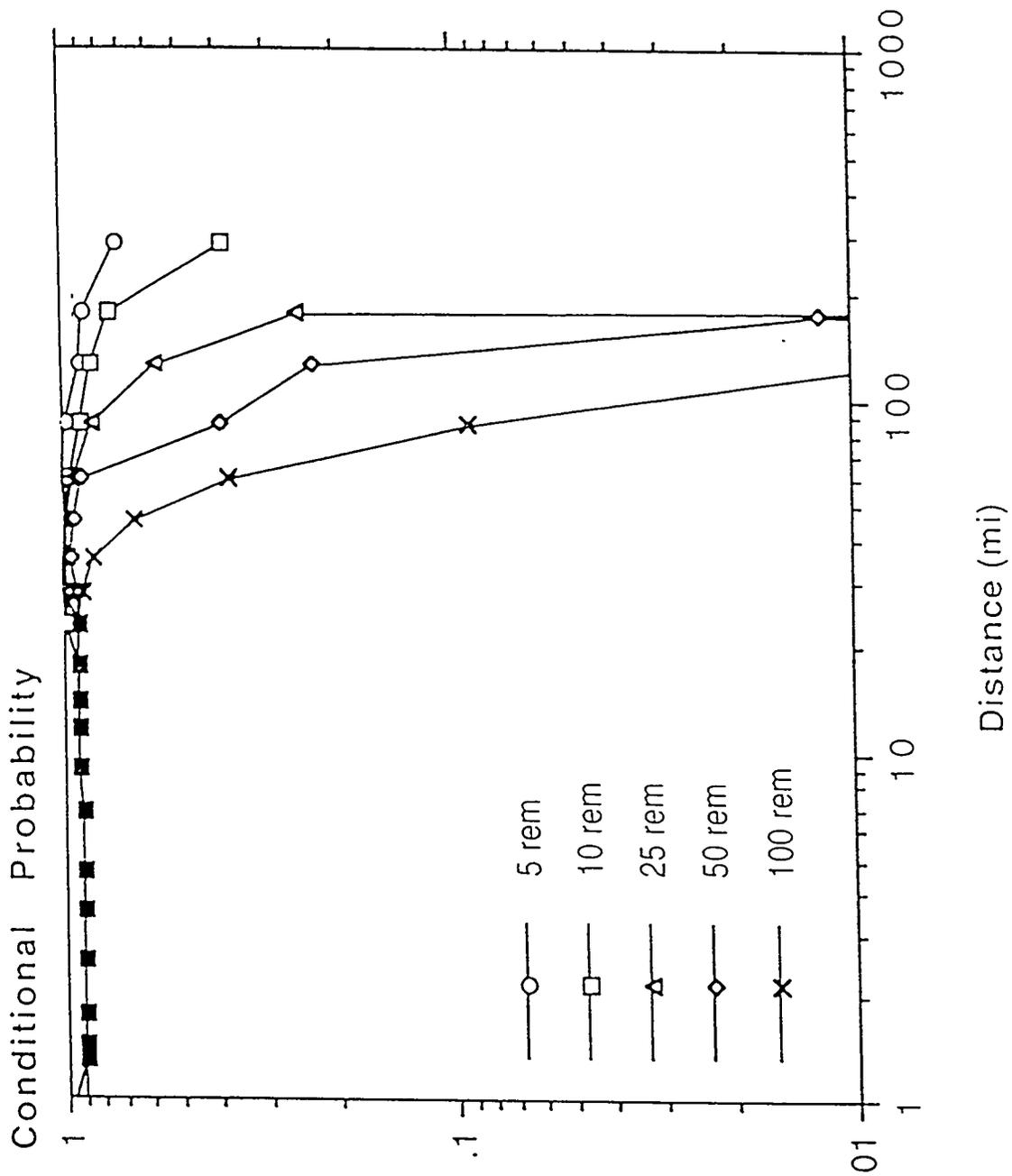


Figure 4-4. Total Thyroid Dose (RSUR-1, Average Person)

4.3.3 Estimates of Population Thyroid Effects

The prophylactic value of KI is limited to reducing internal exposure to the thyroid from radioiodides. It is, therefore, important to identify that component of the total thyroid dose which can be mitigated by stable iodide. Table 4-12 shows the percent contribution to total thyroid dose by inhaled radioiodides and all other sources for distance intervals of 0-25 miles, 25-100 miles, and greater than 100 miles. The ratio of thyroid dose from internal radioiodines to all other components of mean thyroid dose varies among the four accident categories and for a given accident category varies with distance. In general, differences among accident categories and for increased distances are relatively small and reflect small differences in plume depletion rates among radionuclides by deposition and radioactive decay. It is evident from Table 4-12 that (1) the inhalation of radioiodides contributes about 90% or more to the thyroid dose, (2) of the radioiodides, I-131 accounts for 65-86% of dose, and (3) the thyroid dose from the combined inhalation of non-radioiodides, plume immersion, cloud-shine, and ground exposure is a small contributor to the total thyroid dose. The relative contribution of I-131 and other radioiodides to the total thyroid dose is depicted in Figure 4-5.

Table 4-12. Percent Contributions to Thyroid Dose* for Exposed Population Versus Distance

Accident Category	Distance (miles)	Inhaled Radioiodides		All Other (%)	Total (%)
		I-131 (%)	Other Iodides (%)		
RSUR-1	0 - 25	71	23	6	100
	25 - 100	70	20	10	100
	100 - 500	80	12	8	100
RSUR-2	0 - 25	68	28	4	100
	25 - 100	65	24	11	100
	100 - 500	76	17	7	100
RSUR-3	0 - 25	76	18	6	100
	25 - 100	78	15	7	100
	100 - 500	86	8	6	100
RSUR-4	0 - 25	66	27	7	100
	25 - 100	66	23	11	100
	100 - 500	77	14	9	100

* Assumes normal activity.

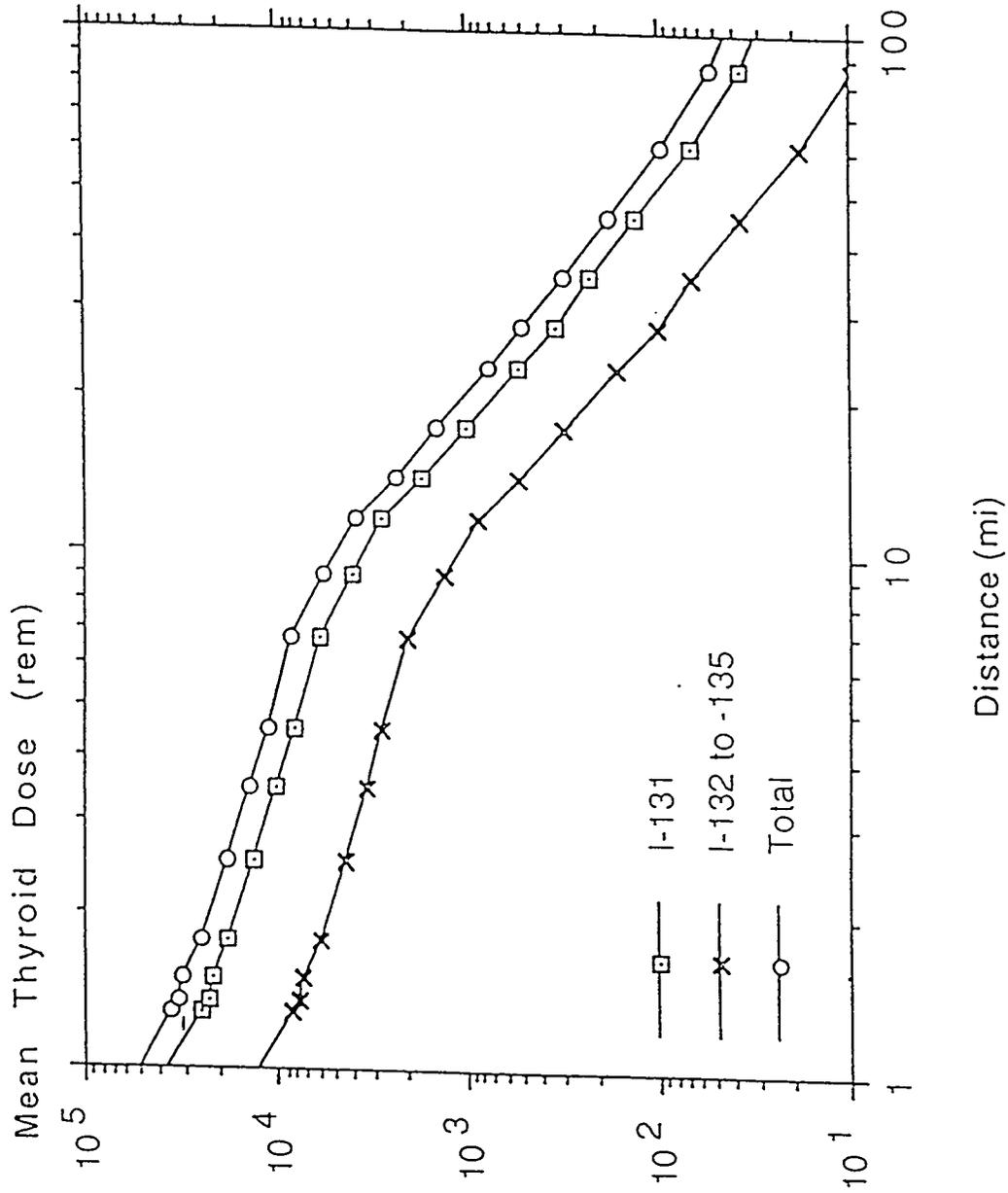


Figure 4-5. Mean Thyroid Dose Contribution from RSUR-1 to Average Person

4.3.4 Population Distribution Around Nuclear Power Facilities in the United States

For risk analyses, it is common practice to use a constant population density estimate that may be expressed as the number of individuals per square mile. Even if such a single value represents an empirically derived average value, it will lead to erroneous results and conclusions if the population is, in fact, not homogeneously distributed. In assessing the cost-benefit of KI prophylaxis, this potential error becomes obvious when it is recognized that the cost of protecting an individual is constant and independent of potential thyroid exposure; the protective "benefit," however, is not constant but decreases proportionately with reducing thyroid doses. For individuals living close to a reactor facility where potential exposures are greatest, the benefit (i.e., avoidance of thyroid effects) is also greatest per unit expense associated with the stockpiling/predistribution of KI tablets. For this reason, an attempt was made to determine representative population densities around reactor facilities as a function of distance.

To date, comprehensive information regarding population densities around nuclear facilities does not exist in the open literature. A suitable alternative was to construct a "Reference LWR Population" density distribution from Final Safety Analysis Reports (FSARs) filed by utilities as part of the NRC licensing process. At the time of filing, FSARs typically contain the most current population data, as well as projected data, typically at ten-year intervals, taking into account national and regional population trends.

FSAR population data were obtained from the NRC's Public Document Room from all currently licensed facilities. For some licensees, however, population data were either insufficiently detailed or formatted in such a way that the data could not be collated with that of other utilities. In total, usable population data were obtained for 55 facilities representing 26 BWRs and 60 PWRs. Population data for 16 sectors were added to yield total population values for each successive annular area starting at the exclusion zone of a facility and out to a 50-mile radius. These facility-specific data are presented in Table 4-13.

Table 4-13. Population Distribution Around United States Nuclear Power Plants

Site	< 1	1-2	2-3	3-4	4-5	5-10	10-20	20-30	30-40	40-50	Reactor
#1	0	55	470	465	1,095	34,020	126,880	188,525	336,980	147,780	Browns Ferry
#2	81	610	3,270	857	1,082	11,712	91,715	70,604	35,330	66,880	Brunswick
#3	3	30	389	227	281	1,598	18,887	34,465	33,100	93,288	Cooper
#4	443	5,052	3,486	5,164	4,387	83,201	349,674	2,020,402	2,855,963	1,961,502	Fermi
#5	3	405	808	1,588	3,548	44,662	68,731	131,168	523,320	422,590	Fitzpatrick
#6	51	143	116	146	1,709	5,412	17,857	74,970	104,459	95,598	Grand Gulf
#7	54	69	146	242	377	4,405	40,295	40,177	60,870	118,600	Hatch
#8	0	0	0	299	1,026	21,550	341,000	623,300	1,992,600	2,367,200	Hope Creek
#9	219	105	111	250	647	14,837	83,972	132,041	327,697	545,504	LaSalle
#10	527	6,082	13,523	34,781	19,671	98,276	767,384	2,371,936	2,217,772	1,356,901	Limerick
#11	1,027	9,200	7,179	2,726	5,673	99,157	296,754	575,046	1,594,268	2,380,116	OC
#12	0	1,718	3,095	2,835	5,275	102,137	260,268	574,520	1,089,403	1,207,703	Perry
#13	53	140	235	1,206	5,797	21,671	304,832	121,065	104,601	136,070	Quad Cities
#14	45	322	514	1,490	728	19,416	71,322	389,315	162,360	212,057	River Bend
#15	248	1,177	1,532	2,531	9,450	46,400	261,400	351,200	419,000	553,600	Susquehanna
#16	630	1,500	1,300	1,100	3,800	27,179	101,897	132,813	373,620	835,442	Vt. Yankee
#17	0	0	0	20	464	98	62,192	62,434	43,841	85,775	WNP-2
#18	6	12	44	77	245	4,755	71,919	310,777	131,436	144,419	Vogtle
#19	133	912	1,666	2,934	5,120	28,910	61,081	96,680	116,634	196,675	Arkansas One
#20	1,025	8,800	4,098	4,093	3,483	204,000	416,000	1,517,000	1,586,000	1,274,000	Beaver Valley
#21	25	62	98	150	508	8,969	29,907	123,452	132,247	122,505	Callaway
#22	173	844	2,817	1,860	2,050	34,372	98,146	190,043	484,858	2,913,440	CalvertCliffs
#23	112	824	3,974	6,843	5,025	64,903	490,593	336,713	294,339	343,853	Catawba
#24	0	0	10	40	489	14,245	9,899	17,796	96,327	128,091	Crystal River
#25	181	410	459	367	585	13,659	109,707	911,289	575,558	1,388,284	Davis Besse
#26	0	4	2	18	52	6,826	111,460	90,500	78,800	56,600	Diablo Canyon
#27	107	1,360	2,996	3,479	3,565	63,147	179,898	526,176	275,281	640,942	D C Cook
#28	450	370	1,210	5,270	5,420	11,550	276,950	407,100	91,200	72,704	Ft Calhoun
#29	577	1,111	2,310	2,955	6,126	23,275	58,940	177,180	202,410	308,857	Robinson
#30	23	39	222	636	1,959	9,500	82,505	57,430	116,652	115,316	Farley
#31	396	2,521	3,516	3,432	2,951	59,776	511,649	1,398,599	1,779,321	1,190,051	Haddam Neck
#32	1,599	16,037	19,198	27,633	45,905	549,818	2,068,626	5,130,383	8,235,939	5,011,505	Indian Pt.
#33	20	175	413	605	1,104	13,626	115,262	214,294	201,162	294,107	Kewaunee
#34	39	494	1,063	1,325	2,207	75,399	707,673	409,946	375,475	318,597	McGuire
#35	98	507	691	1,840	1,975	23,689	63,600	150,600	206,400	128,000	Maine Yankee
#36	0	170	523	592	640	9,017	41,290	175,450	513,190	440,520	N. Anna
#37	0	486	1,128	1,488	1,554	41,576	68,752	300,207	205,258	203,306	Oconee
#38	41	494	1,391	1,390	2,468	29,643	81,632	96,130	281,580	407,146	Palisades
#39	21	0	141	157	175	3,080	11,075	9,645	110,555	1,047,595	Palo Verde
#40	57	252	375	425	524	28,048	88,765	171,360	256,607	260,493	Pt. Beach
#41	106	330	292	571	1,123	17,040	118,110	387,100	1,333,400	1,132,143	Prairie Is.
#42	32	85	144	34	129	6,687	231,574	1,703,641	337,822	575,545	Rancho Seco
#43	0	0	0	602	1,910	34,618	412,757	562,662	1,967,403	2,409,169	PSE&G
#44	0	32	362	792	1,016	19,120	258,350	455,570	381,710	403,760	ShearonHarris
#45	0	2,050	6,460	8,200	10,750	55,390	421,500	756,790	2,021,000	3,251,000	San Onofre
#46	0	4	75	480	665	2,905	31,201	40,636	161,802	203,839	S. Texas
#47	135	1,590	2,265	4,913	5,035	51,502	433,340	163,598	198,253	150,193	Sequoyah
#48	0	908	1,395	5,748	16,323	100,323	101,342	111,697	143,634	319,227	St. Lucie
#49	4	121	207	336	457	5,578	76,704	393,938	191,163	289,707	V C Summer
#50	0	7	69	134	467	160,777	295,789	335,906	610,098	631,214	Surry
#51	736	2,436	8,169	11,004	10,848	160,912	661,598	497,692	313,703	832,235	TMI
#52	284	407	2,522	2,415	3,828	80,103	55,230	148,643	815,022	543,495	Trojan
#53	0	0	0	0	0	168,258	710,158	946,133	723,650	396,115	Turkey Pt.
#54	98	131	329	512	548	16,036	82,801	160,414	345,835	790,932	Yankee Rowe
#55	289	15,217	12,676	4,462	6,599	194,937	321,086	544,362	460,537	4,226,596	Zion

Table 4-14 shows the average values and the standard deviations for each population cell. In all cases, the standard deviations of the mean exceeded their mean values. Population densities were determined by dividing the average number of individuals within each cell by the corresponding area. The first five miles yield population densities of about 140 individuals per square mile. Beyond five miles, the average population density essentially doubles in value (Table 4-14).

Table 4-14. Average Population Distribution for U.S. Nuclear Facilities

Distance (miles)	Average No. Individuals \pm 1 SD	Population Density (No. Ind./Mile ²)
< 1	185 \pm 314	63
1 - 2	1,560 \pm 3,365	166
2 - 3	2,172 \pm 3,698	138
3 - 4	2,977 \pm 6,019	135
4 - 5	3,979 \pm 6,969	141
5 - 10	55,122 \pm 84,811	234
10 - 20	240,581 \pm 318,939	255
20 - 30	507,664 \pm 809,435	323
30 - 40	702,317 \pm 1,228,789	320
40 - 50	831,796 \pm 1,062,887	294

Population densities beyond the 50-mile radius are not defined in FSARs and had to be derived by alternate means. All States in which at least one licensed commercial nuclear facility exists or whose borders are within 50 miles of a reactor facility were identified. The average population density was defined for each State by dividing the 1990 State population by the State's area defined in square miles. States with multiple reactors were weighted proportionately. An overall population density of about 200 individuals per square mile was thus obtained. This value was used to represent population density beyond a 50-mile radius.

Table 4-15 provides the population distribution of the Reference LWR facility used to estimate thyroid dose and health effects for the four reactor accident categories

Table 4-15. Population Distribution for Reference LWR

Distance Interval (miles)	Mean Population		
	Density (person/mile ²)	Total (persons)	
		Radial Segment	Cumulative
< 1	63	185	185
1 - 5	138	10,406	10,591
5 - 10	234	55,142	65,733
10 - 25	284	468,472	534,205
25 - 50	309	1,820,396	2,354,601
50 - 100	200	4,713,000	7,067,601
100 - 150	200	7,855,000	14,922,601
150 - 200	200	10,994,000	25,919,601
200 - 350	200	51,843,000	77,762,601
350 - 500	200	80,121,000	157,883,601

4.4 Population Thyroid Health Effects

Population thyroid health effects for the Reference LWR are estimated by deriving the cumulative population thyroid exposure for each population subgroup and applying the appropriate risk coefficient. The percentage of individuals representing each sub-population for the Reference LWR is assumed to be identical to that of the whole U.S. population, as defined by 1990 census data. By multiplying the age- and sex-adjusted populations at fixed radial distances with the corresponding thyroid dose values of the exposed individuals, population thyroid doses were derived for each distance interval. It is important to note that the exposed population is limited to individuals within the plume pathway, which based on dispersion parameters may represent only a small fraction of the total population residing 360 degrees around a reactor facility. Additionally, thyroid doses within the plume pathway for any given radial distance are assumed to exhibit a Gaussian distribution whose maximum value is equal to the plume centerline values cited in Tables 4-8 through 4-11.

Population thyroid doses are converted to thyroid health effects by means of the previously derived risk coefficients for thyroid cancer, thyroid nodules, and hypothyroidism. The mean numbers of thyroid cancers, nodules, and ablated thyroids estimated to occur within selected distance intervals for the four accident categories are given in Table 4-16. These estimates of thyroid effects represent a population exposed under normal conditions with no KI. The number of expected thyroid effects is highest for RSUR-1, followed by RSUR-4 and RSUR-2. The

small release fraction for RSUR-3 results in small population thyroid doses and yields estimates of less than 0.5 excess thyroid cancers and nodules for all population segments. A less than 0.5 probability of observing a single thyroid cancer or nodule for a population cell is reported as a zero (0) value.

The relative frequencies of total cancers to fatal cancers and to nodules are a constant among population cells. This constancy occurs because the relative frequencies of these thyroid effects are solely defined by the relative magnitude of their corresponding risk coefficients (see Chapter 3). For I-131, the risk coefficients of 23.2, 2.3, and 44.7 per 10^6 thyroid rads were previously cited to correspond to cancer, fatal cancer, and nodule, respectively. On the average, these risk coefficients predict that for every fatal thyroid cancer, there will be nine additional non-fatal cancers, and 19.4 thyroid nodules.

A comparison of the absolute numbers of thyroid effects per population cell for increasing radial distances shows a complex trend reflecting a steady decrease in individual doses and a near exponential increase in the exposed population size. Thus, the total number of thyroid effects for populations at large distances must be viewed in the context of individual risks that fall off precipitously with distance. Individual risks can be readily estimated by dividing the number of thyroid effects for a population cell by the total number of individuals residing within that radial segment.

The number of cases of hypothyroidism for the four accident categories are also shown in Table 4-16. Since hypothyroidism is a non-stochastic effect with a dose-threshold, its occurrence is limited to those populations in which individual thyroid doses exceed threshold values (defined in Table 3-7). With the exception of RSUR-1, the likelihood of exceeding the threshold value is minimal beyond a distance of 25 miles.

Table 4-16. Population Thyroid Effects for Normal Activity Without KI*

Distance Interval (miles)	A Total Thyroid Cancers				B Fatal Thyroid Cancers			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	137	58	0	52	14	6	0	5
5 - 10	278	59	0	105	28	6	0	11
10 - 25	432	72	0	157	43	7	0	16
25 - 50	351	58	0	128	35	6	0	13
50 - 100	232	36	0	84	23	4	0	8
100 - 150	174	27	0	63	17	3	0	6
150 - 200	138	21	0	49	14	2	0	5
200 - 350	264	41	0	93	26	4	0	9
350 - 500	449	72	0	153	45	7	0	16
Distance Interval (miles)	C Thyroid Nodules				D Hypothyroidism			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	361	155	0	139	150	31	0	33
5 - 10	726	157	0	283	186	11	0	49
10 - 25	1123	193	0	420	146	1	0	21
25 - 50	909	154	0	340	11	0	0	0
50 - 100	594	94	0	220	0	0	0	0
100 - 150	438	70	0	162	0	0	0	0
150 - 200	343	55	0	124	0	0	0	0
200 - 350	635	103	0	230	0	0	0	0
350 - 500	962	168	0	340	0	0	0	0

* The administration of KI is assumed to reduce the thyroid dose from inhalation of radioiodides with a 99% efficiency.

4.4.1 Potential Reduction in Thyroid Health Effects

The potential reduction in the mean number of thyroid effects that would result from the use of KI are governed by the fraction of the thyroid dose from the inhalation exposure of radioiodide. When KI is properly administered, it reduces internal thyroid exposures from radioiodides with a 99% efficiency. Thyroid exposure from external radiation and internal exposure from non-radioiodide nuclides is unaffected by the prophylactic administration of KI. Table 4-17 shows the residual number of thyroid cancers, fatal thyroid cancers, thyroid nodules, and ablated thyroids (i.e., ablated thyroids resulting in a clinical state of hypothyroidism). The difference between values shown in Table 4-16 and 4-17 provides an estimate of the net potential reduction in thyroid health effects attributable to KI administration. The number of thyroid health effects that can be potentially avoided if KI is administered under optimal conditions is shown in Table 4-18.

An estimate of fetal thyroid effects employs a similar methodology and uses parameter values previously defined. Critical parameters include the following:

- Fetal thyroid dose: assumed to be twice the maternal dose and corresponds to twice the values for females above 18 years of age (see Tables 4-8 to 4-11).
- Fetal thyroid risk coefficients for cancer, nodules, and thyroid ablation are assumed to be equal to those of males and females under the age of 18, but are adjusted for 75 years at risk.
- The number of fetuses at risk is based on the fact that radioiodide is concentrated in the fetal thyroid only during the second and third trimesters. At the current birth rate of 16 live births per 1,000 individuals per year, the number of fetuses at risk at any moment in time is eight fetuses per 1,000 persons exposed to the plume.

Although the fetus may be considered the most sensitive member of the general population, the number of fetuses likely to be exposed from a passing plume is relatively small.

Table 4-19 identifies the number of fetal thyroid cancers, nodules, and ablated thyroids for maternal plume exposure when no KI is administered. Table 4-20 provides estimates of residual fetal thyroid effects that cannot be avoided even if KI is administered to pregnant women. The difference in corresponding values of Tables 4-19 and 4-20 yields the net potential reduction of fetal thyroid effects attributable to maternal KI prophylaxis (Table 4-21).

Table 4-17. Residual Thyroid Effects for Population Exposed Under Normal Activity and Administered KI*

Distance Interval (miles)	A Total Thyroid Cancers				B Fatal Thyroid Cancers			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	18	16	0	8	2	2	0	1
5 - 10	37	17	0	16	4	2	0	2
10 - 25	58	21	0	24	6	2	0	2
25 - 50	51	17	0	21	5	2	0	2
50 - 100	35	11	0	14	3	1	0	1
100 - 150	26	8	0	11	3	1	0	1
150 - 200	21	7	0	8	2	1	0	1
200 - 350	41	13	0	17	4	1	0	2
350 - 500	61	19	0	25	6	2	0	2
Distance Interval (miles)	C Thyroid Nodules				D Hypothyroidism			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	58	52	0	25	5	4	0	1
5 - 10	117	54	0	51	6	0	0	1
10 - 25	186	68	0	77	1	0	0	0
25 - 50	162	56	0	68	0	0	0	0
50 - 100	111	35	0	45	0	0	0	0
100 - 150	83	26	0	34	0	0	0	0
150 - 200	67	21	0	27	0	0	0	0
200 - 350	131	41	0	53	0	0	0	0
350 - 500	193	62	0	79	0	0	0	0

* The administration of KI is assumed to reduce the thyroid dose from inhalation or radioiodides with 99% efficiency.

Table 4-18. Avoidable Population Thyroid Effects with KI Prophylaxis

Distance Interval (miles)	A Total Thyroid Cancers				B Fatal Thyroid Cancers			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	119	41	0	44	12	4	0	4
5 - 10	241	42	0	89	24	4	0	9
10 - 25	374	51	0	133	37	5	0	13
25 - 50	301	40	0	107	30	4	0	11
50 - 100	197	25	0	70	20	2	0	7
100 - 150	148	18	0	52	15	2	0	5
150 - 200	117	15	0	41	12	1	0	4
200 - 350	223	28	0	77	22	3	0	8
350 - 500	388	53	0	131	39	5	0	13
Distance Interval (miles)	C Thyroid Nodules				D Hypothyroidism			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	303	103	0	114	99	28	0	32
5 - 10	609	103	0	231	180	10	0	48
10 - 25	937	124	0	342	144	1	0	21
25 - 50	748	98	0	272	11	0	0	0
50 - 100	482	60	0	174	0	0	0	0
100 - 150	355	43	0	128	0	0	0	0
150 - 200	276	34	0	98	0	0	0	0
200 - 350	504	63	0	177	0	0	0	0
350 - 500	769	105	0	261	0	0	0	0

Table 4-19. Fetal Thyroid Effects for Normal Activity Without KI*

Distance Interval (miles)	A Total Thyroid Cancers				B Fatal Thyroid Cancers			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	3	1	0	1	0	0	0	0
5 - 10	6	1	0	2	1	0	0	0
10 - 25	9	2	0	3	1	0	0	0
25 - 50	7	1	0	3	1	0	0	0
50 - 100	5	1	0	2	0	0	0	0
100 - 150	4	1	0	1	0	0	0	0
150 - 200	3	1	0	1	0	0	0	0
200 - 350	5	1	0	2	1	0	0	0
350 - 500	9	2	0	3	1	0	0	0
Distance Interval (miles)	C Thyroid Nodules				D Hypothyroidism			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	9	4	0	4	1	0	0	0
5 - 10	18	5	0	7	1	0	0	0
10 - 25	27	6	0	11	1	0	0	0
25 - 50	23	5	0	9	0	0	0	0
50 - 100	15	3	0	6	0	0	0	0
100 - 150	11	2	0	4	0	0	0	0
150 - 200	9	2	0	3	0	0	0	0
200 - 350	16	3	0	6	0	0	0	0
350 - 500	23	5	0	8	0	0	0	0

The administration of KI is assumed to reduce the thyroid dose from inhalation of radioiodides with a 99% efficiency.

Table 4-20. Residual Thyroid Effects for Fetal Exposure Under Normal Activity and Maternal Administration of KI*

Distance Interval (miles)	A Total Thyroid Cancers				B Fatal Thyroid Cancers			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	1	0	0	0	0	0	0	0
5 - 10	1	1	0	1	0	0	0	0
10 - 25	2	1	0	1	0	0	0	0
25 - 50	2	1	0	1	0	0	0	0
50 - 100	1	0	0	1	0	0	0	0
100 - 150	1	0	0	0	0	0	0	0
150 - 200	1	0	0	0	0	0	0	0
200 - 350	2	1	0	1	0	0	0	0
350 - 500	2	1	0	1	0	0	0	0
Distance Interval (miles)	C Thyroid Nodules				D Hypothyroidism			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	3	2	0	1	0	0	0	0
5 - 10	5	2	0	2	0	0	0	0
10 - 25	8	3	0	3	0	0	0	0
25 - 50	7	3	0	3	0	0	0	0
50 - 100	5	2	0	2	0	0	0	0
100 - 150	4	1	0	2	0	0	0	0
150 - 200	3	1	0	1	0	0	0	0
200 - 350	6	2	0	2	0	0	0	0
350 - 500	9	3	0	4	0	0	0	0

* The administration of KI is assumed to reduce the thyroid dose from inhalation or radioiodides with 99% efficiency.

Table 4-21. Avoidable Thyroid Effects for Fetuses with KI Prophylaxis

Distance Interval (miles)	A Total Thyroid Cancers				B Fatal Thyroid Cancers			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	2	1	0	1	0	0	0	0
5 - 10	4	1	0	2	0	0	0	0
10 - 25	7	1	0	2	1	0	0	0
25 - 50	5	1	0	2	1	0	0	0
50 - 100	3	0	0	1	0	0	0	0
100 - 150	3	0	0	1	0	0	0	0
150 - 200	2	0	0	1	0	0	0	0
200 - 350	4	0	0	1	0	0	0	0
350 - 500	6	1	0	2	1	0	0	0
Distance Interval (miles)	C Thyroid Nodules				D Hypothyroidism			
	RSUR-1	RSUR-2	RSUR-3	RSUR-4	RSUR-1	RSUR-2	RSUR-3	RSUR-4
< 5	6	2	0	2	1	0	0	0
5 - 10	13	2	0	5	1	0	0	0
10 - 25	19	3	0	7	1	0	0	0
25 - 50	15	2	0	6	0	0	0	0
50 - 100	10	1	0	4	0	0	0	0
100 - 150	7	1	0	3	0	0	0	0
150 - 200	6	1	0	2	0	0	0	0
200 - 350	10	1	0	3	0	0	0	0
350 - 500	14	2	0	5	0	0	0	0

CHAPTER 5

THE ECONOMIC COSTS AND BENEFITS OF KI PROPHYLAXIS

As a rule, whenever radiation exposure can be reduced by a specific measure, its endorsement by policy-makers is linked to a cost-benefit ratio in which the benefit is perceived to be equal to or greater than the economic impact of the protective measure. A common problem encountered in defining a cost-benefit ratio is the quantification of the major elements that constitute either the cost or the benefit. When the elements are expressed in their normal units, a highly subjective approach is required at the final stage of decision-making. Conversely, an objective and defensible decision is supported by a cost-benefit analysis in which all parameters are expressed in dimensionally-equivalent terms.

The quantification of cost for making KI available can be obtained by the conventional method of assigning monetary values to materials, labor, and other needed resources. The assignment of monetary values to thyroid health effects is less standardized and of considerable complexity. Appendix D of this report provides a detailed description of the methodology used to establish monetary values for (1) the programmatic cost of providing KI and (2) the reduction in thyroid health effects. In this section, only a limited summary is provided which identifies the principal cost elements and their assigned monetary values.

5.1 The Economic Cost of KI Prophylaxis

Critical to a discussion of cost is the method by which KI is made available to the general public. The two principal options include stockpiling and predistribution, and any policy decision must address not only the economic aspects but also logistical factors imposed by either option. Logistical considerations are governed by (1) the potentially short time interval between the initiating events of a serious reactor accident and atmospheric releases of radioiodines and (2) the need to administer KI prior to plume exposure for optimum thyroid protection. The timeliness of KI availability is most critical to persons living in close proximity to a nuclear facility where potential plume exposures are maximal and plume travel times are small.

In spite of the perceived advantage of timeliness for the predistribution option, there are limitations as well as disadvantages, which include the following:

- Accessibility - KI predistributed to households (and assumedly stored at the residence) may not be readily available during times when residents are at work, school, etc.
- Availability - At any point in time, there are transients as well as new residents to whom KI may not have been provided.

- Loss or misplacement - Based on a five-year shelf-life/replacement period, there is a significant probability that tablets will be lost or misplaced during this lengthy time interval.
- Improper storage - Improper storage may adversely affect its shelf-life and potency at time of administration.
- Misuse and accidental administration - Like any pharmaceutical kept by a household, there is a potential for misuse and/or accidental administration with prolonged possession by the general public.
- Improper disposal - For expired tablets, there is a loss of control for proper disposal.

5.1.1 Cost of Stockpiling

Most of the disadvantages associated with predistribution are either eliminated or minimized for the stockpiling option. A program can be developed under the direction of a State's emergency management staff that provides for the necessary controls and oversight of stockpiles. Thus, the benefits include proper storage, controlled access to stockpiles, assurance of adequate replacement and proper disposal of expired capsules.

With a properly trained emergency staff and an informed public, potential problems associated with a timely distribution of KI can be minimized. Timely distribution requires an adequate number of strategically located stockpiles within the community. Suitable locations would include police stations, fire houses, schools, community centers, hospitals and major health care centers, from which an efficient localized door-to-door distribution could be conducted or where residents themselves could procure the needed KI.

Beyond logistical and practical issues, costs must be considered a major factor in a policy decision which selects stockpiling, predistribution, or a combination of these two options.

A unique aspect of the stockpile option is that it is essentially transparent to the public and the cost of distribution to residents only becomes a reality in the unlikely event of a major nuclear emergency. Thus, for the stockpile option, the principal cost is the initial purchase of KI and its periodic replacement from the two FDA approved sources: Carter Wallace and ANBEX.

- Carter-Wallace - At the current purchase price of \$75.00/carton containing 100 vials with 14 tablets of 130 mg KI per vial, the cost per tablet is about five cents. With a suggested five-year shelf-life (i.e., replacement period) and a ten-day supply (i.e., ten tablets/individual), the annual cost of KI prophylaxis per individual is about ten cents for the stockpiling option.

- ANBEX - The initial cost for 14 scored tablets of 130 mg KI in a moisture resistant blister pack is 60 cents per pack with a guaranteed four-year shelf-life. Thereafter, annual payments of 15 cents per package would be required if, and only if, the stockpiled product can pass required FDA tests for stability and effectiveness. The annual stockpiling cost of KI procured from ANBEX would also be about ten cents per individual.

Additional costs might include the amendment of existing emergency plans to include protocols for distribution, public notification and training of the emergency staff. These one-time costs, however, are likely to be modest and may only marginally add to the baseline purchase/replacement cost of KI at ten cents per year per individual.

5.1.2 Cost of Predistribution

For predistribution, the cost of dispensing KI tablets to residents is an integral part of the program cost. Additionally, for a predistribution program to be effective, there has to be a very comprehensive public relations program that not only informs the public of the objectives of iodide prophylaxis and provides supportive information regarding safe storage, proper usage, dosage, contraindications, etc., but also establishes public confidence. In summary, the cost for predistribution of KI includes the purchase/replacement of KI, the predistribution of tablets, and a comprehensive public information program.

An assessment of cost for the predistribution option can be derived from the Tennessee pilot program in which State officials predistributed KI to residents within a 5-mile radius of the TVA's Sequoyah Nuclear Power Plant (see Appendix E of this report). It is estimated that the cost of predistribution of KI to 3704 households around the Sequoyah Nuclear Power Plant was accomplished at \$125,000.00. Conservatively assuming that within the five-year replacement time there is no loss of KI or relocation of households and that the average household represents four individuals, a lower bound cost per individual for the predistribution option is estimated at \$1.70 per year.

The cost estimates for providing KI to specific population segments of the Reference LWR are presented in Table 5-1 for stockpiling with and without predistribution to the less than five-mile resident population.

Table 5-1. Annual Programmatic Costs of KI Prophylaxis

Distance (miles)	Number of Individuals	Distribution Options			
		Stockpile		Combination*	
		segment cost (x \$1,000)	cumulative cost (x \$1,000)	segment cost (x \$1,000)	cumulative cost (x \$1,000)
< 5	10,591	1.1	1.1	18.2	18.2
5 - 10	55,142	5.5	6.6	5.5	23.7
10 - 25	468,472	46.8	53.4	46.8	70.5
25 - 50	1,820,396	182	235.4	182	252
50 - 100	4,713,000	471	706.4	471	723
100 - 150	7,855,000	786	1,492	786	1,509
150 - 200	10,997,000	1,100	2,592	1,100	2,609
200 - 350	51,843,000	5,184	7,776	5,184	7,793
350 - 500	80,121,000	8,012	15,788	8,012	15,805

* includes predistribution for the less than five-mile resident population.

5.2 The Economic Benefits of KI Prophylaxis: The Cost-of-Illness Approach

The "benefits" of protective measures commonly employed to safeguard public health, frequently involve the avoidance of disease, injury, or death. For such cost-benefit analyses, the monetary equivalence of human illness and disease must be assessed for the patient, family, and society. The burden of illness may include financial losses, pain and suffering, reduced quality of life, and premature mortality. At a minimum, the economic benefits must consider the cost of resources used for medical care and the loss of human resources due to morbidity, disability, and premature death. Additional consideration may be given to the impact of disease, injury, or death on the quality of life for the affected individual and family members.

The "cost-of-illness" approach was pioneered by Dorothy Rice, former Director of the National Center for Health Statistics (Rice 1985), and is frequently used to assess the economic burden of disease. In brief, this methodology is defined by three components which include: direct medical costs; morbidity/mortality costs; and psychological costs.

Direct costs include resources used for medical care from the time of diagnosis until total recovery or death. Morbidity and mortality costs, when combined, are referred to as indirect costs (Hodgson 1984). Indirect costs are the time and output lost or foregone by the individual and/or family members from employment (including imputed earnings for domestic work),

volunteer activities, and leisure. Lastly, morbidity and mortality invariably cause patients and family members to incur psychological costs, such as pain and suffering, impaired function in personal relationships, and a general reduction in the quality of life.

5.2.1 Derivation of Direct Costs

Direct cost estimates of radiation-induced thyroid illness include medical costs associated with the initial diagnosis, treatment of the disease, and the long-term management, surveillance, and care of the patient. Estimates of costs for relevant diagnostic procedures, treatments, hospitalization, etc. in this report are based on 1991 Government and private insurers' reimbursement schedules defined by Physicians' Current Procedural Terminology (CPT) Codes. CPT is a listing of descriptive terms and identifying codes for reporting medical services and procedures performed by physicians under Government and private health insurance programs. Additional information was obtained from the Health Care Financing Administration Division (HCFA) of the U.S. Department of Health and Human Services.

- Thyroid Nodules. Benign nodules may or may not require surgery. For either instance, costs include the initial diagnosis, treatment, and long-term follow-up. For long-term follow-up of potential patients resulting from an accidental exposure, an average residual life-expectancy of 30 years is assumed following the initial diagnosis of a nodule. Estimates of costs for long-term patient management and surveillance include routine office visits, hormone replacement therapy, and diagnostic procedures. For a benign thyroid nodule that does not require surgery, a lifetime medical cost of \$5,148 to \$7,375 was identified. When surgery is required, direct medical costs for a benign nodule range between \$11,820 and \$14,047. For either situation, the upper value reflects the discretionary use of ultrasound for patient evaluation. For a detailed analysis of these and subsequent cost estimates, the reader is referred to Appendix D of this report.
- Thyroid Cancer. The major cost difference between a thyroid cancer and a thyroid nodule is the need for aggressive treatment of the former. Medical costs for a thyroid malignancy are estimated at \$15,413 to \$19,348. This range in cost estimates may, nevertheless, be low in instances where residual thyroid tissue is suspected of malignancy following an initial course of treatment. In cases of persistent suspected malignancy, additional I-131 therapies and associated procedures and services are required. It is estimated that each additional I-131 therapy would increase the total cost by about \$4,000. In rare instances, up to ten separate therapeutic treatments may be required for the total eradication of malignancy.

For the ten percent of thyroid malignancies that are fatal, cost estimates are adjusted to reflect (1) the reduced follow-up period of medical care and (2) the terminal patient care costs. Based on mean survival times of papillary and follicular thyroid cancers, the mean follow-up period of 35 years assumed for non-fatal cancer is reduced to 9.4 years. It is estimated that the average terminal care of a cancer patient costs about \$16,000.

Given the options that are available for the treatment and management of thyroid malignancies and the multiple therapeutic treatments, the following direct costs will be assigned to thyroid cancer:

Non-fatal Thyroid Malignancy = \$20,000
 Fatal Thyroid Malignancy = \$32,000

- Hypothyroidism. Medical cost in cases of radiation induced hypothyroidism are limited to initial diagnostic tests, which confirm the reduction or loss of thyroid function, hormone replacement and management, and follow-up evaluation of thyroid status. Cost estimates are based on a 35-year life-expectancy following the diagnosis and loss of thyroid function. For hypothyroidism medical costs are estimated at \$5,669.

Table 5-2 summarizes direct medical cost estimates for the radiation thyroid effects under consideration.

Table 5-2. Summary of Direct Medical Costs

Thyroid Disorder	Total Direct Cost (\$)
Thyroid Nodule*	9,600
Thyroid Cancer	
- Non-fatal	20,000
- Fatal	32,000
Hypothyroidism	5,600

* assumes that 50% of nodules require surgery

5.2.2 Derivation of Indirect Costs

Indirect costs principally reflect the time and output lost or forfeited by the patient due to illness, permanent disability, and premature mortality. Indirect costs may also be incurred by individuals other than the patient who may forego economic activities to accommodate a family member's illness. Economic activities include occupational work that is lost to either the patient or his/her employer, as well as non-occupational (e.g., domestic) work that must be performed by someone else at the expense of the patient. For illness, the loss of time from economic opportunities corresponds to three discrete stages:

- (1) Illness - The period during which the thyroid dysfunction becomes sufficiently symptomatic and prompts the individual to seek medical evaluation and treatment. During this time, the patient may physically suffer from either hyper- or hyposecretion by the thyroid gland.
- (2) Treatment - Thyroidectomy and therapeutic administration of I-131 require hospitalization and convalescence; radioiodine therapy also requires that a patient be first rendered hypothyroid.
- (3) Long-Term Management - Following treatment, the patient, in most instances, is subject to a lifetime dependency on daily doses of thyroxine and must be periodically monitored for proper dosage. The patient must also be monitored for the recurrence of nodule/cancer. Patient management and surveillance require periodic office visits and clinical evaluation. It is estimated that office visits and outpatient clinical evaluation, on the average, represents a loss of one day per year for the residual portion of the patient's life.

Table 5-3 provides estimates of the average total number of days lost from economic activities for the various thyroid disorders.

The number of days appropriated to long-term management of the disorder is based on the average remaining years of life following diagnosis and latency periods previously identified. A special case involves a thyroid malignancy, which may result in premature death.

The indirect cost of permanent impairment. In addition to time lost from economic activity due to illness, a patient may also be permanently impaired and/or disabled. Permanent impairment or disability can reduce a patient's ability to be fully effective in occupational or economic activities and must, therefore, be included in assessing the total indirect cost.

Table 5-3. Time Lost From Economic Activities Due to Radiation Induced Thyroid Illness

Thyroid Disorder	Time Lost (Days)			Total
	Illness	Diagnosis/ Treatment	Long-Term Management	
Thyroid Nodule	14	14	30	58
Thyroid Cancer				
· Non-Fatal	14	14	35	63
· Fatal	14	14	10,731*	≈ 10,750
Hypothyroidism	14	7	35	56

* For a fatal malignancy, this value represents loss of life-expectancy, which is estimated at 29.3 years.

The American Medical Association has published Guides to the Evaluation of Permanent Impairment (AMA 1990). These Guides provide a reference framework within which physicians may evaluate and report medical impairments. Various terms used in the Guides, such as "impairment" and "disability" appear in laws, regulations, and policies of diverse origin and without consistent definition. The Guides define these terms as follows:

- Impairment - an alteration of an individual's health status that is assessed by medical means.
- Disability - an alteration of an individual's capacity to meet personal, social, or occupational demands. Disability is assessed by non-medical means.

On the basis of these definitions, the economic impact of thyroid disorders on indirect costs is most objectively assessed in terms of their permanent medical impairments. The AMA provides guidelines for evaluating permanent medical impairment of the thyroid due to hypothyroidism from radiation exposure or thyroidectomy as follows (AMA 1990):

Class 1 - A patient belongs in Class 1 when: (a) continuous thyroid therapy is required for correction of the thyroid insufficiency or for maintenance of normal thyroid activity, and (b) there is no objective physical or laboratory evidence of inadequate replacement therapy.

Class 1 Level of Impairment of the Whole Person: 0 - 10%

Class 2 - A patient belongs in Class 2 when: (a) symptoms and signs of thyroid disease are present, or there is anatomic loss or alteration, and (b) continuous thyroid hormone replacement therapy is required for correction of the confirmed thyroid insufficiency; but (c) the presence of a disease process in another body system or systems permits only partial replacement of the thyroid hormone.

Class 2 Level of Impairment of the Whole Person: 15 - 20%

In this report, the central value of five percent for Class 1 permanent impairment will be applied to the permanent hypothyroid conditions that are likely to result from (1) high radiation exposure doses received accidentally, (2) from the radiotherapy treatment for toxic nodules/cancer, or (3) the surgical removal of nodules/cancer. It will further be assumed that this five percent medical impairment results in a five percent disability for occupational and non-occupational economic activities for the affected individual, family members, and/or society.

The conversion of time lost from economic activities to equivalent dollars is most fairly achieved by means of the Gross National Product (GNP). The GNP is considered the most comprehensive measure of the country's economic activity and includes the market value of all goods and services that have been bought for final use during a year. From the Gross National Product of \$5,200 billion in 1989, the gross average annual per capita income of about \$21,000 is derived. This value of \$21,000 per year can be used to determine the equivalent dollar value for the number of days lost over the lifetime of an individual afflicted with a thyroid condition. This value can also be applied to determine the equivalent value of a five percent permanent disability (i.e., a five percent disability equates to about \$1,000 annually in reduced income). Table 5-4 provides estimates of the total average indirect costs associated with thyroid disorders.

Table 5-4. Average Lifetime Indirect Costs Associated with Thyroid Disorders

Thyroid Disorder	Lifetime Indirect Costs (\$)		
	For Time Lost	For Disability (%5)	Total
Thyroid Nodule	3,337	30,000	33,337
Thyroid Cancer			
Non-Fatal	3,625	35,000	38,625
Fatal	619,586	9,400	628,986
Hypothyroidism	3,222	35,000	38,222

5.2.3 Derivation of Psychological Costs

Disease may cause numerous changes and impositions in the lives of the patient and family members that may in part be linked to, but are not reflected in, the direct and indirect economic

costs identified above. The wide variety of deteriorations in the quality of life (QOL) brought on by illness are frequently referred to as psychological costs. For thyroid neoplasms and dysfunction, a deterioration in the quality of life may be precipitated by the loss of bodily function, a lifetime dependence on medication, hormonal instability, disfigurement from surgical scars, the uncertainty of normal life expectancy, and reduced financial security. In characterizing psychological costs associated with disease, Thomas Hodgson (Hodgson 1985), chief Economist for the Department of Health and Human Services' Office of Analysis and Epidemiology states:

"Disease may bring about personal catastrophes . . . to the victims of illness, . . . children, spouses, and siblings of victims, friends and co-workers of victims; and those who render care may all be affected. A victim may suffer a loss of a body part or speech, disfigurement, disability, impending death, pain, and grief. He and those around him, may be forced into economic dependence and social isolation, unwanted job changes, loss of opportunities for promotion and education, relocation of living quarters, and other undesired changes in life plans. The environment created by illness often induces anxiety, reduced self-esteem and feeling of well-being, resentment, and emotional problems that often require psychotherapy. Problems of living may develop, leading to family conflict, antisocial behavior, and suicide. The victim and others may experience marked personality changes and reduced sexual function. Disrupted development and delinquency may occur among children. The quality of life may be reduced beyond restorative capability of current rehabilitation efforts. The combination of financial strain and psychological problems can be especially devastating."

Due to the fact that quality of life issues have only recently become the subject of formal investigations among health care professionals, QOL data is both sparse and lacks standardization. In July 1990, the National Institutes of Health (NIH) conducted a workshop on the quality of life assessment in cancer clinical trials (NCI 1990). Among the major objectives of the meeting were to define discrete quality of life elements and to identify currently available instruments (i.e., methods) for QOL assessment. The workshop group consisting of international experts concluded that (1) the quality of life of patients is affected by both the disease and by the treatment of the disease and (2) the quality of life is a multi-dimensional concept which must be evaluated by a set of instruments (i.e., methods) that measures both broad issues and disease/treatment specific phenomena.

Although QOL measurements that specifically deal with thyroid cancer and/or thyroid dysfunction are not currently documented, the literature, nevertheless, identifies age, gender, marital status, educational level, religious beliefs, employment, and economic status, and the number of children living at home as generic variables that affect changes in the quality of life imposed by a given disease.

Valuation of Psychological Costs. In spite of the fact that psychological costs are consistently identified as a major cost component by health care researchers and economists, no formal

attempt has been made to quantify these costs in monetary terms (Hodgson 1984; Rice 1985; Brown 1990). The reason for this omission is obvious. From the foregoing discussion, it is safe to conclude that the intangible dimensions which define the quality of life are (1) highly subjective, (2) vary greatly among individuals, and in time and space, and (3) are not readily expressed in monetary terms. Independent of these difficulties, past instances of excluding psychological costs may have been justified for conditions in which the health effect is of unknown origin, self-inflicted or unavoidable.

The omission of psychological costs, however, is not readily justified for situations in which the health effect is clearly avoidable, or is the consequence of negligence or wrongful action of a second party. In litigation cases of wrongful injury or death, monetary compensation for psychological cost factors generally exceed those involving medical costs or loss of earnings. The thyroid health effects under consideration in this report must clearly be considered avoidable through the administration of KI. Additionally, accidental public exposure to radioiodine is likely to be viewed as the direct or indirect consequence of human negligence or wrongful actions. A complete cost-benefit analysis of KI prophylaxis must, therefore, include estimates of psychological costs expressed in the unit of dollars.

Based on the monetary awards for the radiation and non-radiation injury claims cited in Appendix D, and the opinion expressed by a subject matter expert, the psychological cost component for each radiation-induced thyroid health effect is estimated at \$500,000 and will be applied to the derivation of cost-benefit ratios for KI prophylaxis.

5.3 Summation of Thyroid Health Effects Cost

Table 5-5 summarizes previously derived values for the direct medical costs, the indirect cost of lost economic opportunities, and the psychological costs attributed to the reduced quality of life for each of the thyroid disorders considered in this report. For all three thyroid effects, the direct medical cost for diagnosis, treatment, and follow-up represents the smallest contribution to the total cost. The assigned common value of \$500,000 for psychological costs dominates the total cost of potential thyroid effects¹.

¹ Although the indirect cost of \$629,000 for a fatal thyroid cancer is considerably larger, the low frequency of fatal cancers among thyroid effects (< 3.5%) mitigates its impact on the average indirect cost of thyroid disorders.

Table 5-5. Average Total Cost Per Radiation-Induced Thyroid Effect

Thyroid Effect	Direct (\$)	Indirect (\$)	Psychological (\$)	Total (\$)
Nodule	9,600*	33,300	500,000	542,900
Cancer				
Non-fatal	20,000	38,600	500,000	558,600
Fatal	32,000	629,000	500,000	1,161,000
Hypothyroidism	5,600	38,200	500,000	543,800

* Value represents the midpoint of the range in direct medical cost estimates.

In Utero Cost Estimates. Fetal exposure in utero may also result in thyroid nodules, thyroid cancer, or congenital hypothyroidism. The resultant cost elements are similar to those involving the general population, but are somewhat higher in value, which reflects the reduced age at time of first diagnosis. Affected by this shift in time are costs associated with long-term medical care and surveillance, and indirect costs of lost economic opportunities. When in utero exposure results in thyroid disorders, the costs are based on the following ages of initial diagnosis:

- hypothyroidism: at time of birth
- thyroid nodule: at age ten
- thyroid cancer: at age five
- for fatal thyroid cancer, the time of death is assumed to occur at age 14.4

The cost of thyroid effects which are the result of in utero exposure is summarized in Table 5-6.

Table 5-6. Cost Estimates of Thyroid Effects for In Utero Exposure

In Utero Thyroid Effect	Direct (\$)	Indirect (\$)	Psychological (\$)	Total (\$)
Nodule	17,000	53,000	500,000	570,000
Cancer				
Non-fatal	24,000	56,000	500,000	580,000
Fatal	32,000	N/A	500,000	532,000
Hypothyroidism	11,000	79,000	500,000	590,000

5.4 An Evaluation of the Derived Cost Estimates

The appropriateness of monetary values for thyroid dysfunction and neoplasms derived in this report may be assessed by comparing these values to those that have previously been published by the NRC and other Federal agencies. For example, as part of a study performed by Sandia National Laboratories to estimate the financial consequences of reactor accident health effects (NUREG/CR-2723), cost estimates were determined for on-site emergency workers for five severe accident categories. Health effect "costs" to emergency utility workers were converted to dollar-equivalents using the following conversion: (1) \$1 million per early fatality, and (2) \$100,000 per early injury or latent cancer. These 1983 cost estimates, when adjusted to the current medical costs and market value of the dollar, yield cost estimates that are very comparable to those defined in this report. It may further be argued that cost estimates derived in this report are subject to an adjustment factor, which accounts for the difference in the involuntary non-occupational exposure of a member of the general public and the "voluntary" exposure conditions of the utility emergency worker. As a rule, it is appropriate to assign a higher compensation value in instances of involuntary participation.

In a recent analysis of radiation risks to the public from residential radon exposure, the EPA evaluated the cost-effectiveness of radon testing and mitigation at various levels (EPA 1992). Results of this cost-effectiveness analysis show that at the EPA's recommended action level of 4 pCi/l, the cost per lung cancer death averted is about \$700,000. At this action level, the EPA concluded that ". . . the Radon Program would be as or more cost-effective than many other government programs for personal safety and environmental protection."

The cost-effectiveness of several other Federal programs was recently assessed in a report issued by the Office of Management and Budget (OMB 1991). The range of cost per life saved for three program areas are cited in Table 5-7.

Table 5-7. Ranges in Publicly Implied Valuations of Federal Programs*

Federal Program Area	Range of Cost Per Life Saved (1991 \$'s)
Highway Safety	63,000 - 3,300,000
Air Transportation Safety	100,000 - 1,600,000
Occupational Safety	100,000 - 74,000,000

* Reference: OMB 1991

In summary, values cited in Tables 5-5 and 5-6 fall within the range of existing NRC guidelines used in impact analyses as well as those recently published by the EPA.

CHAPTER 6

THE COST-BENEFIT RATIO OF KI PROPHYLAXIS

A cost-benefit ratio for KI is represented by a dimensionless quotient derived by dividing the programmatic cost of KI stockpiling by the monetary equivalent value of avoided thyroid effects. In Chapter 5 of this report, the programmatic cost of KI prophylaxis for the stockpiling option was assumed to be principally determined by the purchase cost of KI and its periodic replacement.

KI tablets, currently available from two FDA-licensed firms, continue to be evaluated by the FDA for residual potency. At this time, a minimum shelf life of five years can be assumed for KI under proper storage conditions. At the current retail price and a five-year replacement schedule, the programmatic cost of stockpiling KI was estimated at about \$0.10 per person per year. Multiplying the number of persons within each population cell by \$0.10 yields the annual programmatic cost estimates for discrete distance intervals shown in Table 6-1.

Table 6-1. Annual Programmatic Costs of KI Prophylaxis

Distance (miles)	Number of Individuals	Stockpile Option	
		segment cost (x \$1000)	cumulative cost (x \$1000)
< 5	10,699	1.1	1.1
5 - 10	55,142	5.5	6.6
10 - 25	468,472	46.8	53.4
25 - 50	1,820,396	182	235.4
50 - 100	4,713,000	471	706.4
100 - 150	7,855,000	786	1492
150 - 200	10,997,000	1100	2592
200 - 350	51,843,000	5184	7776
350 - 500	80,121,000	8012	15,788

Deriving a monetary equivalence for the thyroid health effects potentially avoided when KI blocks thyroidal uptake of radioiodides with a 99% efficiency was considerably more complex. Chapter 4 identified four specific accident scenarios with the potential to release large quantities of radioiodides into the atmosphere. By means of the MACCS computer code, atmospheric releases of radioiodides were modeled to yield integrated air concentrations at fixed distances and then converted to thyroid doses using age- and sex- specific ventilation rates and dose conversion factors.

Also, in Chapter 4, thyroid doses to individuals in the plume pathway were converted to thyroid health effects by means of risk coefficients. Numbers of thyroid health effects were estimated for the general population and fetuses for discrete population cells defined by distance intervals.

In Chapter 5 (and Appendix D), the monetary equivalence for each thyroid health effect was derived. Estimates of cost equivalence included lifetime medical costs, loss of economic opportunity and psychological costs attributable to pain and suffering, reduction in quality of life, etc.

Multiplying the expected number of avoidable thyroid effects in each population cell (Chapter 4, Tables 4-18 and 4-21) with their economic worth (Chapter 5, Tables 5-5 and 5-6) yielded the economic benefits of avoidable thyroid health effects associated with each of the four reactor accident scenarios.

A cost-benefit ratio in which the programmatic costs are expressed in annual terms, however, requires that the economic benefits of avoided thyroid health effects also be expressed in annual terms. The monetary equivalence of avoided health effects resulting from each accident scenario can be expressed in annual terms by incorporating a factor that defines the probability that a given reactor accident scenario may occur in a year's time. Best estimates of accident frequencies for the four release categories analyzed were previously defined in Table 4-2 and are reproduced in Table 6-2.

Table 6-2. Reactor Accident Frequencies

Release Category	Frequency (year ⁻¹)
RSUR-1	2.9E-7
RSUR-2	2.4E-6
RSUR-3	3.3E-5
RSUR-4	1.6E-6

The multiplicative values of (1) the number of expected thyroid health effects, (2) their monetary equivalence, and (3) the accident frequency for each accident scenario provide an estimate of the yearly economic benefits of KI prophylaxis. Table 6-3 provides a breakdown of the average annual economic benefits. For the population cell defined by the zero to five mile radius, for example, a yearly economic benefit of \$487 is estimated. To ensure that the reader understands the method employed to derive this value, a sample calculation is provided for the zero to five mile population cell.

Table 6-3. Yearly Reduction in Population Thyroid Effects and Their Equivalent Monetary Values

Distance Interval (miles)	Non-Fatal Thyroid Cancers		Fatal Thyroid Cancers		Thyroid Nodules		Hypothyroidism		Total \$-Value
	No. of Cases	Value (\$)	No. of Cases	Value (\$)	No. of Cases	Value (\$)	No. of Cases	Value (\$)	
0 - 5	1.84E-4	103	2.05E-5	24	5.18E-4	281	1.46E-4	79	487
5 - 10	2.83E-4	148	3.14E-5	36	7.95E-4	432	1.54E-4	84	710
10 - 25	4.00E-4	223	4.44E-5	52	1.12E-3	608	7.78E-5	42	925
25 - 50	3.20E-4	179	3.55E-5	41	8.89E-4	483	3.32E-6	2	705
50 - 100	2.06E-4	115	2.29E-5	27	5.63E-4	306	0.00E+	0	448
100 - 150	1.54E-4	86	1.71E-5	20	4.13E-4	224	0.00E+0	0	330
150 - 200	1.21E-4	68	1.34E-5	16	3.18E-4	173	0.00E+0	0	257
200 - 350	2.30E-4	128	2.55E-5	30	5.80E-4	315	0.00E+0	0	473
350 - 500	4.05E-4	226	4.50E-5	52	8.94E-4	485	0.00E+0	0	763

Table 6-3. Yearly Reduction in Population Thyroid Effects and Their Equivalent Monetary Values (Continued)

SAMPLE CALCULATION: Derivation of the Yearly Reduction in Population Thyroid Effects and Their Equivalent Monetary Values for the 0 to 5-Mile Population Cell

1. From Table 4-18, the total number of avoidable thyroid health effects per accident release category for the 0-5 mile population is as follows:

Release Category	Non-Fatal		Fatal	Hypothyroid	
	Cancer	Cancer	Nodules		
RSUR-1	107		12	303	99
RSUR-2	37		4	103	28
RSUR-3	0		0	0	0
RSUR-4	40		4	114	32

2. Annual reduction in avoidable thyroid health effect = (No. of expected effects) x (Accident frequency):

Release Category	Non-Fatal		Fatal	Hypothyroid	
	Cancer	Cancer	Nodules		
RSUR-1	3.1E-5		3.5E-6	8.8E-5	2.9E-5
RSUR-2	8.9E-5	9.7E-6	2.5E-4	6.6E-5	
RSUR-3	0		0	0	0
RSUR-4	6.4E-5		6.4E-6	1.8E-4	5.2E-5
TOTAL	1.84E-4		2.0E-5	5.18E-4	1.46E-4

The total values of 1.84E-4 non-fatal cancers, 2.05E-5 fatal cancers, 5.18E-4 nodules, and 1.46E-4 hypothyroid conditions are given in Table 6-3 for the 0-5 mile population cell.

3. Annual equivalent cost estimates = (No. of thyroid effects) x (equivalent monetary cost)

- Non-fatal thyroid cancer: (1.84E-4 cancers) x (\$558,600/cancer) = \$103
 - Fatal thyroid cancer: (2.05E-5 cancers) x (\$1,161,000/cancer) = \$ 24
 - Thyroid Nodule: (5.18E-4 nodules) x (\$542,900/nodule) = \$281
 - Hypothyroidism: (1.46E-4 hypothyroids) x (\$543,800/hypothyroid) = \$ 79
- TOTAL = \$487

Total yearly economic benefit for the 1-5 population cell = \$242

Using the identical approach, yearly economic benefits of avoided thyroid effects were determined for fetuses exposed in utero. These values are defined in Table 6-4. Fetal values, when added to those of the general population, yield the total economic benefit for each population cell.

Dividing the annual programmatic cost of stockpiling KI by the average annual economic benefits from avoided thyroid effects (i.e., population and fetal) represents the cost-benefit ratio of KI prophylaxis. These two parameters and their quotient are presented in Table 6-5. For example, the annual programmatic cost of stockpiling KI for about 11,000 people living within five miles of the reference LWR is estimated at \$0.10 per person or \$1,100. The economic benefits of avoided thyroid effects for this population cell were estimated at \$495 per year, which gives a cost-benefit ratio of 2.22.

The cost-benefit ratio in effect is a measure of the cost-effectiveness of the prophylactic measure. For the zero to five mile population cell, it can be estimated that \$2.22 would be spent in order to avoid the economic equivalent cost of \$1.00.

The cost-benefit ratios for population cells increase nearly exponentially with distance. This is to be expected inasmuch as the programmatic cost of ten cents per person per year is a constant while the integrated air concentration, which defines individual thyroid dose, can be expected to drop off exponentially with distance. Thus, the cost-benefit ratio for the 50-100 mile population cell is reduced to 1,033. Within this distance interval \$1,033.00 would be spent for stockpiling to avoid the economic equivalent of \$1.00.

Table 6-5 also provides cumulative cost-benefit ratios, which define the cumulative areas of the circle. If, for example, on the basis of thyroid intervention levels, cost-benefit consideration, logistical factors, etc., a decision was made to provide stockpiles for populations out to a distance of 100 miles, the cumulative cost-benefit ratio of 212 can be estimated. The limitations and the significance of these cost-benefit ratios with regard to a policy decision are discussed in the next chapter.

Table 6-4. Yearly Reduction in Fetal Thyroid Effects and Their Equivalent Monetary Values

Distance Interval (miles)	Non-Fatal Thyroid Cancers		Fatal Thyroid Cancers		Thyroid Nodules		Hypothyroidism		Total Value (\$)
	No. of Cases	Value (\$)	No. of Cases	Value (\$)	No. of Cases	Value (\$)	No. of Cases	Value (\$)	
0 - 5	4.12E-6	2.40	0.00E+0	0	9.74E-6	5.50	2.90E-7	0.20	8.10
5 - 10	6.08E-6	3.50	0.00E+0	0	1.66E-5	9.50	2.90E-7	0.20	13.20
10 - 25	6.87E-6	4.00	7.63E-7	0.40	1.38E-5	8.00	2.90E-7	0.20	12.60
25 - 50	6.35E-6	3.70	7.05E-7	0.40	1.87E-5	10.70	0.00E+0	0	14.80
50 - 100	2.22E-6	1.30	0.00E+0	0	1.17E-5	6.70	0.00E+0	0	8.00
100 - 150	2.82E-6	1.60	0.00E+0	0	9.23E-6	5.30	0.00E+0	0	6.90
150 - 200	1.96E-6	1.10	0.00E+0	0	7.34E-6	4.20	0.00E+0	0	5.30
200 - 350	2.48E-6	1.40	0.00E+0	0	1.01E-5	5.80	0.00E+0	0	7.20
350 - 500	6.01E-6	3.50	7.34E-7	0.40	1.69E-5	9.60	0.00E+0	0	13.50

Table 6-5. The Cost-Benefit Ratio of KI Prophylaxis

Distance Interval (miles)	KI Cost: Stockpiling		KI Benefits: Reduced Thyroid Effects		Cost/Benefit Ratio	
	Per Distance Interval (\$/yr)	Cumulative (\$/yr)	Per Distance Interval (\$/yr)	Cumulative (\$/yr)	Per Distance Interval	Cumulative
< 5	1100	1100	495	495	2.22	2.22
5 - 10	5500	6600	723	1218	7.61	5.42
10 - 25	46,800	53,400	938	2156	49.9	24.8
25 - 50	182,000	235,400	720	2876	253	81.8
50 - 100	471,000	706,400	456	3332	1033	212
100 - 150	786,000	1,492,400	337	3669	2332	407
150 - 200	1,100,000	2,592,400	262	3931	4199	659
200 - 350	5,184,000	7,776,400	480	4411	10,800	1763
350 - 500	8,012,000	15,788,400	777	5188	10,311	3043

CHAPTER 7

THE APPLICABILITY OF KI COST-BENEFIT RATIOS TO A POLICY DECISION

In Chapter 6, cost-benefit ratios were derived which conveniently expressed the ratio of programmatic costs and the avoidance of thyroid effects in the common unit of dollars. It would appear that an assessment of these cost-benefit ratios could lead directly to a defensible policy decision. In other words, a ratio value of one or less in which the programmatic cost of stockpiling KI was equal to or less than the equivalent cost of thyroid effects avoided, should logically provide the basis for a policy decision to use KI. Conversely, cost-benefit ratios of values that are significantly greater than one could justify a policy decision to reject the use of KI.

The unencumbered and direct application of the derived cost-benefit ratios for KI in a policy decision can in fact be justified only under the following two conditions:

Condition #1: The derived cost-benefit ratio values are absolute. Absolute values imply that all parameter values used to derive the cost-benefit ratio are 100% representative of the universe and, therefore, have an uncertainty value of zero.

Condition #2: The prophylactic use of KI is applied independently of existing protective measures.

For reasons explained in the following sections, these two conditions do not exist. A valid policy decision must weigh the potential impact of model uncertainties and the prophylactic use of KI in the context of other protective measures.

7.1 Condition #1: Uncertainties and Their Impact on Cost-Benefit Ratios

Primary assumptions and model parameters, which must be defined for reactor accident consequence analysis in this report, are numerous and potentially have a wide range of uncertainties. While the uncertainty value for some assumptions/parameters may have little impact on the final cost-benefit ratios, other parameter uncertainties could potentially shift the cost-benefit ratio by as much as one to two orders of magnitude.

A highly quantitative treatment of uncertainties and their collective impact on the derived cost-benefit ratios is beyond the scope of this report. This chapter will identify the most important model parameters and assumptions used and will assess their relative effects on the derived cost-benefit ratios.

7.1.1 Reactor Accident Frequencies

By far, the single most significant parameter for accident consequence analysis is the probability of reactor accident occurrence. The probability values of the reactor accident frequencies used in this report were derived in NUREG-1150 (1987). Appendix A of NUREG-1150 discusses in detail the risk analysis steps and the interrelationships among steps. Using Monte Carlo techniques, frequency distributions of individual parameters were combined to yield frequency distributions of accident sequences, plant damage conditions, and total core damage. Although bounding values of the frequency distribution were "described," they were not quantified in NUREG-1150 (see Exhibit 8-1; this figure is reproduced as it appears in NUREG-1150, Appendix A, page A-21).

In 1978, NRC chartered a risk assessment review group to evaluate the 1975 Reactor Safety Study (NUREG-75/014, also known as WASH 1400), which defined similar accident frequencies. This review committee concluded in NUREG/CR-0400:

" . . . We are unable to determine whether the absolute probabilities of accident sequences in WASH-1400 are high or low, but we believe that the error bounds on those estimates are, in general, greatly understated."

In a separate assessment, the authors of NUREG-1433 evaluated the probability of different types of reactor accidents. The following bounding estimates of core melt accidents were provided:

" . . . the probability of core melt is less than 1.5×10^{-3} with 50 percent confidence, and less than 6.7×10^{-3} with 95 percent confidence . . . These upper bound probabilities are approximately factors of 25 and 100 times the RSS values above ($4.6 \times 10^{-5} + 1.4 \times 10^{-5} = 6.0 \times 10^{-5}$)."

Applying a similar range of uncertainty to accident frequencies derived in NUREG-1150 would profoundly affect the cost-benefit ratio values defined in Chapter 6. Assuming that reactor accident frequencies are potentially 100 times higher than assumed in this report, the cost-benefit ratios defined in Chapter 6, Table 6-5, could be reduced by two orders of magnitude. A reduction of the cost-benefit ratios by 100 would yield a cost-benefit ratio of about 1.0 out to a radial distance of nearly 50 miles (i.e., the cumulative cost-benefit ratio out to 50 miles is 81.8 and, when divided by 100, yields a 95% bounding ratio value of 0.818).

In summary, the values of reactor accident frequencies used in this report must be regarded as the single most significant uncertainty affecting the cost-benefit ratio cited in Table 6-5.

Exhibit 7-1

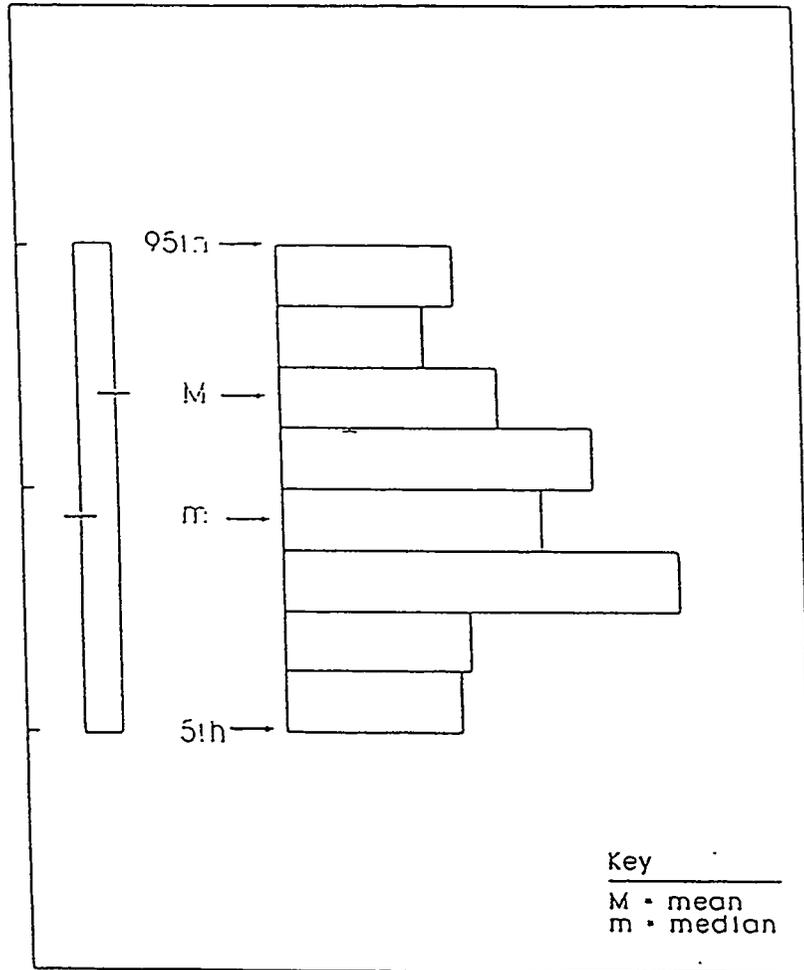


Figure A.6 Example display of core damage frequency distribution.

NUREG-1150

7.1.2 Core Inventory and Release Fraction

Time-weighted variations in core inventory of radioiodines during power operations are relatively minor and, therefore, may be ignored. The physico-chemical nature of iodide/iodine is relatively well understood. Under severe accident conditions of core melt, techniques used to retain iodine in the primary coolant (which were used during the TMI accident) may not be possible. It can, therefore, be assumed that the release fraction applied to radioiodines in this report is appropriate and exhibits a low error band.

7.1.3 Atmospheric Dispersion and Meteorological Factors

The MACCS computer code, like all other codes used for risk or consequence analysis, has associated uncertainties with regard to modeling plume dispersion in the environment. Limitations of the code that result in these uncertainties involve the absence of site-specific data such as topography. Other limitations involve assumptions such as the wind blows in a continuous straight line for extended periods of time, or assumptions about the meteorological conditions applied to the long-range transit of a released plume. For example, a single weather file is assumed to apply at all times and at all places of the plume pathway. Thus, if a site weather file assumes rain at the site, the code assumes that it rains everywhere at that time. Although such assumptions are commonly made to solve complicated differential equations for atmospheric dispersion models, they introduce uncertainties in the dispersion of radioactivity. Uncertainties in dispersion modeling have two major effects:

- (1) For population risk analyses, the impact of uncertainties regarding the atmospheric dispersion of radioactivity is relatively minor. Meteorological parameters have a profound effect on individual doses but only a limited impact on cumulative population doses. For example, a very stable condition producing a very narrow plume results in high air concentrations and high individual doses. In contrast, a very unstable condition disperses radioactivity resulting in a larger number of exposed individuals with lower individual doses. For extreme conditions of high and low stability, the cumulative population exposures and expected thyroid health effects may, nevertheless, be nearly identical. It is important to note that the cumulative population thyroid dose, which is relatively unaffected by dispersion, determines the denominator of the cost-benefit ratio.
- (2) In contrast, uncertainties regarding atmospheric dispersion may have a profound effect on the numerator of the cost-benefit ratio. Table 6-5 clearly demonstrates that the cost-effectiveness of KI prophylaxis deteriorates exponentially as a function of distance from the source term. Thus, a meteorological model, which maintains a straight-line plume over extended periods of time (i.e., the plume does not meander), projects unrealistically high centerline doses to populations at great distances.

The programmatic cost of stockpiling is principally determined by the size of the stockpile, which in turn, is determined by the radial distance at which the plume centerline thyroid exposure dose exceeds a predetermined intervention level. From this

relationship, it becomes readily apparent that a conservative computer dispersion model adversely affects the derived cost-benefit ratio and falsely implies a reduced cost-effectiveness.

The MACCS code undoubtedly uses conservative assumptions that project unrealistically high plume centerline exposures.

7.1.4 Age- and Sex-Specific Parameters and DCF Values

Individuals vary considerably in their physiology, which affects the internal exposure dose from the inhalation/ingestion of radionuclides. This report considers age- and sex- specific parameters, which have been well studied and reported in the literature, in converting time-integrated air concentrations of radioiodide to thyroid doses. Nevertheless, the dose conversion values (DCFs) represent average values that vary symmetrically about their means. When applied to a large random population, however, dose variations among individuals for a given group defined by age and sex are likely to cancel out. It can, therefore, be assumed that uncertainties regarding individual variations in thyroid doses do not contribute significantly to an estimate of cumulative population thyroid doses and thyroid health effects.

7.1.5 Thyroid Risk Coefficients

The risk coefficients used in this report represent consensus values defined by the BEIR V Committee and the NCRP. These scientific groups did not provide estimates of uncertainty regarding their risk coefficients. Thyroid risk coefficients like all other risk coefficients are extrapolated from epidemiological data, which contain uncertainties and confounding variables. Based on historical trends in which risk coefficients for other radiation health effects have generally increased, it should not be assumed that the thyroid risk coefficients used in this report are conservatively high and overestimate the consequences of thyroid exposure to radioiodine.

7.1.6 Uncertainties of Other Assumptions Used in Deriving Cost-Benefit Ratios

The following is a partial list of major assumptions that affect the cost-benefit ratio either positively or negatively. A positive effect on the cost-benefit ratio by an assumption is defined as one that reduces the cost-benefit ratio. A reduction in cost-benefit ratio improves the cost-effectiveness and supports the use of KI prophylaxis. A negative effect on the cost-benefit ratio by an assumption is defined as one that increases the cost-benefit ratio. An increase in cost-benefit ratio reduces the cost-effectiveness and opposes the use of KI prophylaxis.

- Efficiency Factor. This report assumes that KI is administered to all individuals under optimal conditions. Thyroid exposures from internal radioiodides are assumed to be reduced with a 99% efficiency. This is a highly unrealistic assumption. The use of more realistic efficiency values (i.e., less than 99%) would have a negative effect on the cost-benefit ratio that is inversely proportional to the reduction in efficiency. Thus, if an efficiency of about 50% had been

used, the cost-benefit ratios would effectively increase by a factor of two, which also reduces the cost-effectiveness of KI prophylaxis by a factor of two.

- Shelf-Life of KI. A conservative shelf-life of five years has been assumed, which in effect dictates the cost of stockpiling. An increase in shelf-life proportionately reduces the numerator of the cost-benefit quotient and has a positive effect. Thus, if the shelf-life could be increased to ten years, the cost-benefit ratio decreases by a factor of two and improves the cost-effectiveness by a factor of two.
- KI Stockpile Redundancy. No redundancy in stockpile quantities was assumed. This assumption is unrealistic. For efficient distribution, a stockpile is needed containing at least twice the quantity of KI that would be distributed in the event of an accident. A more realistic redundancy of 100% has a negative effect by increasing the cost-benefit ratio by a factor of two.
- Sheltering. Population exposure is assumed to occur under conditions of normal activity. If in fact KI were administered under conditions of sheltering, thyroid dose reduction by KI would be lower (see Table 4-7). Under more realistic conditions of sheltering, the cost-benefit ratio is negatively affected.
- Population Distribution. The assumed population distribution for the Reference LWR has large standard deviations for each population cell. For actual nuclear facilities, the cost-effectiveness varies in proportion to differences in population distribution relative to the Reference LWR. For facilities having disproportionately larger percentages of their population closer to the source term, cumulative cost-benefit ratios are lower.
- Adverse Reaction to KI. Potential adverse reactions and an adverse reaction incidence rate were identified in this report (Chapter 2 and Appendix C). Due to their infrequency and their uncertain monetary value, adverse reactions to KI were not factored into the cost-benefit ratio. The inclusion of adverse reactions to KI in the cost-benefit ratio would have a minor but negative effect on the cost-benefit ratio.
- Partial Predistribution. The derivation of cost-benefit ratios was confined to the stockpiling option only. The inclusion of KI predistribution to the proximal population would increase the programmatic cost of KI prophylaxis and have a negative effect.
- Multiple Plants per Site and Overlapping Populations. The cost-effectiveness of KI prophylaxis increases for facilities with more than one reactor per site or for facilities that are close to other facilities and share portions of the target populations. The assumption of a single reactor per site with no overlapping

target population used to derive the cost-benefit ratio in this report has a negative effect. For nuclear facilities with as many as three reactors per site and emergency zones overlapping with other neighboring facilities, the cost-benefit ratios are improved by at least a factor of three.

7.2 Condition #2: The Relationship of KI Prophylaxis to Other Protective Measures

In the event of a major accident involving a commercial nuclear power plant, a large-scale release of radioiodines would most likely occur along with a massive release of noble gases and varying quantities of other radionuclides. Thyroid and whole body exposures are, therefore, inextricably linked. Current protective action guidelines relating to population plume exposures are, therefore, defined by exposure limits to the whole body and the thyroid to doses of 1 to 5 rem and 5 to 25 rem, respectively.

Figure 7-1 depicts thyroid and whole body doses for the four accident categories considered in this report. Quantitative values of thyroid and whole body exposures for RSUR-1 are provided in Table 7-1. The relative magnitude of thyroid to whole body exposures is defined as a ratio in the right-hand column of the table.

To safeguard against primary plume exposure, current protective measures are limited to sheltering or evacuation. Sheltering and evacuation are clearly not interchangeable, but represent a first and second priority for public protection. Sheltering would most likely be recommended when expected doses span the lower limits of whole body and thyroid exposures. Projected doses in incremental excess of lower limits could be expected to change the recommendation from sheltering to evacuation. The relevance of KI prophylaxis to these two protective measures is simple: since KI cannot reduce external exposure and internal exposure from non-radioiodines, its usefulness is restricted to the concurrent recommendation for sheltering. In combination, these two independent measures are complementary in reducing whole body exposure and thyroid exposure and are compatible in time and space.

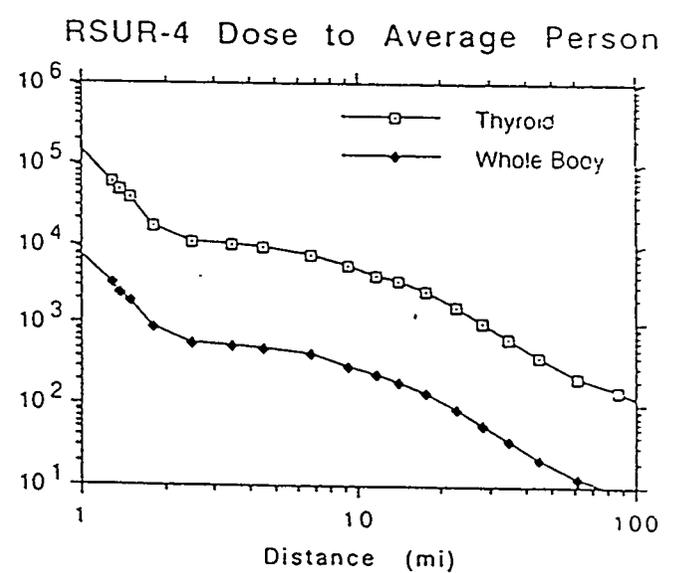
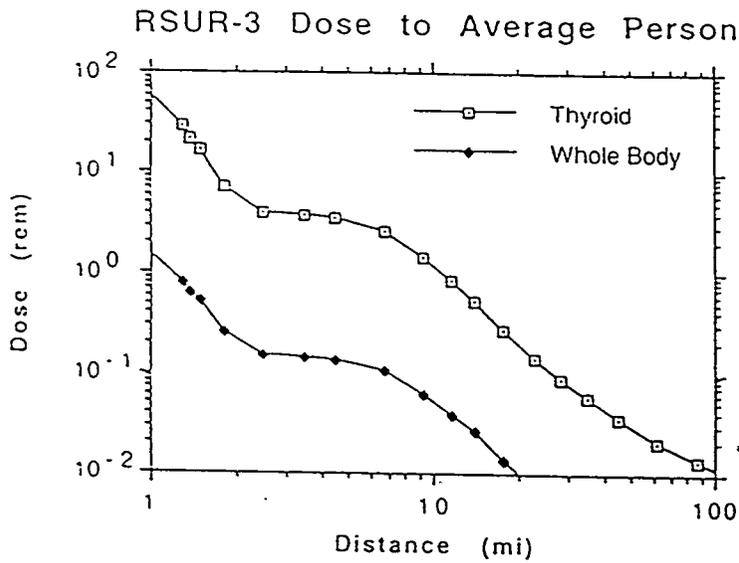
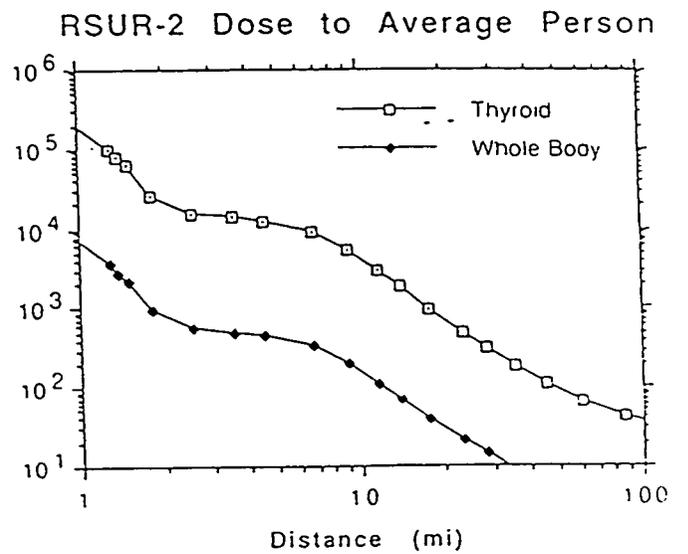
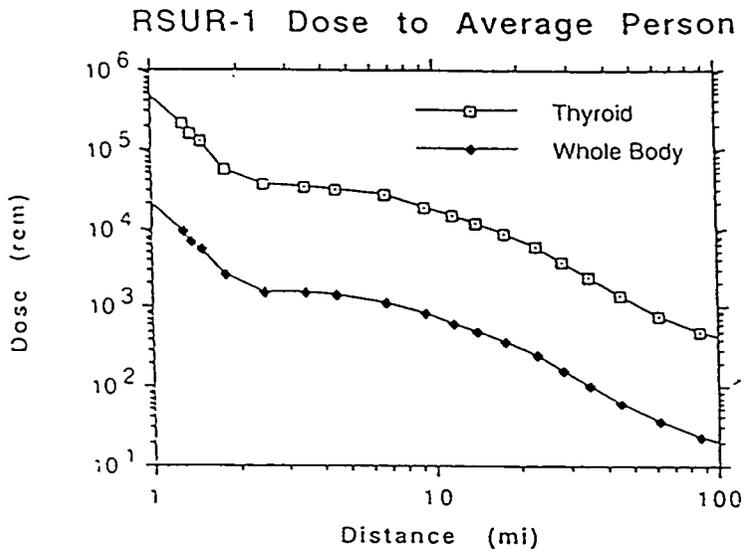


Figure 7-1. The Relationship of Thyroid to Whole Body Doses

Table 7-1. The Relationship of Thyroid to Whole Body Exposure for RSUR-1

Distance (miles)	Thyroid dose (rem)		Whole Body Dose (rem)	Dose Ratio (Thyroid/ Whole Body)
	Radioiodines	Total (All Pathways)		
0 - 5	1.9E+04	2.0E+04	8.7E+02	23.0
5 - 10	6.9E+03	7.3E+03	3.2E+02	22.8
10 - 25	1.7E+03	1.9E+03	7.9E+01	24.0
25 - 50	2.7E+02	3.0E+02	1.4E+01	21.4
50 - 100	6.2E-01	7.0E+01	3.6E+00	19.4
100 - 150	2.8E+01	3.2E+01	1.5E+00	21.3
150 - 200	1.7E+01	1.9E+01	9.6E-01	19.8
200 - 350	7.8E+00	8.5E+00	4.3E-01	19.8

In contrast, the prophylactic use of KI and the evacuation of residents must be regarded as mutually exclusive protective measures. The principal purpose of evacuation is to avoid primary plume exposure; KI prophylaxis is intended to mitigate its impact. More important is the potential conflict in time and space. Under conditions of evacuation, it would be counterproductive to request that residents either delay evacuation until KI is distributed door-to-door, or reroute and delay evacuation by first obtaining KI from a local distribution center.

The relationship of KI prophylaxis to existing protective measures and the need to assess the cost-benefit in context with these existing protective measures may best be illustrated by the following hypothetical example:

A major population center of 150,000 people resides in a downwind sector from the source term. Doses to this population center are projected to reach levels as high as 2.5 rem to the whole body and 50 rem to the thyroid. Sheltering is estimated to reduce these maximal doses to about 1 rem and 20 rem, respectively. Based on the residual high thyroid dose, a recommendation is made for this group of residents to evacuate the area immediately.

In this scenario, it can be assumed that the prompt distribution of KI from local stockpiles could readily reduce thyroid exposures to less than the lower limit of five rem and in the process shift the recommended protective measure from evacuation to sheltering.

The value of KI prophylaxis, therefore, has two discrete components: the first involves the reduction of thyroid health effects, as defined in the preceding chapter in terms of cost-benefit

ratios; the second is the economic benefit of the potential shift from evacuation to sheltering for select target populations.

A thorough and quantitative treatment of this second economic benefit is complex and influenced by a host of modifiers. Critical modifiers that may influence a decision to shelter or evacuate include logistical problems affected by (1) the time interval before plume arrival, (2) the time of day, (3) the season of the year, (4) weather and road conditions, (5) plume direction(s) relative to evacuation routes, (6) the size of the exposed population, and (7) the ability to provide temporary shelter.

The literature contains limited information addressing logistical issues and comprehensive cost estimates associated with evacuation. A baseline cost estimate can be extracted from studies involving the Three Mile Island Accident. At the time of the TMI accident, it was estimated that there were about 14,300 households within the 0-5 mile radius, 40,000 between 5-10 miles, and 72,000 in the 10-15 mile ring (Houts 1980). Although voluntary evacuation began almost immediately following the announcement of the emergency status at TMI, the number of evacuees was initially minimal. Only 5 to 6% of the population within the 0-5 mile radius evacuated within the first two days. On the third day, however, nearly 50% of the 0-5 mile population had evacuated (Houts 1980). The increase was largely precipitated by the Governor of Pennsylvania's advisory on Friday, March 30, 1979, for voluntary evacuation of pregnant women and young children residing within five miles of the TMI facility. Over the two-week period, the percent of households that evacuated corresponded to 63%, 49%, and 32%, for the 0-5, 5-10, and 10-15 mile populations, respectively. In total, about 50,000 households, representing about 150,000 people, evacuated. Evacuation cost estimates were divided into two categories: (1) direct cost outlays and (2) loss of earned income. Direct cost outlays included the cost of travel, lodging, meals, and other incidental costs directly related to evacuation. Loss of earned income included either loss of wages or loss of business income for store owners. The median distance traveled by evacuees was 100 miles and the average household left the area for about four to five days during the two-week period (Flynn 1979).

The NRC estimated that the cost of evacuation was \$100 per household for direct cost outlays and \$100 per evacuee whose income was affected. The total cost was estimated at around \$20 million (Flynn 1979). The reason that the costs were relatively low was that fully two-thirds of the evacuated households stayed with relatives, 15% stayed with friends, and only 8% elected to stay at a hotel/motel. The apparent low estimate for lost earnings was not explained.

A major factor not included in the baseline estimates of evacuation costs was the economic impact of psychological stress. Psychological stress was one of the most widely studied aspects of the Three Mile Island crisis (Houts 1980(a), Houts 1980(b), Hu 1980, Houts 1981(a), Houts 1981(b), Houts 1984). Between 20 and 30% of the TMI population reportedly suffered from heightened levels of distress. Psychological distress was most acute during the period of evacuation and, for a considerable number of individuals, persisted for up to a year. Stress symptoms consisted of somatic and behavioral changes. Common symptoms included headache, digestive and eating disorders, abdominal pain, sweating spells, memory loss, impaired sleep,

irritability, inability to work, etc. (Hu 1980, Houts 1984). Associated with these symptoms, investigators reported an increased consumption of cigarettes, alcohol, sleeping pills, and tranquilizers. Personal factors influencing psychological stress included proximity to TMI; age, sex, and education of the household decision-maker; and the presence of children.

Psychological distress produces somatic and behavioral symptoms not too different from those of organic diseases. The economic value of psychological distress can be defined by the following three components:

- direct cost - medical costs incurred from the treatment of somatic and psychological symptoms
- indirect costs - loss of economic opportunity imposed by psychological distress
- psychological costs - a reduction in the quality of life precipitated by somatic or behavioral problems.

(This report's approach to assigning monetary values to these cost components is described in detail in Appendix D.)

No attempt was made to give monetary values to psychological distress and incorporate these values into the TMI economic impact analysis. Several studies, however, did assess the utilization of medical care following the Three Mile Island crisis (Hu 1980; Houts 1984). These studies assessed the utilization of medical care by means of: (1) Blue Cross-Blue Shield records of claims by primary care physicians in the vicinity of TMI; (2) utilization rates in family practices located near the facility; (3) interviews with persons living within five miles of TMI; and (4) responses to a questionnaire by primary care physicians practicing within 25 miles of TMI. Although all four study methods showed increased trends in utilization rates during the year following the crisis, a reliable estimate of direct medical costs attributable to psychological stress could not be extracted from the data.

CHAPTER 8

CONCLUSION

The principal purpose of this report was to provide a comprehensive analysis of the costs and benefits associated with the prophylactic use of KI by the general public in the event of a nuclear accident. The most currently available data were used to define the programmatic costs for stockpiling KI and the equivalent monetary values of thyroid health effects that are potentially avoidable when KI is administered. Dividing the stockpiling costs of KI by the monetary values of thyroid health effects yielded cost-benefit ratios that provide a limited basis for a policy decision.

Although these cost-benefit ratios are as credible and objective as current data allow, caution must be exercised in using these values in a policy decision. Existing uncertainties in reactor accident frequencies and dispersion modeling could easily reduce the cost-benefit ratios derived in Chapter 6 by two orders of magnitude or more.

Additionally, the derived cost-benefit ratios do not represent a total assessment of the cost-effectiveness of KI prophylaxis protective measures. The cost-effectiveness of KI prophylaxis must be assessed in the context of other protective measures.

APPENDIX A

SUMMARY FINDINGS OF THE CRCPD E-6 COMMITTEE'S SURVEY

Stimulated by new information relating to the Chernobyl experience and by the urging of the American Thyroid Association (ATA), the Federal Radiological Preparedness Coordinating Committee (FRPCC) requested that the Conference of Radiation Control Program Directors (CRCPD) E-6 Committee conduct a survey to assess the emergency plans of individual States with regard to KI. States with commercial nuclear power plants or whose border(s) is within a ten-mile range of a nuclear facility were sent a survey questionnaire. A facsimile of the questionnaire is provided in Addendum A-1. Specific information sought pertained to target populations and available quantities of KI for the ten-mile emergency protection zones (EPZ) for nuclear facilities.

A total of 32 States provided information regarding the use of KI for the ten-mile emergency planning plume exposure pathway zone(s). Data provided by States are summarized in Table A-1. Because the data were not consistent in format, some interpretation of the data was required for compilation. The following statements summarize the survey data:

- All States provide KI to off-site emergency workers.
- Of the 32 States, 21 have provisions to distribute KI to institutionalized persons within the ten-mile EPZ.
- Only three States have provisions to distribute KI to the general public residing in the ten-mile EPZ.
- Depending on anticipated size of the target population(s), which ranges from as few as 200 up to 50,000 persons, the size of KI stockpiles ranges from a few thousand tablets up to 700,000 tablets.
- Reflected in the size of target populations and stockpiles is the total number of EPZs in a State.
- The cumulative stockpile for all 32 States is estimated to be between 2.5 and 3 million tablets.

Based on the information presented in this report, which indicates that a target population out to 100 miles or greater may be exposed to thyroid doses in excess of intervention level(s), the combined stockpiles of all States represent less than four percent of what might be required to protect the general public from thyroid exposure in the event of a nuclear emergency.

**Table A-1
Current KI Stockpiles Maintained by States**

State	Answer to Question #1 ^a				Total No. of Tablets Stockpiled	Estimated No. of Persons Targeted for Distribution	Duration for KI Prophylaxis (Days)
	A	B	C	D			
AL	X		X		35,000	9,000	4
AR	X	X			28,000	4,000	7
AZ	X		X		5,600	2,000	2
CA	X	X			NI ^b	NI ^b	3
CT	X				14,000	1,000	14
DE	X	X			NI ^b	NI ^b	NI ^b
FL	X				53,200	7,600	7
GA	X				8,400	600	14
IL	X	X			196,000	14,000	14
IA	X	X			48,188	3,400	14
KS	X	X			5,600	800	7
LA	X				NI ^b	NI ^b	10
ME	X	X			NI ^b	NI ^b	14
MD	X	X			10,000	2,100	NI ^b
MA	X	X			16,100	1,150	14
MI	X	X			9,800	700	14
MS	X	X			14,000	1,000	14
MO	X	X			30,800	2,200	10
NE	X				1,400	200	7
NH	X	X			99,120	9,912	10
NY	X	X			11,200	1,120	7-10
NC	X	X			210,000	15,000	14
OH	X	X			165,000	11,757	10-14
OR	X	X			NI ^b	400	14
PA	X	X			700,000	50,000	14
SC	X	X			84,000	7,000	14
TN	X		X		425,000	26,800	14
TX	X	X			2,400	200	10-14
VA	X	X			39,200	2,800	14
WA	X				51,800	3,700	14
WV	X				6,000	600	10
WI	X				9,000	900	10

^a See Question #1 in attached Addendum

^b NI = Not Identified.

ADDENDUM A-1

CRCPD E-6 COMMITTEE QUESTIONNAIRE ON STOCKPILE AND DISTRIBUTION OF KI

In view of European experience following the Chernobyl incident in which several million doses of KI were distributed, and in response to renewed interest within the medical community, the Federal Emergency Management Agency (FEMA) is re-evaluating the need for federal stockpile of Potassium Iodide (KI) for distribution in the event of an inadvertent release of radioiodine from a nuclear power generating facility.

FEMA has requested that the CRCPD E-6 Committee on Emergency Response Planning survey state programs on this issue.

Regardless of whether you do or do not at this time plan to distribute KI to emergency workers, institutionalized persons and/or the general public, please respond to the following questions, adding any brief narrative which you feel is necessary to clarify your response. Unless your plans specify otherwise, for the purposes of this survey, the affected general public is assumed to be the resident and transient population within the Plume Exposure Pathway (approximately ten miles) emergency planning zone surrounding each commercial nuclear power generating facility. If parts of the ten-mile EPZ for a plant lie within two or more different states, answer only for that portion which is within your state.

In your answers, do not include utility employees or other persons for whom the utility would be responsible for providing KI.

1. What groups has your state targeted for possible distribution of KI?

- Off-site Emergency Workers
- Institutionalized Persons
- General Public
- No plans at this time to distribute KI

2. Do you (or the responsible agency) maintain a stockpile of KI for these groups?

3. How many tablets (or liquid daily doses) would you issue to each person?

4. How many courses (7 to 10 day supply for one individual) do you have on hand? (If you maintain separate supplies for multiple EPZs, please report the respective quantity for each EPZ.)

CRCPD E-6 Committee KI Questionnaire

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5. Including inventories already on hand, how many courses (7 to 10 day supply of KI for 1 individual) would you need to complete distribution in accordance with your plan? If your state includes part or all of the ten-mile EPZ for more than one plant, please answer this question for each EPZ.

6. If you anticipate a need for additional supplies, possibly from a federal stockpile, to what agency at what location should those supplemental supplies be delivered? (If your state is responsible for responding to more than one power plant, please specify a location and responsible agency for each fixed nuclear facility to which you might respond.)

7. Please provide the name and telephone number of a cognizant individual within your state from whom clarification and/or additional information could be obtained.

8. Additional details/information/comment (Identify item number referred to):

Please provide your answers to:

CRCPD E-6 Committee KI Survey
c/o Mr. Terry Devine
Conference of Radiation Control Program Directors, Inc.
205 Capitol Avenue
Frankfort, KY 40601

APPENDIX B

RECOMMENDATIONS BY THE WORLD HEALTH ORGANIZATION ON THE USE OF KI

The World Health Organization (WHO) and the Commission of the European Communities (CEC) organized a joint workshop in July of 1988 to assess current knowledge and to make recommendations for National contingency plans involving nuclear emergencies.

The workshop committee submitted recommendations, which were subsequently adopted as WHO guidelines, for iodine prophylaxis in behalf of the following population groups:

- pregnant women
- lactating mothers
- infants
- children and adolescents
- adults

Pregnant Women

Radioiodine uptake by the maternal thyroid may be elevated during pregnancy due to enhanced stimulation of the maternal thyroid by human chorionic gonadotrophin which reaches maximal levels in the first trimester. For this reason, protection of the maternal thyroid gland from radioiodine exposure is desirable. However, the potential fetal adverse health effects from radioiodine as well as KI must be carefully considered. These fetal effects vary over the period of pregnancy.

First Trimester. Although the placenta has been shown to freely transfer iodide (or radioiodide), the fetal thyroid is undeveloped and lacks the ability to concentrate iodine. The extent to which maternal thyroid hormone transfers across the placenta and serves as a surrogate source of thyroid hormone to the fetus is the subject of considerable debate. The significance of this uncertainty is that if there is fetal dependency on maternal thyroid hormones, care should be taken that maternal thyroid levels do not fall. The administration of KI to the mother for several days could result in temporary reduction of serum levels of the thyroid hormones T_4 and T_3 .

WHO Recommendations. Administration of stable iodine during the first trimester of pregnancy should be restricted to the minimum daily dosage and duration that still provides adequate maternal thyroid protection.

Second Trimester. During this time, the fetal thyroid is rapidly increasing in mass and has the ability to actively concentrate iodine. Due to its limited mass, the fetal thyroid dose is higher than that of its mother. Although fetal thyroid secretion of T_4 may begin at mid-gestation, fetal dependency on maternal T_4 for normal organogenesis inclusive of the brain may exist.

WHO Recommendations. If the predicted dose to the thyroid is likely to exceed the agreed intervention level, stable iodine should be given to pregnant women in the second trimester to protect both the fetal thyroid and the maternal thyroid. The duration of stable iodine prophylaxis in pregnant women should be limited to the minimum time frame that still provides adequate protection. Other countermeasures such as evacuation, and control of ingestion of contaminated foods/water are particularly important for this group.

Third Trimester. During this time of gestation, the fetal thyroid continues to concentrate iodine and secrete increasing amounts of the thyroid hormone. Up to this time the feedback control mechanism involving the pituitary thyroid stimulating hormone has not been fully developed, and the fetus has an enhanced vulnerability to thyroid overload by stable iodine (Wolff-Chaikoff effect). This transient iodine overload can result in primary hypothyroidism in utero, which may adversely affect organ and brain development.

WHO Recommendations. If the predicted dose to the thyroid is likely to exceed the agreed intervention level for KI, prophylaxis should be given to women in the third trimester to protect the fetal thyroid gland and to protect the maternal thyroid gland. The duration of stable iodine prophylaxis should be limited to the minimum that still provides adequate protection. The fetus will need to produce T_4 and T_3 at birth and is likely to be susceptible to the Wolff-Chaikoff effect. Therefore, fetal TSH and T_4 levels should be assessed at birth for neonates whose mothers were administered iodine prophylaxis in the third trimesters. Replacement therapy must be administered as needed.

Neonates (birth to 1 month). At birth there is a dramatic rise in TSH levels that is followed by a rise in T_4 and T_3 levels. During this time, the fraction of iodine taken from blood and concentrated by the thyroid (i.e., f_2' fraction) reaches values in excess of 90%. A neonatal exposure to radioiodine during this time leads to unusually high thyroid doses. However, the neonate is still vulnerable to the Wolff-Chaikoff effect from iodine overload. The long-term effects of transient thyroid depression are not established, and therefore monitoring of thyroid hormone levels in the neonate is advised.

WHO Recommendations. Stable iodine should be given to protect the neonatal thyroid. Thyroid hormone levels should be assessed following iodine prophylaxis. The dosage and duration of prophylaxis should be kept to the minimum level that still offers adequate protection, with other countermeasures such as evacuation and sheltering given high priority.

Lactating Mothers

Iodine is concentrated in breast milk and may become a source of both stable iodine and radioiodine for a nursing infant. If the mother is given stable iodine as well as the baby, the baby will receive stable iodine from two sources, which may increase the risk of iodine overload.

WHO Recommendations. Lactating mothers should be given stable iodine to protect the maternal thyroid but at minimal dosage and duration.

Infants, Children, Adolescents

Due to higher thyroid doses, increased thyroid sensitivity, and longer periods at risk than adults, the youngest members of the population are at highest risk and, therefore, are most likely to benefit from iodine prophylaxis. Adverse reactions to stable KI involving intrathyroidal and extrathyroidal effects are less likely than for adult populations.

WHO Recommendations. Stable iodine should be given to infants, children, and adolescents to protect the thyroid. Because of the low probability of adverse effects to stable iodine, a less restrictive policy may be adopted to include individuals in the far-field where thyroid doses may not necessarily exceed intervention levels. Stable iodine should be withheld from those individuals with known allergies to iodine or who have previously been treated to thyroid disorders.

Young Adults (18-45 years)

Neither the radiation risks nor the adverse risks to stable iodine are extraordinary for this group.

WHO Recommendations. Iodine prophylaxis is recommended for those individuals who may exceed intervention levels of thyroid exposure. Individuals with known thyroid disorders or allergies toward iodine should avoid the use of stable iodine.

Older Adults

With increasing age and diminishing years of life expectancy, the risk of thyroid cancer expression decreases. The incidence of thyroid diseases increases significantly with age, especially among women. Stable iodine can exacerbate or precipitate thyrotoxicosis among individuals treated for or with asymptomatic Graves' Disease or with autonomously functioning thyroid nodules. Among this susceptible group, iodine prophylaxis can be life-threatening, especially if recognition is delayed.

WHO Recommendations. Because the potential side effects of stable iodine are likely to be greatest in this age group, iodine prophylaxis is recommended only when intervention levels have a high probability of being exceeded. Emphasis must be placed on contraindications with instructions strongly discouraging KI use among individuals with known iodine allergies, known thyroid pathologies (i.e., goiters; autoimmune thyroid disease), hypocomplementemic vasculitis, and dermatitis herpetiformis.

The Applicability of WHO Guidelines for U.S. Population

When evaluating WHO Guidelines for U.S. populations, it is important to acknowledge the major difference in dietary intakes between the population of the United States and those of other countries. The average daily dietary intake of about 200 μg of iodide in the United States is considered high compared to that in other countries.

When iodine deficiency is present, the thyroid has a higher avidity for iodine (and, therefore, radioiodine) than the thyroid of a person with a normal or high iodine intake. In areas with low iodine intake, the amount of radioiodine accumulated in the thyroid can be expected to be up to as much as two to three times higher from an identical environmental exposure than in a population with normal or high iodine intake (Delange 1989). Stated somewhat differently, the prophylactic benefit of KI is higher for individuals with low dietary intake.

Along with its higher thyroid protection among persons with lower dietary intake of iodine, the potential side effects of KI are also more likely. This is because nodular goiter is more prevalent with low dietary intakes of iodine. Since some goitrous nodules are likely to be autonomous (i.e., function independently of thyroid-stimulating hormone (TSH)), this sudden increase in available iodine can facilitate the increased synthesis of thyroid hormone. Similarly, individuals with Graves' Disease whose condition is sub-clinical due to dietary restrictions of iodine, when given KI, would be subject to the full expression of the disease.

APPENDIX C

ADVERSE REACTIONS TO IODIDE AND ESTIMATION OF ADVERSE INCIDENCE RATE

The frequency of potential adverse reactions to iodide when taken orally in daily doses of 130 mg can be assumed to be very small based on extrapolation from documented data. Potassium iodide is a major ingredient in cough syrups and expectorants whose principal purpose is to liquify tenacious bronchial secretions associated with respiratory infections, allergic bronchitis, asthma, pulmonary emphysema, etc.

The Food and Drug Administration's Division of Epidemiology and Surveillance (DES) maintains a computerized data base of adverse drug reactions. Known as either the Adverse Reaction Reporting System (ARRS) or the Spontaneous Reporting System (SRS), the present data base contains over 400,000 reports that have been collected since 1969. The primary purpose of this data base is to serve as an early warning system for adverse reactions not detected during pre-market testing.

Approximately 90% of the reports in the SRS data base are submitted by drug manufacturers, who must, by law, report adverse events that become known to them. The remaining 10% of reports are received directly by DES from sources other than manufacturers (i.e., health professionals and consumers).

Adverse Reactions to KI

For the period of 1969 through July 1991, the SRS data base contained only 97 reports of suspected adverse reactions to KI. Summary data supplied by the FDA concerning these 97 cases are furnished as Addendum-1 in this appendix. Table C-1 characterizes these cases with respect to age and gender of the subjects and quantifies exposure. Individuals tended to be above the age of 40, with about twice as many males as females. The duration of therapy was skewed and bimodal, having a mean of 19 days and a standard deviation of 60 days. While most individuals were medicated for less than two weeks, there were few individuals whose therapy lasted months and up to one year. Although the FDA provided daily dosage information, the data could not be converted into milligram quantities of KI. An estimate of daily doses administered was derived from the recommended doses prescribed by pharmaceutical firms (see Table C-4). No adverse reactions were reported for children.

Table C-1. Adverse Reaction Profile to KI¹

Total # of Individuals	Route of Administ.	Gender			Avg. Age ±/SD	Duration of Therapy (days)	Daily Dose ² (mg)
		M	F	U			
97	PO	61	28	8	54 ± 16	19 ± 60	100 - >1,000

¹ Source: Addendum-1 of this appendix.

² See Table C-4.

Table C-2 identifies specific adverse reactions among these subjects and the frequency of their occurrence. With rare exceptions, the adverse reactions cited were not life-threatening and were quickly reversed upon discontinuation of medication. The sum of adverse reactions exceeds the number of individuals because some individuals reported more than one reaction. Of the 97 individuals, recovery was cited for 65 without medical intervention; for 31 individuals, the patient outcome was not addressed in the initial report received by the FDA and is, therefore, identified as "unknown;" in one instance, the adverse reaction was sufficiently severe to require hospitalization; and one death was reported. The adverse reactions cited in the case requiring hospitalization included fever, skin necrosis, eye pain, and petechia. For the fatality, the major adverse reaction identified in the report was limited to vesiculobullous rash.

Cause and effect interpretation from these data must be done with caution. The FDA issued the following caveats (personal communications):

1. "For any report, there is no certainty that the suspected drug caused the reaction. This is because physicians are encouraged to report all suspected adverse drug events, not just those that are known to have been caused by the drug. The event may have been related to an underlying disease for which the drug was given, to other drugs being taken concurrently, or may have occurred by chance at the time the suspected drug was taken."
2. "Accumulated case reports cannot be used to calculate incidence or estimates of drug risk. They must be carefully interpreted as reporting rates and not occurrences or incidence rates. Comparison of drug safety cannot be made from these data."

Table C-2. Suspected Adverse Reactions to KI Reported Since 1969

Adverse Reaction	No. of Occurrences	Definition/Description
ACNE	4	Pustular skin eruption.
ALLERGIC REACTION	1	Unspecified response which could range from a fever type symptom to severe asthma.
ANAPHYLACTOID REACT	1	Life-threatening allergic reaction usually manifested by severe spasm of the bronchi in the lung with associated like syndrome.
ANGIOEDEMA	3	Another form of allergic reaction manifested by swelling of the mucus membranes of the eyes, nose, mouth, pharynx, and occasionally the larynx. Also in its more diffuse form will cause diffuse soft tissue swelling throughout the body and is associated with giant hives.
ANTHRALGIA	1	Bone pain.
ASTHMA	1	Wheezing respiration due to bronchial restriction.
CONJUNCTIVITIS	4	Redness of the eye membrane.
COUGH INCREASED	1	Self-explanatory.
DERMATITIS, EXFOLIATIVE	1	Another form of toxic reaction to medication where the superficial layers of the skin become inflamed and desquamate.
DIARRHEA	1	Self-explanatory.
EDEMA FACE	2	Self-explanatory. Again a form of allergic reaction.
EOSINOPHILIA	2	A type of white blood cell which is increased in its numbers.
ERYTHEMA MULTIFORME	2	Another form of toxic skin reaction.
ERYTHEMA NODOSUM	1	A nodular form of inflammatory disease of the skin. Again, usually associated with toxic reaction to some medication.
FEVER	5	Self-explanatory.
GLOSSITIS	1	Swelling and inflammation of the tongue.
GOITER	2	An enlarged thyroid.
HEADACHE	1	Self-explanatory.
HEMATURIA	1	Blood in the urine.
HYPOTHYROIDISM	1	Lack of thyroxine hormone.
LYMPHADENOPATHY	1	Swelling of the lymph nodes, usually multiple.
NECROSIS OF SKIN	1	Again similar exfoliated dermatitis.
PAIN	1	Self-explanatory.
PAIN EYE	1	Self-explanatory

Table C-2. Suspected Adverse Reactions to KI Reported Since 1969 (Continued)

Adverse Reaction	No. of Occurrences	Definition/Description
PAROTID ENLARGEMENT	3	Self-explanatory. Parotid is the salivary gland just in front of the ear.
PETECHIA	1	Small hemorrhagic skin spots usually associated with toxic reaction to medication.
PRURITUS	3	Skin itch.
RASH	9	Non-specific term.
MACULOPAPULAR RASH	24	Multiple skin areas of punctate erythema with slight elevation.
PURPURIC RASH	1	Quite similar to petechia.
PUSTULAR RASH	2	Very similar to acne.
VESICULAR BULLOUS RASH	3	Superficial layers of the skin develop considerable inflammation with fluid accumulation causing bubble-like lesions.
REACTION UNEVALUATED	1	Self-explanatory.
SALIVARY GLAND ENLARGEMENT	11	Related to parotid enlargement which includes submandibular salivary glands.
SARCOIDOSIS	1	A granulomatous noninfectious disease of unknown etiology.
SERUM SICKNESS	1	A delayed type of allergic reaction to foreign protein. It can be life-threatening.
SIALADENITIS	4	Inflammation of the salivary glands.
SPUTUM, INCREASED	1	Self-explanatory.
STOMATITIS	1	Inflammation of the oral cavity; frequently associated with glossitis.
URTICARIA	7	Hives.
VASODILATATION	1	Dilatation of the small blood vessels.
VOMITING	1	Self-explanatory.
SALIVARY GLAND ENLARGEMENT	1	Self-explanatory.
IODISM		A morbid clinical condition characterized by salivary gland enlargement, cutaneous eruption, etc. induced by iodine.
LYMPHADENOPATHY		Previously described.
PHARYNGITIS		Inflammation of the pharynx.
PRURITIS		Previously described.
RASH		Previously described.
RASH MACULA PAPULAR		Previously described.
PHINITIS		Inflammation of the mucus membranes of the nose.
TASTE PERVERSION		Self-explanatory.

Nevertheless, the NCRP in 1977 (NCRP 1977) attempted to use FDA's SRS data to establish incidence rate estimates. At the time of the NCRP study, six pharmaceutical firms were identified as manufacturers of products containing KI. However, only two companies provided production data, which was only for 1975. By using the average annual number of adverse reactions reported between 1969 and 1975, and 1975 manufacturing data from only two out of six companies, a conservative adverse reaction rate of about 5×10^{-7} was estimated. To determine a baseline estimate of the potential adverse reaction incidence rate, it is necessary to correlate the number of adverse reactions for a fixed time frame to the total quantity of KI consumed.

In an attempt to update earlier data and refine the adverse reaction incidence value, five pharmaceutical firms were identified in the Physicians' Desk Reference as manufacturers of drugs containing KI (a sixth company producing SSKI was not included). The companies were contacted and asked to provide information regarding production quantities for their KI-containing products. Without exception, all companies stated that production information dating back to 1969 was not available. Data, however, were available for the most recent five years. Company representatives also warned that recent production data could not be used to extrapolate production quantities back to 1969. There was emphatic consensus among firms that production quantities of KI-containing drugs have been drastically reduced over the past two decades. This trend is strongly supported by the frequency distribution of the number of adverse drug reactions reported to the FDA between 1969 and 1991 (Table C-3).

Table C-3. Number of Adverse Reactions to KI by Year

Year													
'69	'70	'71	'72	'73	'74	'75	'76-79	'80	'81-83	'84	'85	'86-90	'91
7	37	23	9	12	2	2	none	1	none	1	1	none	1

The five companies provided the product information and production estimates given in Table C-4.

Table C-4. Product Profile and Production Quantity for 1986-1990

Pharm. Firm	Product Description	KI Content or Concentration	Recommended Daily Dose (daily KI)	Quantity Manufactured	Equivalent Doses (130 mg ea.)
A	liquid	324 mg/5 ml	20-60 ml (1,300-1,900 mg)	830,000 oz*	12,410,000*
B	tablet	320 mg/tablet	3-4 tablets (960-1,280 mg)	15,106,000 tablets	37,648,800
C	liquid	75 mg/5 ml	20-30 ml (300-450 mg)	4,662,544 oz	16,139,575
D	tablets	195 mg/tablet	3-4 tablets (585-780 mg)	2,000,000 tablets*	3,000,000
E	liquid	130 mg/15 ml	30-45 ml (260-390 mg)	1,264,280 oz	2,528,560

* Values represent best estimates by pharmaceutical firms.

For the most recent five-year period, pharmaceutical firms produced oral medication containing approximately 10,000 kilograms of KI. To convert quantities manufactured to quantities consumed, it is necessary to estimate what percentage of the manufactured quantities is actually sold to wholesalers/retailers, the quantity sold by retailers to consumers, and the percentage actually consumed. In response to these questions, pharmaceutical firms stated that essentially 100% of their manufactured products are sold to wholesalers and retailers, with no significant quantities discarded for reasons of shelf-life expiration, etc. When asked about the potential quantities consumed, representatives of pharmaceutical firms speculated that an estimate of 50% may be appropriate for the following reasons: the symptoms of coughs, colds, and allergies are frequently of shorter duration than the quantity prescribed or purchased, and the use of medication is frequently confined to that period of time when individuals feel the need for medication. This is especially true for KI-containing medication that also contains codeine and barbiturates. For the most recent five-year period, therefore, it will be estimated that about 5,000 kg of KI was consumed, which corresponds to 38 million equivalent doses of 130 mg each. During this same five-year period, only a single adverse reaction to KI was reported (see Addendum-1: Report Accession No. 91040801600011). This adverse reaction was classified as "unevaluable" and did not involve a biological reaction. In fact, the complaint was confined to the physical discoloration of the medication. In summary, for the most current data involving 38 million equivalent doses of KI consumed, there were no reports of adverse reactions.

While the absence of adverse reactions for the most recent five-year period does not imply a zero risk, the data do suggest that the previous risk coefficient of 5×10^{-7} as estimated by the NCRP (NCRP 1977) is conservative. If the NCRP's risk coefficient were applied to the consumption of about 38 million equivalent doses, a total of 19 adverse reactions would be expected.

The current data support an adverse reaction incidence rate value of 1×10^{-7} or less per unit dose of 130 mg of KI.

Adverse Reactions to Iodinated Contrast Media

A second source for deriving potential risk estimates involves iodinated x-ray contrast media and their occasionally toxic side effects that are presumed to be caused in part by their high iodide content. For a single diagnostic procedure, the dose of organically bound iodide may involve quantities of several grams. Adverse reactions to iodinated contrast media are usually of mild to moderate severity. About 95% of these reactions include aches and pain, stiffness, nausea, and vomiting. These reactions, usually occurring 1 to 10 hours after the injection, last for a few hours and usually disappear within 24 hours. Severe life-threatening anaphylactoid reactions, mostly of cardiovascular origin, have been observed. Cardiovascular complications include arrhythmias (including PVCs and PACs), angina, hypotension, and cardiac arrest.

Studies assessing adverse reaction incidence rates are fragmented. Frequently, the size, selection criteria of study subjects, and the type of reported adverse reaction are of limited scope. The following provides a brief summary.

- In one of the earliest studies involving iodinated contrast media, the unfavorable sequelae and deaths were assessed for a total of 662,000 urographic examinations (Pendergrass 1942). A total of 26 deaths was reported of which eight were attributed to the medical condition under investigation. If the remaining 18 deaths were exclusively the consequence of iodine reactions, the fatal incidence rate would be 27 per 10^6 exposures (one fatality per approximately 37,000 examinations) involving doses of iodine between 2.5 and 16.8 grams per examination.
- This incidence rate appears consistent with the data of Tucker and diBago (Tucker 1956) who observed no severe reactions/fatalities among 2,000 patients who had received either Neo-iopax with 5.2 grams of iodine per examination or Urokon with 4.9 grams of iodine.
- In a study of 196 Japanese hospitals involving 77,040 injections of ionic and 42,581 injections of non-ionic iodinated contrast media, one fatality and 38 severe reactions were reported. Severe reactions were defined as those requiring hospitalization of the patient. The overall incidence of severe reactions is 34 per 10^5 with a fatality incidence of 1.7×10^{-5} (Katayama 1963).

Because iodine/iodide is considered a significant risk to the fetus, iodinated pharmaceuticals and diagnostic x-ray media are avoided during pregnancy. No reliable medical data, therefore, exist concerning fetal risks.

- A study of 3,808 hospital patients investigated for various thyroid disorders showed that the frequency of hyperthyroidism increased from 3.7% to 5.4% when patients were segregated on the basis of exposure (within the previous 12 months) to iodinated x-ray contrast medium (Oberhausen 1988).
- In controlled clinical trials involving 1,270 patients administered the contrast medium OMNIPAQUE, one fatality occurred. A cause and effect relationship between this death and iohexal, the pharmacological ingredient of OMNIPAQUE, has not been established (PDR 1991).

To obtain more current and comprehensive data, information from the Food and Drug Administration's Adverse Reactions Reporting System was requested. Adverse reactions to iodide-containing diagnostic contrast media have been reported to the FDA since 1969. Between 1969 and August 1991, 5,131 cases of adverse reactions were reported in which iodinated contrast media were suspected as the causative agent. The majority of adverse reactions involved extrathyroidal effects that were transient, mild to moderate in severity, and required no medical intervention for patient recovery. In a few cases, adverse reactions were severe and included cardiac arrest, myocardial infarction, anaphylactoid reactions, shock, and death. Table C-5 identifies the most severe adverse reactions in the context of the total number of reactions reported.

Table C-5. Adverse Reactions to Iodinated Contrast Media Reported to the FDA Between 1969 and August 1991

Iodinated Contrast Media*	Anaphylactoid Reactions	Cardiac Arrest & Myoc. Infarct.	Shock	Death	Total Cases of Adverse Reactions
Domestic	157	122	88	26	4,933
Foreign	6	8	9	4	198
TOTAL	163	130	97	30	5,131

* Includes all manufacturers of contrast media approved by the FDA.

To convert the FDA's ARRS data to adverse reaction incidence rate data requires knowledge of the total quantity of diagnostic contrast media used for the corresponding time frame. The quantity of diagnostic contrast media that had been used was estimated based on (1) the total quantity manufactured, (2) the total number of diagnostic procedures performed, and (3) the total reimbursements made by Federal and private insurers for procedures involving iodinated contrast media. Statistical data were sought from pharmaceutical firms, the HFCA, FDA, other governmental agencies, and private organizations (e.g., American Medical Association; Commission on Professional and Hospital Activities, IMS America). In all instances, data were either incomplete, lacked the necessary specificity for reliable quantification, or were considered confidential.

The inability to convert FDA's ARRS data to an adverse reaction incidence rate for iodinated contrast media, however, is not significant for this report. Any extrapolation of adverse reaction incidence data involving iodinated contrast media to potassium iodide would likely have been considered inappropriate for the following reasons:

- The one to five grams of iodine per diagnostic procedure involving iodinated contrast media represents quantities that are 10 to 50 times higher than the recommended 100 mg of iodide contained in a 130 mg tablet of KI.
- Iodinated contrast media, in most instances, exist in organically bound form. The iodinated protein globulin is water soluble and remains non-dissociated (nonionic) in the bloodstream with little or no metabolism, deiodination, or biotransformation prior to rapid urinary excretion. Serum levels of free iodide for thyroid metabolism are, therefore, either unknown or assumed minimal.
- The role of the organic component in extrathyroidal hypersensitivity reactions is uncertain but must be suspected.
- Unlike KI that is administered orally, iodinated contrast media are infused intravascularly or intrathecally.
- The underlying medical condition warranting the diagnostic procedure involving iodinated contrast media must be viewed as a confounding variable with respect to the etiology of the reported adverse reactions.

ADDENDUM C

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE

REPORT SOURCE	COSTART	TOTAL OCCURRENCES
DOMESTIC	ACNE	4
DOMESTIC	ALLERG REACT	1
DOMESTIC	ANAPHYL	1
DOMESTIC	ANGIOEDEMA	3
DOMESTIC	ARTHRALGIA	1
DOMESTIC	ASTHMA	1
DOMESTIC	CONJUNCTIVITIS	4
DOMESTIC	COUGH INC	1
DOMESTIC	DERM EXFOL	1
DOMESTIC	DIARRHEA	1
DOMESTIC	EDEMA FACE	2
DOMESTIC	EOSINOPHILIA	2
DOMESTIC	ERYTHEMA MULT	2
DOMESTIC	ERYTHEMA NOD	1
DOMESTIC	FEVER	5
DOMESTIC	GLOSSITIS	1
DOMESTIC	GOITER	1
DOMESTIC	HEADACHE	2
DOMESTIC	HEMATURIA	1
DOMESTIC	HYPOTHYR	1
DOMESTIC	LYMPHADENO	1
DOMESTIC	NECRO SKIN	1
DOMESTIC	PAIN	1
DOMESTIC	PAIN EYE	2
DOMESTIC	PAROTID ENLARGE	3
DOMESTIC	PETECHIA	3
DOMESTIC	PRURITUS	3
DOMESTIC	RASH	9
DOMESTIC	RASH MAC PAP	24
DOMESTIC	RASH PURPUR	1
DOMESTIC	RASH PUST	2
DOMESTIC	RASH VESIC BULL	3
DOMESTIC	REACT UNEVAL	1
DOMESTIC	SALIV GLAND ENLARGE	11
DOMESTIC	SARCOIDOSIS	1
DOMESTIC	SERUM SICK	1

* These data sheets were provided by the FDA's Division of Drug Experience under the Freedom of Information Act.

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE	COSTART	TOTAL OCCURRENCES
REPORT SOURCE		
DOMESTIC	SIALADENITIS	4
DOMESTIC	SPUTUM INC	1
DOMESTIC	STOMATITIS	1
DOMESTIC	URTICARIA	7
DOMESTIC	VASODILAT	1
DOMESTIC	VOMIT	1
FOREIGN	SALIV GLAND ENLARGE	1
DOMESTIC		96
FOREIGN		1
THE GRAND TOTAL IS		97

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL DRUGS

ALL REACTIONS

MESSAGE

6911011101961	06000741	060.000	M	S	PO		057	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
PAROTID ENLARGE RASH MAC PAP										
69110110500601	00001138	005.000	CC	S	PO	00002	048	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH MAC PAP										
69122008212001	00001642			S			063	F	DOMESTIC	RECOVER
POTASSIUM IODIDE PHENOBARBITAL										
RASH MAC PAP										
69100400600101	00001884	030.000	M	S	PO	00005	053	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH MAC PAP										
70010108800201	00001992	020.000	M	S	PO	00005	041	F	DOMESTIC	RECOVER
POTASSIUM IODIDE										
FEVER										
70020105503901	00002770	004.000	CC	S	PO	00001	072	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE										
ANGIOEDEMA										
7001011102201	00004397	060.000	M	S	PO	00180	075	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE										
ACNE										
69010115700501	00004556	040.000	M	S	PO	00002	053	M	DOMESTIC	RECOVER
POTASSIUM IODIDE PHENOBARBITAL										
RASH MAC PAP										

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

ACCESSION NUMBER	POTASSIUM IODIDE CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
ALL DRUGS										
ALL REACTIONS										
MESSAGE										
7001011101101	00004579	040.000	M	S	P0		056	M	DOMESTIC	RECOVER
	POTASSIUM IODIDE									
70030108100201	00005053	040.000	M	S	P0	00003	047	M	DOMESTIC	RECOVER
	POTASSIUM IODIDE									
	RASH MAC PAP									
70030108300701	00006070			S	P0	00002	075	F	DOMESTIC	UNKNOWN
	POTASSIUM IODIDE									
	GANTRISIN POTASSIUM IODIDE									
70010116200101	00006307	030.000	M	S	P0	00014	064	M	DOMESTIC	RECOVER
	POTASSIUM IODIDE									
	FEVER									
70040111100201	00006489	045.000	M	S	P0	00021	055	M	DOMESTIC	RECOVER
	POTASSIUM IODIDE									
	RASH									
70040108300701	00006739	030.000	M	S	P0	00042	074	M	DOMESTIC	UNKNOWN
	POTASSIUM IODIDE									
	RASH MAC PAP									
70050401500901	00007829			S				M	DOMESTIC	RECOVER
	POTASSIUM IODIDE									
	SALIV GLAND ENLARGE									
70050116200301	00008616	040.000	M	S	P0	00001		M	DOMESTIC	RECOVER
	POTASSIUM IODIDE									
	EOSINOPHILIA									
	PENICILLIN G PROCAINE									

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL DRUGS

ALL REACTIONS

MESSAGE

70010106400301	00009970	020.000	ML	S	PO	00090	060	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
HYPOTHYR										
70060111102401	00011483	040.000	M	S	PO	00001	061	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
CONJUNCTIVITIS										
70060105001401	00012169	030.000	M	S	PO	00004	054	M.	DOMESTIC	RECOVER
POTASSIUM IODIDE LASIX										
RASH MAC PAP										
70050108800101	00012657	040.000	M	S	PO	00001	023	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
SALIV GLAND ENLARGE										
70070203200301	00012925	030.000	M	S	PO	00044	065	M	DOMESTIC	RECOVER
POTASSIUM IODIDE EPHEDRINE										
PRURITUS										
70070201100101	00012926			S	PO	00017	031	F	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH										
70070105000701	00013798	020.000	M	S	PO	00004	062	M	DOMESTIC	RECOVER
PENICILLIN G PROCAINE POTASSIUM IODIDE STREPTOMYCIN										
RASH PURPUR										
70080119000301	00014487	300.000	MG	S	PO	00007	170	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH MAC PAP										

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE										
ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
ALL DRUGS										
ALL REACTIONS										
MESSAGE										
70100119400101	00016501	030.000	M	S	S	00001	039	F	DOMESTIC	RECOVER
POTASSIUM IODIDE										
70080116800401	00016801	030.000	MG	S	P0	00003	040	M	DOMESTIC	RECOVER
PRURITUS RASH										
POTASSIUM IODIDE										
70080400400201	00017171	030.000	M	S	P0	00002	036	M	DOMESTIC	RECOVER
RASH										
POTASSIUM IODIDE										
70110116800401	00017484	030.000	M	S	P0	00002	023	F	DOMESTIC	RECOVER
PAROTID ENLARGE										
POTASSIUM IODIDE										
70110116800801	00017486	030.000	M	S	P0	00004	049	M	DOMESTIC	RECOVER
SALIV GLAND ENLARGE										
POTASSIUM IODIDE										
70100202000701	00017489	040.000	M	S	P0	00001	049	M	DOMESTIC	RECOVER
SIALADENITIS										
POTASSIUM IODIDE										
70120104504601	00017864			S	P0	00014		F	DOMESTIC	UNKNOWN
HEADACHE VASODILAT										
POTASSIUM IODIDE										
70090105001701	00017874			S	P0		059	M	DOMESTIC	UNKNOWN
URTICARIA										
POTASSIUM IODIDE										
RASH MAC PAP										

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL DRUGS

ALL REACTIONS

MESSAGE

70090108301201	00017957	015.000	MG	S	PO	00005	068	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE										
70100105002501	00018292	030.000	M	S	PO	00004	060	M	DOMESTIC	UNKNOWN
SIALADENITIS										
70120116200301	00018304	060.000	MG	S	PO	00004	061	F	DOMESTIC	RECOVER
RASH PUST										
70090115301201	00018425	004.000	TB	S	PO	00002	069	F	DOMESTIC	UNKNOWN
RASH MAC PAP										
70120106901501	00018564	021.000	M	S	PO	00004		U	DOMESTIC	UNKNOWN
ERYTHEMA MULT HEMATURIA										
70120108300101	00018614	040.000	M	S	PO	00012	045	M	DOMESTIC	UNKNOWN
RASH										
70080119700301	00019532	010.000	M	S	PO	00001	036	F	DOMESTIC	UNKNOWN
RASH MAC PAP RASH VESIC BULL										
71010108100401	00020479	020.000	CC	S	PO	00002	071	M	DOMESTIC	RECOVER
ANAPHYL										
PENICILLIN POTASSIUM IODIDE GENTAMICIN										
RASH MAC PAP										

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE		CONTROL NUMBER	DAILY DOSE	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME

ALL DRUGS										

ALL REACTIONS										

MESSAGE										

71010105001001	00020683	POTASSIUM IODIDE	030.000	M	S	PO	00365	M	DOMESTIC	RECOVER
		RASH MAC PAP								
71010108300201	00021032	POTASSIUM IODIDE	040.000	M	S	PO	00008	M	DOMESTIC	UNKNOWN
		RASH								
71010111104601	00021105	POTASSIUM IODIDE	030.000	M	S	PO	00003	F	DOMESTIC	RECOVER
		URTICARIA								
71010112600401	00021454	POTASSIUM IODIDE	020.000	M	S	PO	00029	F	DOMESTIC	RECOVER
		URTICARIA								
71030115300301	00022830	KEFLIN AMPICILLIN KANAMYCIN SULFATE POTASSIUM IODIDE	020.000	M	S	PO	00015	M	DOMESTIC	UNKNOWN
		RASH MAC PAP								
71030107500701	00022922	POTASSIUM IODIDE	030.000	M	S	PO	00002	M	DOMESTIC	RECOVER
		ACNE								
71040116801001	00023451	POTASSIUM IODIDE	030.000	M	S	PO	00003	M	DOMESTIC	RECOVER
		RASH								
71040107501201	00023615	POTASSIUM IODIDE	030.000	M	S	PO	00002	F	DOMESTIC	UNKNOWN
		ERYTHEMA NOD								

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
71040107502901	00023776	017.000	CC	S	PO	00003	048	M	DOMESTIC	RECOVER
71040107505201	00023905	030.000	M	S	PO	00029	054	M	DOMESTIC	RECOVER
70100108100401	00024245	030.000	M	S	PO	00009	074	F	DOMESTIC	RECOVER
69020117100101	00024888	032.000	M	S	NAS	00008	035	M	DOMESTIC	RECOVER
71050111101601	00025006	040.000	M	S	PO	00014	082	M	DOMESTIC	RECOVER
69020111102601	00025162	030.000	M	S	PO	00015	055	M	DOMESTIC	RECOVER
70100202700301	00025290	010.000	M	S	PO	00040	041	F	DOMESTIC	RECOVER
71060105000701	00025553	030.000	M	S	PO					RECOVER

ALL DRUGS

ALL REACTIONS

MESSAGE

71040107502901 00023776
 POTASSIUM IODIDE
 LYMPHADENO

71040107505201 00023905
 POTASSIUM IODIDE
 SIALADENITIS

70100108100401 00024245
 POTASSIUM IODIDE
 SERUM SICK

69020117100101 00024888
 AMPICILLIN POTASSIUM IODIDE DILANTIN
 RASH MAC PAP

71050111101601 00025006
 POTASSIUM IODIDE CODEINE CHLORAL HYDRATE
 FEVER URTICARIA

69020111102601 00025162
 POTASSIUM IODIDE KANAMYCIN SULFATE
 RASH MAC PAP

70100202700301 00025290
 PENICILLIN V POTASSIUM IODIDE
 RASH MAC PAP

71060105000701 00025553
 POTASSIUM IODIDE
 FEVER

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL DRUGS

ALL REACTIONS

MESSAGE

71060107502601	00025908	030.000	M	S	P0	00001	019	F	DOMESTIC	RECOVER
POTASSIUM IODIDE										
SIALADENITIS										
71060116800301	00025998	030.000	M	S	P0	00005	081	M	DOMESTIC	RECOVER
POTASSIUM IODIDE AMPICILLIN										
DIARRHEA GLOSSITIS STOMATITIS										
71070304400501	00027327	040.000	M	S	P0	00009	051	F	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH										
70100105500301	00030547	040.000	MG	S	P0	00004	067	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE										
ASTHMA										
71090107500401	00032998	030.000	M	S	P0	00003	044	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH PUST										
71090401500901	00033606			S	P0	00001		M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH MAC PAP										
71101000100201	00034505	030.000	M	S	P0		055	F	DOMESTIC	UNKNOWN
POTASSIUM IODIDE										
SARCOIDOSIS										
71110107507801	00035374	015.000	M	S	P0	00002	056	F	DOMESTIC	RECOVER
POTASSIUM IODIDE										
ANGIOEDEMA PAROTID ENLARGE										

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
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POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL DRUGS

ALL REACTIONS

MESSAGE

71120109501101	00035641	030.000	M	S	PO	00001	057	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH MAC PAP										
71120104502601	00035643	040.000	M	S	PO	00002	069	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
RASH MAC PAP										
72040107501701	00038235	040.000	M	S	PO	00006	023	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
ACNE										
71070106505601	00038469	040.000	M	S	PO	00003	084	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE										
SALIV GLAND ENLARGE										
72020401503301	00040063			S				M	DOMESTIC	RECOVER -
POTASSIUM IODIDE										
SALIV GLAND ENLARGE										
72060107502001	00040658	045.000	M	S	PO	00031	074	F	DOMESTIC	RECOVER
POTASSIUM IODIDE										
DERM EXFOL EOSINOPHILIA										
72070401501601	00042159	010.000	M	S				U	DOMESTIC	RECOVER
POTASSIUM IODIDE										
EDEMA FACE SALIV GLAND ENLARGE										
72100400600101	00044623	010.000	M	S	PO	00001	065	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
SALIV GLAND ENLARGE										

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE										
ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG ADM.	ROUTE	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
ALL DRUGS										
ALL REACTIONS										
MESSAGE										
72110107500101	00045546	052.000	M	S	PO		019	F	DOMESTIC	RECOVER
POTASSIUM IODIDE QUADRINAL GOITER										
72120107503101	00045906	030.000	M	S	PO	00002	055	M	DOMESTIC	RECOVER
POTASSIUM IODIDE										
72120107501701	00045934	060.000	M	S	PO	00004	060	M	DOMESTIC	DIED
URTICARIA										
72120107504101	00045959	001.000	GM	S	PO	00004	055	F	DOMESTIC	UNKNOWN
RASH VESIC BULL POTASSIUM IODIDE										
73010202001901	00046198	002.000	GM	S	PO	00005	061	M	DOMESTIC	RECOVER
URTICARIA										
73010202002001	00046251	030.000	M	S	PO	00001	049	M	DOMESTIC	RECOVER
POTASSIUM IODIDE CONJUNCTIVITIS EDEMA FACE										
73020109501601	00047266	020.000	M	S	PO	00007		F	DOMESTIC	UNKNOWN
SALIV. GLAND ENLARGE ERYTHEMA MULT										
73041000204701	00049311	015.000	M	S	PO	00002		U	DOMESTIC	UNKNOWN
POTASSIUM IODIDE TEDRAL SALIV GLAND ENLARGE										

FDA SPONTANEOUS REPORTING SYSTEM
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POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS	SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL DRUGS

ALL REACTIONS

MESSAGE

73040116001401	00049621	500.000	MG		S	PO	00001	083	F	DOMESTIC	RECOVER
- POTASSIUM IODIDE											
ALLERG REACT											
73040116001601	00049810	500.000	MG		S	PO	00001	019	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE											
SALIV GLAND ENLARGE											
73050202201801	00050248	010.000	M		S	PO	00001	060	M	DOMESTIC	RECOVER
POTASSIUM IODIDE											
ARTHRALGIA PAIN											
73050107501801	00053931	040.000	M		S	PO	00004	053	M.	DOMESTIC	RECOVER
POTASSIUM IODIDE											
RASH VESIC BULL											
73061000207101	00054676	060.000	M		S	PO			U	DOMESTIC	UNKNOWN
POTASSIUM IODIDE QUIBRON SUMYCIN HCL											
SALIV GLAND ENLARGE											
73110305000101	00056028	150.000	MG		S	PO	00014	037	F	FOREIGN	RECOVER
POTASSIUM IODIDE											
SALIV GLAND ENLARGE											
73110107502901	00056258	040.000	M		S	PO	00365	023	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE											
ACNE											
73120201000101	00057454	030.000	M		S	PO	00003	074	M	DOMESTIC	UNKNOWN
POTASSIUM IODIDE POLYCYLLIN AMINOPHYLLINE											
PRURITUS RASH MAC PAP											

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
 CANNOT BE ESTABLISHED WITH CERTAINTY IN ALL CASES

POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS SUSPECT DRUG ADM.	ROUTE	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL DRUGS

ALL REACTIONS

MESSAGE

74041000200901	00060089								UNKNOWN
AARANE MARAX POTASSIUM IODIDE									
COUGH INC SPUTUM INC									
74120707100503	00072041								UNKNOWN
POTASSIUM IODIDE AARANE									
GOTTER									
75040301700301	00072618	030.000	M	S	PO	00004	046	M	RECOVER
POTASSIUM IODIDE									
RASH MAC PAP									
75060107506401	00075045	010.000	M	S	PO	00003	052	F	RECOVER
POTASSIUM IODIDE									
VOMIT									
80011100100201	00107326								UNKNOWN
POTASSIUM IODIDE ORAGRAFIN CALCIUM									
CONJUNCTIVITIS									
HERPES-LIKE ERUPTIONS AND DRAINAGE FROM EYES.									
84080801800011	00189743	003.000	M	S	OPH	00009	060	M	RECOVER
POTASSIUM IODIDE ASPIRIN									
CONJUNCTIVITIS PAIN EYE URTICARIA									
EXTEMPORAMENOUSLY COMPUDED PRESCRIPTION FOR USE IN RETAIDING THE GROWTH OF CATARACTS.									
85031100100161	00332693								HOSPITAL
POTASSIUM IODIDE PREMARIN									
FEVER NECRO SKIN PAIN EYE PETECHIA									
YX OF ALLERGIES TO STREPTOMYCIN, CHLORDIAZEPOXIDE; OCCUPATION:NURS'S AID.									
91040801600011	00736896								UNKNOWN
POTASSIUM IODIDE									
REACT UNEVAL									

POTASSIUM IODIDE IS AN EXPECTORANT AND IS NOT USED AS A POTASSIUM SUPPLEMENT AS STATED IN THE REPORT. THE COMPLAIN DISCOLORATION OF THE PRODUCT AND IT IS NOT AN ADR.

FDA SPONTANEOUS REPORTING SYSTEM
 CAUSE-EFFECT RELATIONSHIP BETWEEN EACH DRUG AND REACTION
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POTASSIUM IODIDE

ACCESSION NUMBER	CONTROL NUMBER	DAILY DOSE	UNITS SUSPECT DRUG	ROUTE ADM.	DURATION THERP.	AGE	SEX	REPORT SOURCE	PATIENT OUTCOME
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ALL-DRUGS

ALL REACTIONS

MESSAGE

7912100010000 70009047
 POTASSIUM IODIDE
 RASH

S 064 M DOMESTIC UNKNOWN

APPENDIX D

COST-BENEFIT ANALYSIS

Introduction

The rapid proliferation of commercial nuclear power in the 1970's gave rise to increasing concerns among policy makers to control radiation exposure to the worker and the general public. Policy decisions relating to radiation protection standards had to balance the benefits of exposure reduction to the economic impacts of protective measures. As a rule, whenever radiation exposure can be controlled by a protective measure, its endorsement by policy makers is linked to a favorable cost-benefit ratio. A major difficulty that is frequently encountered, however, is that the cost-benefit requires value judgements for which there are few points of reference, and on which administrative and political authorities must, nevertheless, take a stand. In 1972, Sagan (Sagan 1972) assessed the human cost of nuclear power by establishing a monetary link between radiation exposure and the primary health consequence of cancer. Applying the 1972 BEIR Committee's risk coefficient of 10^{-4} fatal cancers per person-rem to an assigned value of life at \$300,000, he established the monetary equivalence of \$30 per person-rem.

Over the years, cost-benefit analyses have adopted this or other simplistic models in which radiation exposure is directly converted to monetary terms. While this model approach may be appropriate for some applications, it is grossly inadequate for others. For example, the previously cited 1972 figure of \$300,000 would yield a current value of about \$1 million for a human life. This value may be considered appropriate since it is well within the range of values currently used by Federal agencies as discussed below.

The limitation of this model is demonstrated, however, when it is applied to complex situations such as the 1979 accident at the Three Mile Island Nuclear Station. Exposure to the general public was estimated at 3,300 person-rem (Behling 1986). At \$30 per person-rem, the total economic impact to the general public at the time of the accident would have been estimated to be between \$100,000 and \$200,000. For the complex condition of a major accident, the need for more sophisticated models is obvious.

The first step in the conduct of an impact-value analysis is the identification of pertinent factors that constitute the cost and the benefit. Included are subjective factors that must assess logistical/practical problems, public perceptions, etc. The second and more difficult requirement is the coherent quantification of all factors, inasmuch as these are not normally expressed in commensurate terms. When cost-benefit parameters are expressed in their usual units, a highly subjective approach is required at the final stage of decision making. A cost-benefit analysis, in which all parameters are expressed in monetary units, can support a more objective and defensible decision.

The quantification of cost for the protective measure can be made by the conventional method of assigning monetary values to materials, labor, and other resources needed. In special circumstances, however, the cost of providing a protective measure must also incorporate a term that represents the potential harm associated with the protective measure itself. For potassium iodide prophylaxis, the cost of public protection must consider the potential adverse reactions to KI that some individuals may experience (see Appendix C).

The assignment of monetary values to avoidable radiation health effects is less standardized and of considerable complexity. This appendix provides a comprehensive cost-benefit analysis that compares the programmatic cost of providing KI to the public to the avoidance of costs associated with radioiodine induced thyroid effects. In order to minimize the need for a subjective decision, all major elements that define the cost or the benefit of KI prophylaxis are expressed in terms of their dollar value.

The Economic Cost of KI Prophylaxis

Critical to a discussion of cost is the method by which KI is made available to the general public. The two principal options include stockpiling and predistribution and any policy decision must address the logistical and economic aspects for either option. Logistical considerations are governed by (1) the potentially short time interval between the initiating events of a serious reactor accident and atmospheric releases of radioiodines and (2) the need to administer KI prior to plume exposure for optimum thyroid protection. The timeliness of KI availability is most critical to persons living in close proximity to a nuclear facility where potential plume exposures are maximal and plume travel times are small.

In spite of the apparent advantage of timeliness for the predistribution option, there are limitations as well as disadvantages that include the following:

- Accessibility - KI predistributed to households (and stored at the residence) may not be readily available during times when residents are at work, school, etc.
- Availability - At any point in time, there are transients as well as new residents to whom KI was not provided.
- Loss or misplacement - Based on a five-year shelf-life/replacement period, there is a significant probability that tablets will be lost or misplaced.
- Improper storage - Improper storage may adversely affect its shelf-life and potency.
- Misuse and accidental administration - Like any pharmaceutical kept by a household, there is a potential for misuse and/or accidental administration.
- Improper disposal - For expired tablets, there is a loss of control for proper disposal.

Most of the disadvantages associated with predistribution are either eliminated or minimized for the stockpiling option. A program can be developed under the direction of a State's emergency management staff that provides for the necessary controls and oversight of stockpiles. Thus, the advantages for the stockpiling option include proper storage, controlled access to stockpiles, assurance of adequate replacement and proper disposal of expired capsules.

With a properly trained emergency staff and an informed public, potential problems associated with a timely distribution of KI can be minimized. Timely distribution requires an adequate number of strategically located stockpiles within the community. Suitable locations would include police stations, fire houses, schools, community centers, hospitals and major health care centers, from which an efficient localized door-to-door distribution could be conducted or where residents themselves could procure the needed KI.

Beyond logistical and practical issues, a major factor that must be considered in a policy decision that selects stockpiling, predistribution, or a combination of these two options is cost.

A unique aspect of the stockpile option is that it is essentially transparent to the public, and the cost of distribution to residents only becomes a reality in the unlikely event of a major nuclear emergency. Thus, for the stockpile option, the principal cost is the initial purchase of KI and its periodic replacement from the two FDA approved sources: Carter Wallace and ANBEX.

- Carter-Wallace - At the current purchase price of \$75.00/carton, containing 100 vials with 14 tablets of 130 mg KI per vial, the cost per tablet is about five cents. With a suggested five-year shelf-life (i.e., replacement period) and a ten-day supply (i.e., ten tablets/individual), the annual cost of KI prophylaxis per individual is about ten cents for the stockpiling option.
- ANBEX - The initial cost for 14 scored tablets of 130 mg KI in a moisture resistant blister pack is 60 cents per pack with a guaranteed four-year shelf-life. Thereafter, annual payments of 15 cents per package would be required if, and only if, the stockpiled product can pass required FDA tests for stability and effectiveness. The annual stockpiling cost of KI procured from ANBEX would also be about ten cents per individual.

Additional costs might include the amendment of existing emergency plans to include protocols for distribution, public notification and training of the emergency staff. These one-time costs, however, are likely to be modest and may only marginally add to the baseline purchase/replacement cost of KI at ten cents per year per individual.

For predistribution, the cost of dispensing KI tablets to residents is an integral part of the program cost. Additionally, for a predistribution program to be effective, there has to be a very comprehensive public relations program, which not only informs the public of the objectives of iodide prophylaxis and provides supportive information regarding safe storage, proper usage, dosage, contraindications, etc., but also establishes public confidence. In summary, the cost for

predistribution of KI includes the purchase/replacement of KI, the predistribution of tablets, and a comprehensive public information program.

An assessment of cost for the predistribution option can be derived from the Tennessee pilot program in which State officials predistributed KI to residents within a five-mile radius of the TVA's Sequoyah Nuclear Power Plant. (For a detailed cost analysis of this pilot project, see Appendix E of this report.) It is estimated that the cost of predistribution of KI to 3,704 households around the Sequoyah Nuclear Power Plant was accomplished at \$125,000.00. Conservatively assuming that within the five-year replacement time there is no loss of KI or relocation of households and that the average household represents four individuals, a lower bound cost per individual for the predistribution option is estimated at \$1.70 per year.

The cost estimates for providing KI to specific population segments of the Reference LWR are presented in Table D-1 for stockpiling with and without predistribution to the less than five-mile resident population.

Table D-1. Annual Programmatic Costs of KI Prophylaxis

Distance (miles)	Number of Individuals	Distribution Options			
		Stockpile		Combination*	
		segment cost (x \$1000)	cumulative cost (x \$1000)	segment cost (x \$1000)	cumulative cost (x \$1000)
< 5	10,699	1.1	1.1	18.2	18.2
5 - 10	55,142	5.5	6.6	5.5	23.7
10 - 25	468,472	46.8	53.4	46.8	70.5
25 - 50	1,820,396	182	235.4	182	252
50 - 100	4,713,000	471	706.4	471	723
100 - 150	7,855,000	786	1,492	786	1,509
150 - 200	10,997,000	1,100	2,592	1,100	2,609
200 - 350	51,843,000	5,184	7,776	5,184	7,793
350 - 500	80,121,000	8,012	15,788	8,012	15,805

* includes predistribution for the < 5-mile resident population

The Economic Benefit of KI Prophylaxis

The "benefits" of protective measures commonly employed to safeguard public health, frequently involve the avoidance of disease, injury, or death. For such cost-benefit analyses, the monetary equivalence of human illness and disease must be assessed for the patient, family, and society. The burden of illness may include financial loss, pain and suffering, reduced quality of life, and premature mortality. This collective burden may extend to family members who must share the

emotional trauma and economic losses associated with morbidity and mortality. At a minimum, the economic benefits must consider the cost of resources used for medical care and the loss of human resources due to morbidity, disability, and premature death. Additional consideration should be given to the impact of disease, injury, or death on the quality of life for the affected individual and family members.

To aid decision-makers in situations where allocations of resources can affect health and life-expectancy, economists have offered several valuation methods. Methods and models commonly used to assess disability, impairment, and loss of life in monetary terms include, (1) publicly implied valuation, (2) court compensation, and (3) direct valuation by the "cost of illness" approach. These three approaches are briefly discussed below.

Publicly Implied Valuation

It is clear that society uses implicit values in order to make administrative decisions on resource allocations in areas where human health and lives are at risk. It is reasonable to conclude that administrative decision-makers in their role as public servants, make decisions from which a "social value" of life can be calculated. In the most recent annual report issued by the Office of Management and Budget (OMB 1991), the cost effectiveness of several Federal programs was assessed. The range of cost per life saved for three Federal program areas are cited in Table D-2. Specific example values for medical and traffic safety programs are provided in Table D-3 and D-4, respectively.

Table D-2. Ranges in Publicly Implied Valuations of Federal Programs*

Federal Program Area	Range of Cost Per Life Saved (1991 \$'s)
Highway Safety	63,000 - 3,300,000
Air Transportation Safety	100,000 - 1,600,000
Occupational Safety	100,000 - 74,000,000

* Reference: OMB 1991

Table D-3. Publicly Implied Valuation of Life-Saving Medical Programs¹

Program	\$ / Life-Saved ²
Cervical Cancer Screening	63,000
Breast Cancer Screening	204,000
Lung Cancer Screening	178,000
Colo-Rectal Screening	
Fecal Blood Test	26,000
Proctoscopic Exams	76,000
Hypertension Control	191,000
Kidney Dialysis	510,000
Mobile Intensive Care Units In Small Towns	153,000

¹ Reference: Cohen, 1980
Costs as presented in original reference were for 1975. Because health care costs have more than doubled since 1975, these costs have been adjusted to 1991 \$'s by multiplying original costs by 2.55.

Table D-4. Publicly Implied Valuation of Traffic Safety Measures¹

Traffic Safety Measure	\$ / Life - Saved ²
Improved Traffic Signs	31,000
Improved Lighting	80,000
Upgrade Guard Rails	101,000
Breakaway Sign Supports	125,000
Obstacle Removal	160,000
Median Barrier	163,000
Impact Attenuator	167,000
Median Strip	181,000
Channels; Turn Lanes	290,000
New Flashing Lights at Railroad Crossings	295,000

Reference: DOT 1984
Costs are based on fatal accidents and assume that there are 1.1 fatalities per fatal accident. Costs are expressed in 1984 dollars.

The relatively wide range in values is not surprising inasmuch as the only common denominator is a reduction in mortality rates. Not reflected in these sets of cited values are important variables, which include (1) average years of life-lost per mortality, (2) the ratio of mortality to morbidity/injury and, (3) property damage. Additionally, there may be a host of value judgements that may include the potential contribution of the victim by his own conduct, the

degree with which individual participation is voluntary/involuntary, and the moral, ethical, and/or legal obligation to provide protection.

The public's willingness to pay to save a "statistical life" (i.e., buy risk reduction) was reviewed by the EPA. In a 1983 study, the EPA concluded that the public appears to value risk reduction at a cost between \$600,000 and \$9,900,000 per life saved (EPA 1983).

In summary, publicly implied valuations may serve as a reference. However, there are too many ill-defined variables that obscure their direct application in assigning definitive monetary values to thyroid related morbidity and mortality.

Compensation in Legal Claims

The second method commonly used to assess the monetary value of injury, morbidity, or death involves the legal system. In instances of medical malpractice, product failure, negligence, etc., the courts must frequently assess the monetary awards granted to the injured party or the survivors. The Court's purpose and function are decision-making on the basis of conflicting evidence. In court, the burden is on the plaintiff and defendant to present information that is believable and accepted by the judge and jury. It can be argued that the size of the awards of damages reflects society's values of compensation for the "collective detriment" of a given situation involving injury or death. In addition to awards of punitive damages, compensatory awards determined by litigation (or out-of-court settlements) frequently represents the sum of medical costs, property damage, loss of earnings, and psychological factors involving pain and suffering, loss of quality of life, etc. An assessment of monetary judgements awarded plaintiffs in personal injury cases involving radiation and other injurious agents are discussed below (pages D-28 through D-33).

The "Cost-of-Illness" Approach

The "cost-of-illness" approach is the third and last method discussed in this report. Because it is the most common and defensible of the methods used among health-policy researchers and health care administrators, a more detailed analysis of this method will be provided. The "cost-of-illness" approach was pioneered by Dorothy Rice, former Director of the National Center for Health Statistics (Rice 1985), and is frequently used to assess the economic burden of disease. In brief, this methodology is defined by three components that include: direct medical costs; morbidity/mortality costs; and psychological costs.

Direct costs include resources used for medical care from the time of diagnosis until total recovery or death. Morbidity and mortality costs, when combined, are referred to as indirect costs (Hodgson 1984). Indirect costs are the time and output lost or foregone by the family members and others from employment (including imputed earnings for domestic work), volunteer activities, and leisure. Lastly, morbidity and mortality invariably cause patients and family members to incur psychological costs, such as pain and suffering, impaired function in personal relationships, and a general reduction in the quality of life.

National estimates of the direct and indirect economic burden of neoplasms were originally reported for the year 1980 (Rice 1985). Direct costs were derived from data collected by the Health Care Financing Administration, which has estimated national health expenditures according to type of service (e.g., hospital care and physician services) and source of funds (Gibson 1983). The direct costs of personal health care are summarized in Table D-5 below.

For 1980, the American Cancer Society estimated that there were over five million living Americans with a history of cancer, of which two million were diagnosed within the previous five years and with new cases occurring at the rate of 900,000 per year (ACS 1982). For that same year, neoplasms required 26 million days of hospital care and 27 million visits to physicians for diagnosis and treatment. The total costs for medical care of neoplasms for the five million cancer patients were \$13.6 billion in 1980. This yields an average annual medical cost of about \$2,700 per cancer patient.

Table D-5. Summary of Direct Health Care Expenditures for Neoplasms in 1980¹
(cost expressed in millions of dollars)

Neoplasms	Hospital Care	Physician Services	Nursing Home Care	Drugs	Other Profess. Services	Total
All Neoplasms	9,130	3,163	469	677	184	13,623
Malignant	7,462	2,264	---	430	166	10,322 ²
Benign	1,667	900	---	247	18	2,832 ²

¹ Reference: Rice 1985

² Does not include expenditures for Nursing Home Care.

The indirect costs for morbidity were derived from work-loss days due to illness data obtained from the National Health Interview Study. Morbidity costs of neoplasms were estimated for the currently employed, persons not institutionalized, who were unable to work, and women unable to keep house because of illness or disability (Table D-6).

Table D-6. Summary of Morbidity Costs of Neoplasms¹
(in millions of dollars)

Type	Currently Employed	Unable To Work	Keeping House	Total
All Neoplasms	1,017	1,205	342	2,563
Malignant	582	1,096	205	1,882
Benign	435	109	137	681

¹ Reference: Hodgson 1984

Morbidity and disability from neoplasms in 1980 resulted in nearly \$2.6 billion of the output and productivity foregone as measured wages and salaries of idled labor and housekeepers. Morbidity losses from malignant neoplasms were nearly three times those of benign neoplasms. For each of the five million living cancer patients in 1980, the average indirect cost due to loss of economic opportunity was \$512 per year.

Lastly, the indirect costs due to cancer mortality were based on estimates of the number of years lost to premature cancer-induced deaths using cancer-mortality data from the National Center for Health Statistics (Table D-7). The number of years lost for each age/sex category was multiplied by the expected earnings for each category, including imputed value of housekeeping services. For the 422,702 persons who died of neoplasms in 1980, it is estimated that their premature death represented a total of 6.8 million person-years lost. The average number of years lost per individual was estimated at 14 for males and 18 for females. These values yield an average monetary value of about \$64,000 per premature cancer death or about \$4,000 for every year of life lost.

**Table D-7. Summary of Mortality Costs for Neoplasms in 1980
(in millions of dollars)**

	Both Sexes	Males	Females
All Neoplasms	26,994	15,713	11,280
Malignant	26,506	15,438	11,068
Benign	488	275	212

The economic impact of neoplasms for 1980 was updated for the year 1985 (Rice 1989) and more recently for 1990 (Brown 1990). Table D-8 is a summary of the direct and indirect costs of neoplasms for 1990.

**Table D-8. Estimated Direct and Indirect Costs
for Neoplasms for 1990**

Cost Category	Cost for 1990 (millions of \$)
<u>Direct Costs</u>	35,256
Malignant	29,328
Benign	5,928
<u>Indirect Costs</u>	
Morbidity	11,896
Malignant	9,895
Benign	2,001
Mortality	56,788
Malignant	55,127
<u>Total (Direct and Indirect)</u>	103,940
Malignant	94,350
Benign	9,590

While the above cited prevalence-based data provides useful information regarding the economic burden incurred for a given year for various diagnostic groups of neoplasms, this type of information is not without criticism (Robinson 1986; Shiell 1987) and has a limited value in the application of a cost-benefit analysis (Weinstein 1986).

A frequent criticism of the prevalence-based approach is that it represents the aggregate economic burden of direct and indirect costs incurred only in the current year due to all prevalent disease in that same year.

It is generally assumed that a cost-benefit analysis is more accurately defined by an "incidence-based" cost, which represents the direct and indirect costs of a disease as they occur from the time of diagnosis until recovery/death. These dated costs can then be summed, using the economic principle of discounting. In principle this states that when costs to be incurred in the future are discounted, they are reduced when compared with current costs in order to account for the fact that dollars invested in productive resources today will yield returns in the future. A discount rate of five percent is commonly used in cost-benefit studies of health care issues (Luce 1990).

Federal agencies are currently coordinating efforts to construct incidence-based cost-of-illness estimates (Brown 1990). This involves the linkage of data between NCI's Surveillance, Epidemiology, and End Results (SEER) Program, and the Medicare program files maintained by the Health Care Financing Administration (HCFA). The successful linkage of these databases will, in the future, provide cost estimates of illness on a patient by patient basis from the time of diagnosis to the time of death or total recovery.

Preliminary direct cost-of-illness data have recently been obtained on this basis (Baker 1989). From the continuous Medicare History Sample File (CMHSF) maintained by the Health Care Financing Administration, 125,832 individuals were identified with an "initial" diagnosis of cancer among the 1.6 million CMHSF sample cohort. Data analyzed for these Medicare beneficiaries included costs for inpatient hospital stays, skilled nursing facility stays, home health agency use, physician services, and outpatient care. Costs were assigned to three time intervals; (1) initial treatment (i.e., first three months following diagnosis); (2) continuing care (i.e., interval between initial and terminal treatment); and (3) terminal treatment (i.e., final six months prior to death).

Table D-9 lists phase-specific treatment costs for each of the 13 cancer diagnostic groups.

Table D-9. Charges Made to Medicare for Treatment During the Initial, Continuing, and Terminal Phases of Cancer of 13 Sites (in 1984 dollars)

Cancer Site	Cancer Phase				
	Initial (3 months)	Continuing (Monthly)	Terminal (6 months)		
Colorectal	\$14,190	(96.5) ^a	\$572	\$15,776	(222.3)
Lung	12,916	(147.1)	690	15,565	(273.1)
Prostate	8,112	(69.4)	560	14,613	(283.2)
Breast	7,606	(58.1)	483	15,136	(301.9)
Bladder	8,470	(122.2)	766	18,577	(447.3)
Leukemia	9,068	(307.7)	676	19,777	(692.9)
Pancreas	14,009	(468.5)	677	14,790	(737.9)
Stomach	14,443	(314.7)	660	16,132	(639.5)
Uterine Corpus	9,260	(134.8)	424	17,623	(741.2)
Kidney	12,608	(241.1)	670	19,302	(994.2)
Ovary	11,055	(272.5)	647	18,650	(867.9)
Uterine Cervix	8,979	(269.6)	493	16,414	(924.6)
Melanoma	6,954	(201.8)	488	16,194	(905.9)
All sites combined	10,039	(35.1)	578	16,280	(98.7)

^a (Standard error of the mean)

Initial treatment of a cancer varied in average cost from about \$7,000 for melanoma to more than \$14,000 for digestive system cancers. Differences in initial costs are thought to reflect the extent of surgery involved as well as the need for short-term post-surgical care representing the 13 cancer sites. Continuing care costs do not show as much variation by site as do initial treatment costs. Continuing care costs were, however, defined per unit of time (i.e., month) and provide no cost estimate for the full duration. Terminal care costs show the least variability

by site, when compared to the initial or continuing care phases of cancer treatment. The weighted average direct costs for all cancer sites yielded values of \$10,039 for the initial, \$578 per month for continuing, and \$16,280 for terminal care of cancers expressed in 1984 dollars.

Conclusion

For a cost-benefit analysis involving radiation induced thyroid disorders, currently available incidence-based cost-of-illness data is neither sufficiently detailed nor complete. This is due to the following reasons: (1) thyroid neoplasms have not been identified as a distinct cancer category, (2) costs such as psychological costs have not been quantified for any cancer site, and (3) even if incidence-based thyroid cost values were extracted from the CMHSF database, these values would require extensive modification to account for a shift in age: CMHSF prevalence-based cost-of-illness values presented above correspond to spontaneous occurring/idiopathic cancers in the U.S. population. On the average, thyroid cancer induction by accidental exposure to radioiodine would undoubtedly occur at a younger age than spontaneously occurring thyroid cancers. This shift in age would have a significant impact on indirect costs.

In summary, there currently exists insufficient incidence-based data for quantifying costs for thyroid disorders. In order to assess the cost-benefit of KI prophylaxis, the author of this report considered it necessary to derive cost estimates for each thyroid disorder, on the basis of (1) direct medical expenditures, (2) individual costs resulting from the loss of economic opportunities, and (3) psychological costs imposed by the intangible impacts of the thyroid disorder. The derivation of these monetary values is presented below.

Derivation of the Monetary Value of Avoidable Thyroid Health Effects

Derivation of Direct Costs

Direct cost estimates of radiation-induced thyroid illness include medical costs associated with the initial diagnosis, treatment of the disease, and the long-term management, surveillance, and care of the patient. Estimates of costs for relevant diagnostic procedures, treatments, hospitalization, etc. are based on 1991 government and private insurers' reimbursement schedules defined by Physicians' Current Procedural Terminology (CPT) Codes. CPT is a listing of descriptive terms and identifying codes for reporting medical services and procedures performed by physicians under government and private health insurance programs. Additional information was obtained from the Health Care Financing Administration Division (HCFA) of the U.S. Department of Health and Human Services. The HCFA maintains a computer database that identifies current health care costs for specific Diagnosis Related Groups (DRGs). DRG 290 identifies surgical procedures involving the thyroid.

Thyroid Nodules. Table D-10 identifies specific cost elements for a benign nodule that may or may not require surgery. Costs are segregated on the basis of belonging to the initial diagnosis, treatment, or long-term follow-up. For long-term follow-up of patients, an average residual life-

expectancy of 30 years is assumed following the initial diagnosis of a nodule. Estimates of costs for long-term patient management and surveillance include routine office visits, hormone replacement therapy, and diagnostic procedures. For a benign thyroid nodule that does not require surgery, a lifetime medical cost of \$5,148 to \$7,375 was identified. When surgery is required, direct medical costs for a benign nodule range between \$11,820 and \$14,047. For either situation, the upper value reflects the discretionary use of ultrasound for patient evaluation.

Table D-10. Medical Costs for Benign Thyroid Nodule

Medical Services and Procedures	CPT Code	Nodule Without	Nodule With
		Surgery	Surgery
		Cost (\$)	Cost (\$)
<u>Diagnosis</u>			
- Consultation	99243	87	87
- Laboratory			
· Free T ₄	88439	29	29
· TSH	88433	42	42
- Nuclear Medical Scan	78011	99	99
- Ultrasound	76536	73	73
- Needle Aspiration	60100	60	---
- Cytology	88173	59	---
<u>Treatment (Surgery)</u>			
- Consultation	99243	N/A	87
- Anesthesia	00320	N/A	460
- Lobectomy	60220	N/A	627
- Surgical Assistant	88331	N/A	125
- Pathology			
· Frozen	88331	N/A	32
· Permanent	88307	N/A	60
- Hospital	(DRG 290)	N/A	5,400
<u>Follow-up Evaluation¹</u>			
- Office Visits	99213	1,190	1,190
- Laboratory			
· Free T ₄	88437	986	986
· TSH	22433	1,428	1,428
- Medication (Thyroxine)	---	1,095	1,095
- Ultrasound (Discretionary)	76536	2,227	2,227
<u>TOTAL DIRECT COST</u>			
	LOW:	\$5,148	\$11,820
	HIGH:	\$7,375	\$14,047

¹ Follow-up evaluation assumes an average of 30 years of residual life-expectancy following initial diagnosis of benign nodule. Patient follow-up evaluations are four times in first year, two times in second year, and once a year for the remaining 28 years.

Thyroid Cancer. The major cost difference between a thyroid cancer and a thyroid nodule is the need for aggressive treatment of the former. Table D-11 cites medical costs for a thyroid malignancy that is estimated to range between \$15,413 and \$19,348. This range in cost estimates may, nevertheless, be low in instances where residual thyroid tissue is suspected of malignancy following an initial course of treatment. In cases of persistent suspected malignancy, additional I-131 therapies and associated procedures and services are required. It is estimated that each additional I-131 therapy would increase the total cost by about \$4,000. In rare instances, up to ten separate therapeutic treatments may be required for the total eradication of malignancy.

For the ten percent of thyroid malignancies that are fatal, cost estimates are adjusted to reflect (1) the reduced follow-up period of medical care and (2) the terminal patient care costs. Based on mean survival times of papillary and follicular thyroid cancers, the mean follow-up period of 35 years assumed for non-fatal cancer is reduced to about nine years. From the previous Table D-9, it was conservatively estimated that the average terminal care of a cancer patient costs about \$16,000.

Given the variable options available for the treatment and management of thyroid malignancies and the range of virulence that may require multiple therapeutic treatments with I-131 or result in premature death, the following direct costs were assigned to thyroid cancer:

Non-fatal Thyroid Malignancy	= \$20,000
Fatal Thyroid Malignancy	= \$32,000

Table D-11. Medical Costs for Thyroid Cancer

Medical Services and Procedures	CPT Code	Costs (\$)
<u>Diagnosis</u>		
- Consultation	99243	87
- Laboratory: Free T ₄	88437	29
TSH	88433	42
- Nuclear Medical Scan	78011	99
- Ultrasound	76536	73
<u>Treatment</u>		
<u>Surgery</u>		
- Consultation	99243	87
- Anesthesia	00320	576
- Total Thyroidectomy	60252	975
- Surgical Assistant	---	195
- Pathology: Frozen	88331	32
Permanent	88307	60
- Hospital	(DRG 290)	5,400
<u>I-131 Ablation Therapy</u>		
- Consultation	99243	87
- Laboratory: Free T ₄	88437	29
TSH	88433	42
- Nuclear Med., Neck & Chest		
· Survey	78015	115
· (2-10 mCi I-131)	79900	90-120
- I-131 Therapy	79035	129
· (100-200 mCi I-131)	79900	564-1,064
- Hospital	(DRG 290)	1,350
<u>Initial Follow-up</u>		
- Hormone replacement		
· Consultation	99213	35
· Laboratory: Free T ₄	88437	29
TSH	88433	42
- Effectiveness of I-131 Therapy		
· Consultation	99213	35
· Laboratory: Free T ₄	88437	29
TSH	88433	42
Thyroglobulin	86318	19
· Neck & Chest Survey	78015	115
- (2-10 mCi I-131)	79900	90-120
- Follow-up Hospitalization for I-131 Therapy		
· Consultation	99221	110
· I-131 Therapy	78015	115
· (100-200 mCi I-131)	79900	564-1,064
· Hospital	(DRG 290)	1,350
<u>Long-Term Follow-up Eval. (35 yr)</u>		
- Minimum follow-up at 1-3 yrs.		<u>3 Yr</u> or <u>1 Yr</u>
· Office Visit	99213	420 1,225
· Laboratory: Free T ₄	88437	348 1,015
TSH	88433	504 1,470
Thyroglobulin	88318	228 665
- Thyroxine (35 years)	---	1,277
TOTAL DIRECT COSTS:		
LOWER RANGE COSTS: \$15,413 - \$19,348		
UPPER RANGE COSTS: > \$50,000		

For some thyroid malignancies, several repeat I-131 therapeutic treatments are required for total eradication of malignancy. Each therapy, which includes a battery of medical procedures/services, and hospitalization, is assigned a cost of \$4,000.

Hypothyroidism. Medical cost in cases of radiation induced hypothyroidism are limited to initial diagnostic tests that confirm the reduction or loss of thyroid function, hormone replacement and management, and follow-up evaluation of thyroid status. Specific cost elements are identified in Table D-12. Cost estimates are based on a 35-year life-expectancy following the diagnosis and loss of thyroid function. For hypothyroidism, medical costs are estimated at \$5,669.

Table D-12. Medical Costs for Hypothyroidism

Medical Service or Procedure	CPT Code	Cost (\$)
<u>Diagnosis</u>		
- Consultation	99243	87
- Laboratory: Free T ₄	88439	29
TSH	88433	42
- Nuclear Medicine Scan	78011	99
<u>Follow-up Evaluations* (35 yr)</u>		
- Office Visit	99213	1,365
- Laboratory: Free T ₄	88439	1,131
TSH	88433	1,638
- Hormone Replacement (medication)	----	1,278
TOTAL DIRECT COSTS:		\$5,669

Assumes four times in first year, two times in second year, and once for remaining years.

Table D-13 provides a summary of direct medical costs estimates for the four radiation thyroid effects under consideration.

Table D-13. Summary of Direct Medical Costs

Thyroid Disorder	Total Direct Cost (\$)
Thyroid Nodule*	9,600
Thyroid Cancer	
- Non-fatal	20,000
- Fatal	32,000
Hypothyroidism	5,600

* assumes that 50% of nodules require surgery

Derivation of Indirect Costs

Loss of Time. Indirect costs principally reflect the time and output lost or forfeited by the patient due to illness, permanent disability, and premature mortality. Indirect costs may also be incurred by individuals other than the patient who may forego economic activities to accommodate a family member's illness. Economic activities include occupational work that is lost to either the patient or his/her employer, as well as non-occupational (e.g., domestic) work that must be performed by someone else at the expense of the patient. For illness, the loss of time from economic opportunities corresponds to three discrete stages:

- (1) Illness - The period of time during which the thyroid dysfunction becomes sufficiently symptomatic and prompts the individual to seek medical evaluation and treatment. During this time, the patient may physically suffer from either hyper- or hyposecretion by the thyroid gland.

Hypersecretion by the thyroid due to a toxic nodule/cancer may be manifested by nervousness, weight loss, heat intolerance, tachycardia, palpitation, diarrhea, tremor, and muscle weakness.

Hyposecretion due to ablation of the thyroid gland may be manifested by slowing of mental processes, lethargy, weakness, cold intolerance, dry skin, constipation and possible myocardial insufficiency.

Either of these conditions is likely to render an individual physically unfit for normal work and leisure activities.

- (2) Treatment - Thyroidectomy and therapeutic administration of I-131 require hospitalization and convalescence; radioiodine therapy also requires that a patient be first rendered hypothyroid.
- (3) Long-Term Management - Following treatment, the patient in most instances, is subject to a lifetime dependency on daily doses of thyroxine and must be periodically monitored for proper dosage. The patient must also be monitored for the recurrence of nodule/cancer. Patient management and surveillance require routine office visits and clinical evaluation. It is estimated that office visits and outpatient clinical evaluation on the average, represents a loss of one day per year for the life of the patient.

Table D-14 provides estimates of the average total number of days lost from economic activities for the various thyroid disorders.

Table D-14. Time Lost From Economic Activities Due to Radiation Induced Thyroid Illness

Thyroid Disorder	Time Lost (Days)			Total
	Illness	Diagnosis/ Treatment	Long-Term Management	
Thyroid Nodule	14	14	30	58
Thyroid Cancer				
· Non-Fatal	14	14	35	63
· Fatal	14	14	10,731 ¹	≈ 10,750
Hypothyroidism	14	7	35	56

¹ For a fatal malignancy, this value represents loss of life-expectancy. See discussion below.

The number of days appropriated to long-term management of the disorder is based on the average remaining years of life following diagnosis and latency periods previously identified. A special case involves a thyroid malignancy that may result in premature death.

Years of Life-Lost to Malignant Thyroid Cancer. Radiation-induced thyroid cancers are essentially confined to the papillary and follicular kind. The proportion of papillary and follicular thyroid carcinomas when induced by radiation are assumed to be 90% and 10%, respectively (Beach 1962). The fatality rate for this ratio of thyroid carcinomas is assumed to be about 10% which, therefore, results in years of life-lost. The times at which deaths from papillary and follicular thyroid cancer occur following diagnosis have been documented by McConahey (1981) and Cady (1976) who collectively analyzed a population of 1,595 thyroid cancer patients treated between 1931 and 1971. The distribution for the time of death for each of the cancer types as well as their weighted mean values are provided in Table D-15.

Table D-15. Time Distribution of Deaths Due to Papillary and Follicular Carcinoma of the Thyroid

Time after Diagnosis (Years)	Papillary (%)	Follicular (%)	Weighted Average Value (%)
1 - 5	44	51	44.7
6 - 10	22	17	21.5
11 - 15	10.5	8.5	10.3
16 - 20	3.5	20.5	5.2
21 or more	20	3	18.3
TOTAL	100	100	100

Using the midpoint of time-intervals and the corresponding percentage value as a weighting factor, an overall mean survival time of 9.3 years following cancer diagnosis can be estimated. From 1990 United States population data (see Chapter 3, Table 3.3) and a cancer induction of five years, it can be estimated that the average number of years lost per fatal thyroid cancer is 29.4 years or 10,731 days.

The Indirect Cost of Impairment. In addition to time lost from economic activity due to illness, treatment, long-term management of the disease, and premature death, a patient may also be permanently impaired and/or disabled. Permanent impairment or disability can reduce a patient's ability to be fully effective in occupational or economic activities and must, therefore, be included in assessing the total indirect cost.

The American Medical Association has published Guides to the Evaluation of Permanent Impairment (AMA 1990) that provides a reference framework within which physicians may evaluate and report medical impairments. Various terms used in the Guides, such as "impairment," "disability," and "handicap" appear in laws, regulations, and policies of diverse origin and without consistent definition. The Guides define these terms as follows:

- Impairment - an alteration of an individual's health status that is assessed by medical means.
- Disability - an alteration of an individual's capacity to meet personal, social, or occupational demands. Disability is assessed by non-medical means.

The Guides amplify these definitions by stating that:

". . . 'impairment' is what is wrong with a body part or organ system and its function; 'disability' is the gap between what the individual can do and what the individual would have been able to do or needs to do. Thus, an individual who is 'impaired' is not necessarily 'disabled'. Impairment only gives rise to disability when the medical condition limits the individual's capacity to meet the demands of life's activities. For example, losing the distal phalanx of the little finger, right hand, will impair the function of the digit and hand of both a concert pianist and a bank president, but the bank president is less likely to be disabled than the pianist."

"The concept of 'handicap' is related to, yet independent of the terms 'impairment' and 'disability', although some use it interchangeably with these terms. Under provision of Federal Law, an individual is identified as 'handicapped' if he or she has an impairment that substantially limits one or more of life's activities, has a record of such impairment, or is regarded as having such an impairment."

On the basis of these definitions, the economic impact of thyroid disorders on indirect costs is most objectively assessed in terms of their permanent medical impairments. The AMA provides guidelines for evaluating permanent medical impairment of the thyroid due to hypothyroidism from radiation exposure or thyroidectomy (AMA 1990).

Class 1 - A patient belongs in Class 1 when; (a) continuous thyroid therapy is required for correction of the thyroid insufficiency or for maintenance of normal thyroid activity, and (b) there is no objective physical or laboratory evidence of inadequate replacement therapy.

Class 1 Level of Impairment of the Whole Person: 0 - 10%

Class 2 - A patient belongs in Class 2 when, (a) symptoms and signs of thyroid disease are present, or there is anatomic loss or alteration, and (b) continuous thyroid hormone replacement therapy is required for correction of the confirmed thyroid insufficiency; but (c) the presence of a disease process in another body system or systems permits only partial replacement of the thyroid hormone.

Class 2 Level of Impairment of the Whole Person: 15 - 20%

In this report, the central value of five percent for Class 1 permanent impairment will be applied to the permanent hypothyroid conditions that are likely to result from (1) high radiation exposure doses received accidentally, (2) from the radiotherapy treatment for toxic nodules/cancer, or (3) the surgical removal of nodules/cancer. It will further be assumed that this five percent medical impairment results in a five percent disability for occupational and non-occupational economic activities for the affected individual, family members, and/or society.

Up to this point of the discussion, indirect costs have been quantified in terms of time lost. The conversion of time lost from economic activities to equivalent dollars is most fairly achieved by means of the Gross National Product (GNP). The GNP is considered the most comprehensive measure of the country's economic activity and includes the market value of all goods and services that have been bought for final use during a year. From the Gross National Product of \$5,200 billion in 1989, the gross average annual per capita income of about \$21,000 is derived. This value of \$21,000 per year can be used to determine the equivalent dollar value for the number of days lost over the lifetime of an individual afflicted with a thyroid condition. This value can also be applied to determine the equivalent value of a five percent permanent disability (i.e., a five percent disability equates to about \$1,000 annually in reduced income). Table D-16 provides estimates of the total average indirect costs associated with thyroid disorders.

Table D-16. Average Lifetime Indirect Costs Associated with Thyroid Disorders

Thyroid Disorder	Lifetime Indirect Costs (\$)		Total
	For Time Lost	For Disability (5%)	
Thyroid Nodule	3,337	30,000	33,337
Thyroid Cancer			
Non-Fatal	3,625	35,000	38,625
Fatal	619,586	9,400	628,986
Hypothyroidism	3,222	35,000	38,222

Derivation of Psychological Costs

Disease may bring about numerous changes and impositions in the lives of the patient and family members that may in part be linked to, but are not reflected in the direct and indirect economic costs identified above. The wide variety of deteriorations in the quality of life (QOL) brought on by illness are frequently referred to as psychological costs. For thyroid neoplasms and dysfunction, a deterioration in the quality of life may be precipitated by the loss of bodily function, a lifetime dependence on medication, hormonal instability, disfigurement from surgical scars, the uncertainty of normal life expectancy, and reduced financial security. In characterizing psychological costs associated with disease, Thomas Hodgson (Hodgson 1984), chief Economist for the Department of Health and Human Services' Office of Analysis and Epidemiology states:

"Disease may bring about personal catastrophes . . . to the victims of illness, . . . children, spouses, and siblings of victims, friends and co-workers of victims; and those who render care may all be affected. A victim may suffer a loss of a body part or speech, disfigurement, disability, impending death, pain, and grief. He and those around him, may be forced into economic dependence and social isolation, unwanted job changes, loss of opportunities for promotion and education, relocation of living quarters, and other undesired changes in life plans. The environment created by illness often induces anxiety, reduced self-esteem and feelings of well-being, resentment, and emotional problems that often require psychotherapy. Problems of living may develop, leading to family conflict, antisocial behavior, and suicide. The victim and others may experience marked personality changes and reduced sexual function. Disrupted development and delinquency may occur among children. The quality of life may be reduced beyond restorative capability of current rehabilitation efforts. The combination of financial strain and psychological problems can be especially devastating."

Qualitative Elements Affecting QOL. Due to the fact that quality of life issues have only recently solicited a formal interest among health care professionals, QOL data is both sparse and

lacks standardization. In July of 1990, the National Institutes of Health (NIH) conducted a workshop on the quality of life assessment in cancer clinical trials (NCI 1990). Among the major objectives of the meeting were to define discrete quality of life elements and to identify currently available instruments (i.e., methods) for QOL assessment. The workshop group consisting of international experts concluded that (1) the quality of life of patients is affected by both the disease and by the treatment of the disease and (2) the quality of life is a multidimensional concept that must be evaluated by a set of instruments (i.e., methods) which measure both broad issues and disease/treatment specific phenomena.

Data on a number of QOL dimensions have been collected from among cancer patients (Kaplan 1990; Patrick 1989; Patrick 1988). The most frequently cited dimensions that characterized the quality of life include (1) physical symptoms of pain and discomfort, (2) functional ability, (3) family well-being, (4) emotional well-being, (5) spirituality, (6) financial concerns, (7) future orientation (planning and hope), (8) sexuality/intimacy (including body image), (9) social functioning, and (10) occupational functioning. Research over the past 20 years has also identified a host of socio-economic variables that modulate these quality of life dimensions (Mor 1987; Teta 1986; Houts 1986). Given the literature, there is justification to identify age, gender, marital status, educational level, religious beliefs, employment and economic status, and the number of children living at home as crucial variables that affect changes in the quality of life imposed by a given disease.

Quantitative Methods for QOL Assessment. Various questionnaires and protocols inclusive of psychometric evaluation have recently been developed and have been used in clinical trials to provide QOL measurements among cancer patients (Schag 1990; Ganz 1990; Schipper 1984) and patients with chronic debilitation medical conditions (Stewart 1988 and 1989; McCorkle 1983 and 1989).

QOL measurements that specifically deal with thyroid cancer and/or thyroid dysfunction are not currently documented. Additionally, available quality of life measurement data frequently focused not on the disease itself but on specific treatment options in which the risks and benefits of the treatment were assessed relative to their impact on the patients' lives. Factors considered in these studies included treatment toxicity, physical disfigurement, and bodily/sexual dysfunction. Not surprisingly, therefore, among the limited number of clinical studies the most frequently evaluated cancers with regard to QOL issues are those that involve the lung, female breasts, ovaries, and prostate.

In summary, while various QOL measurement protocols have been developed and used to aid health care practitioners in clinical decisions, no standard format exists that would allow such measurements to be used for economic or other non-clinical purposes. Of limited application is the Social Security Administration's (SSA 1985) guidelines for assessing impairment due to mental and behavioral disorders. (The term "limited" refers to the fact that mental and behavioral disorders are but two of several dimensions that may characterize QOL changes.) Severity is assessed in terms of functional limitations on activities of daily living; social functioning; concentration, persistence and pace; and adaptive functioning in response to stressful

circumstances. Table D-17 provides the SSA’s guide for rating impairment in each of the four areas of functional limitation on a five-point ordinal scale, ranging from none to extreme:

- None means there is no impairment noted in this area of function.
- Mild implies that any impairment that is discerned is compatible with most useful function.
- Moderate means that impairments that are found are compatible with some but not all useful functions.
- Marked is a level of functional impairment that significantly impedes useful function.
- Extreme signifies that the impairment is not compatible with useful function.

Table D-17. Social Security Administration’s Guidelines for Assessing Impairments

Area of Function	Class 1 No impairment	Class 2 Mild Impairment	Class 3 Moderate Impairment	Class 4 Marked Impairment	Class 5 Extreme Impairment
Activities of Daily Living	No impairments noted	Impairments levels compatible with most useful function	Impairment levels compatible with some but not all useful function	Impairment levels significantly impede useful function	Impairment levels preclude useful function
Social Functioning					
Concentration					
Adaptation					

To illustrate these ratings, extreme limitation in activities of daily living implies complete dependency on another for personal care. In the area of social functioning, extreme impairment implies that the individual engages in no meaningful social contact. An extreme limitation in concentration, persistence, or pace means that the individual cannot contribute to conversation or any productive/occupational tasks at all. In an otherwise ordinary individual, a single area of extreme impairment would be likely to preclude performance of any complex task, such as recreation or work. Two or more areas of marked limitation would also be likely to preclude performance of complex tasks without special support or assistance. An individual who was impaired to a moderate degree in all four areas of function would be expected to be limited in many, but not all, complex tasks. Mild and moderate limitations reduce overall performance but do not preclude performance.

The AMA warns, however, that:

"Translating these guidelines for rating individual impairment on *ordinal* scales into a method for assigning percentage impairments, as if the ratings were made on precisely measured *interval* scales, is not recommended. For example, we cannot be certain that the difference in impairment between a rating of mild and moderate is the same as the difference between moderate and marked. Furthermore, a moderate impairment does not imply 50% limitation in useful function. Similarly, a rating of moderate impairment in all four areas of function does not imply a 50% impairment of the whole person. In reality, however, physicians often are required to make such judgments. It is important to remember that such judgments are based on clinical impression rather than on empirical evidence. In those circumstances in which it is essential to make a percentage rating, the ordinal scale might be of some help: one could assume that the extreme rating approaching 100% mental impairment is similar to a coma, which is the extreme impairment of central nervous system function and level of consciousness.

Eventually research may support the direct link between medical findings and percentage of mental impairment. Until that time the medical profession must refine its concepts of mental impairment, improve its ability to measure limitations and continue to make clinical judgments."

In the absence of thyroid-specific clinical data, as well as a standardized generic protocol for assessing QOL dimensions, the author of this report consulted with medical professionals experienced in the diagnosis, treatment, and surveillance of patients with thyroid cancers.

Consensus opinion of several qualified physicians is that the QOL impact of thyroid cancers, in general, ranks low in comparison to most other cancers. This view is supported by the fact that thyroid cancers of papillary or follicle cell origin have a relatively low mortality rate and patients are reassured of a high survival probability. In addition to a good prognosis, treatment for a primary thyroid cancer (i.e., thyroidectomy and/or radioiodine) involves well-established protocols and procedures. Absent is the toxic side effects of chemotherapy and/or extensive whole body irradiation that is associated with many other cancers. Following successful treatment of the cancer, proper replacement levels with exogenous thyroid hormone in most patients is readily established with only "minor" discomfort to the patient. In fact some physicians regard the functional loss of the thyroid gland as a mere "medical nuisance."

While the physicians' opinions may be understandable, they are not without bias. Given the high mortality rate and toxic treatment for other cancer sites, it is understandable why physicians view thyroid cancer more casually and without the usual intensity reserved for more virulent cancers.

For the patient, however, who up to the time of diagnosis of a thyroid neoplasm may have been perfectly healthy, the anticipation of surgery, radioiodine therapy, hormonal instability, a lifetime dependence of hormone replacement therapy, and the probability of one chance in ten of dying is not likely to be inconsequential with regard to the patient's quality of life. This discrepancy between patients and physicians has been documented in several studies, which have shown that the attending physicians of patients were not a suitable source for patient QOL ratings (Slavin 1988; Martini 1976; Wartman 1983). When patient QOL ratings were compared to those of their attending physicians, a correlation value of only 0.63 was found to exist. In one study, for example, physicians did not recognize 34% of both psychiatric problems and life crises reported by patients (Wartman 1983). The conclusion among the QOL researchers was that individual patients provide the most accurate information for evaluating the impact of a cancer or a chronic disease.

For this reason and at the recommendation of the NRC, the author of this report, in the presence of a health care professional, sought the personal testimony of an individual with a long and complex history of thyroid cancer. The patient who provided testimony is a white male in his late forties. He is a professional, currently employed, married, and the father of one child. In the time frame of 1948/1949, this individual received external medical radiation for the treatment of enlarged tonsils/adenoids. It has been estimated that this exposure resulted in a thyroid dose of about 750 rads.

In 1973, the patient was first diagnosed to have a thyroid carcinoma of mixed papillary/follicular cell origin. Following the surgical removal of about 80% of thyroid tissue, the patient was treated for thyroid insufficiency with desiccated bovine thyroid extract. This treatment resulted in cyclic fluctuation of serum levels that were either too high or too low. The patient, during this time, suffered many symptoms commonly associated with hypo- and hyperthyroid conditions inclusive of emotional and behavioral changes, depression, fatigue, hyperactivity, etc. Substitution of desiccated bovine thyroid extract with synthetically produced thyroid hormone (Synthroid), which became available in 1978, did not eliminate these problems.

Because of persistent hormone imbalance thought to be, in part, the result of residual thyroid activity, the patient received two separate radioiodine doses of 30 mCi I-131 each in 1983.

As part of the continuing patient's surveillance, doctors identified a "new" thyroid malignancy in 1988 for which the patient received another 100 mCi dose of I-131. In 1989, the patient was subjected to yet a fourth therapeutic dose of radioiodine involving 150 mCi of I-131. As part of each I-131 therapy, the patient was intentionally rendered hypothyroid in order to maximize the uptake of radioiodine and to ensure maximum therapeutic tissue destruction. Subsequent thyroid scans showed residual evidence of viable thyroid tissue/ cancer. As of 1992, future treatment is likely to include surgery and more radioiodine therapy. To date, the prospect for successful treatment and hence the patient's prognosis remains uncertain.

The disease and its symptoms, its persistence, the prescribed intermittent treatments, and the uncertain prognosis have had a significant impact on the patient. There were extended periods

of time during which the patient was unable to function in his professional capacity. He stated that he felt debilitated from fatigue, depression, and anxiety, which also affected his relationship and the well-being of his wife, child, and other members of his family. The emotional trauma was particularly acute prior to each radioiodine therapy when the patient's normal hormone replacement therapy had to be altered and following radioiodine therapy when the patient, for radiological reasons, was isolated from family and the normal hospital environment. Due to the uncertain prognosis, the patient and his wife have made a decision not to have any additional children. The patient also feels that his career has been significantly impacted by his disease. The patient stated that he sought counseling and psychiatric help at various times over the course of his illness for reasons that were directly linked to his thyroid illness.

Valuation of Psychological Costs. In spite of the fact that psychological costs are consistently identified as a major cost component by health care researchers and economists, no formal attempt has been made to quantify these costs in monetary terms (Hodgson 1984; Rice 1985; Brown 1990). The reason for this omission is obvious. From the foregoing discussion, it is axiomatic to conclude that the intangible dimensions, which define the quality of life, are (1) highly subjective, (2) vary greatly among individuals, and in time and space, and (3) are not readily expressed in monetary terms. Independent of these difficulties, the exclusion of psychological monetary costs in some instances may be justified for conditions in which the health effect is of unknown origin, self-inflicted or unavoidable. The omission of psychological costs, however, is not readily justified for situations in which the health effect is clearly avoidable, or is the consequence of negligence or wrongful action. A complete cost-benefit analysis of KI prophylaxis must, therefore, include estimates of psychological costs expressed in the unit of dollars.

There are several potential approaches that can be used to estimate the monetary value of psychological costs associated with disease or impaired health. Mooney (1977) and Schelling (1968) proposed the use of survey techniques. Survey methods associated with quality of life valuation can be based on the amount an individual is either prepared to pay to avoid a reduction in the quality of life or would accept in compensation for an existing reduction in the quality of life. Such a survey technique, however, is not without flaws.

Survey-solicited responses may reflect a limited and unrealistic interpretation of the proposed hypothetical condition and are, therefore, difficult to evaluate. Moreover, the valuation of death cannot be assessed by such a survey technique. (Nevertheless, the reader may ask this very question of himself in assigning a monetary value for a thyroid cancer and/or loss of thyroid function.)

Another approach is to analyze data on health and life insurance premiums, which cover disability and death. Again, there is difficulty in the interpretation of this type of data due to socio-economic variables that motivate individuals. For instance, it cannot be assumed that (1) a person who does not purchase health or life insurance does not value his health or life or (2) that there is a proportional relationship between premium and personal valuation of health and life.

The most credible approach to monetize psychological costs is to assess the judgements awarded to plaintiffs in cases of wrongful injury or death. Traditional legal remedies of monetary awards in personal injury and wrongful death litigation are also generally applicable in cases involving radiation exposure.

To date, litigation data involving claims of radiation injury and death, are relatively sparse. In spite of numerous legal claims that have been filed in recent years, many radiation cases have been resolved on other legal issues with no damages being awarded. Only a few cases have gotten as far as a specific economic valuation. Three prominent cases in which plaintiffs were granted financial compensation are briefly summarized below:

Allen versus United States.

In this landmark case, actions were brought against the United States by 24 plaintiffs in 1982, to recover for cancer or leukemia allegedly caused by the Atomic Energy Commission testing of atomic devices prior to 1963. The District Court held that the United States had been negligent in its conduct of the testing program by failing to properly monitor radioactive fallout and by failing to properly inform and warn the people in the vicinity of the test site. Of the ten plaintiffs awarded compensation, eight were wrongful death cases and two involved personal injuries.

Under Utah Law, the court stated that in an action alleging wrongful death, ". . . the full value of the life of the deceased is determined and recovered." The judge highlighted the following elements as important in assessing recoverable damages: "(1) financial support furnished, (2) loss of affection, counsel and advice, (3) loss of deceased's care and solicitude for the welfare of the family, and (4) loss of the comfort and pleasure the family of the deceased would have received" (Switzer versus Reynolds, 606 P. 2d, 244 Utah 1980, p.246).

Among the eight leukemia cases compensated for wrongful death, four involved children. When a wrongful death involves the loss of a child, there is minimal tangible monetary compensation. However, the intangible loss to family and society involving human relationships is considered the greatest loss.

In summary, for the eight plaintiffs in Allen et al. versus the United States, four elements were considered in determining compensation to survivors in wrongful death actions: (1) loss of support; (2) loss of assistance and service to the family; (3) loss of society, companionship and happiness of association; and, (4) loss of the possibility of inheritance, if the decedent is an adult. Awards in the eight cases of wrongful death ranged from \$235,000 to \$625,000 with an average value of \$320,000.

The Utah/Arizona Law concerning damages to personal injury is also clear. The laws allow injured plaintiffs to recover general and special damages that naturally and necessarily result from the harm done, including damages for the loss of time and

earnings, impairment of future earning capacity, all costs pertaining to medical treatment and care, pain and suffering, and other psychological impacts. ♪

Of the two claims involving injury, one involved an adenocarcinoma of the thyroid of a twenty-one year old female suspected of having received a thyroid dose between 30 and 340 rads from the fallout of radioiodine during early childhood. For the benign thyroid cancer, the plaintiff was awarded \$100,000.

Silkwood versus Kerr-McGee.

In November 1974, plutonium contamination was found in the private apartment of a chemical technician (Karen Silkwood) an employee of the Kerr-McGee Corporation. Following her death in a fatal car accident, post mortem analysis of tissue samples were conducted. It was estimated that the total body-burden for plutonium was less than 10 nCi, yielding 50-year committed organ doses of about 0.5, 2, and 0.8 rads, respectively to the lung, liver, and bone. Based on the 1972 BEIR Committee risk estimates, her lifetime risk of fatal cancer was calculated to be between zero and 0.0005.

Two key issues presented in the subsequent jury trial involved (1) the liability of Kerr-McGee for the contamination and (2) the injury question due to a plutonium exposure that was less than permissible limits for occupational exposure. (The death of Karen Silkwood in the automobile accident was not a point of contention in the trial).

The jury found Kerr-McGee negligent in its operation of the facility under the strict liability and also found that Silkwood had been injured by plutonium according to the Court's definition of injury. The court ruled that . . . "Certainly physical injury can include a nonvisible or non-detectable injury and may include injury to bone, tissue, or cells. If a person has suffered physical injury . . . on the basis of expert medical opinion, it is only necessary that a person believe he or she has been physically injured as a basis for mental pain and suffering to occur."

The jury awarded the Estate of Karen Silkwood \$500,000 for injury, \$10,000,000 for punitive damages, and \$5,000 for property damage. In the appeal decision, the Tenth Circuit Federal Court decided that the case should have been tried under the Oklahoma Workman's Compensation Law rather than under common tort law. Thus, the 10.5 million judgement was reversed.

Kerksieck versus McDermott Inc.

The plaintiff (Kerksieck) was the owner of a Cable Television business located next to McDermott's pipe fabrication facility, which engaged in radiographic pipe testing of welds. The plaintiff alleged he had been exposed to gamma radiation between 1978 and 1984. Dosimetry experts for the plaintiff estimated his exposure between 75 and 300 rem. Experts for the defendant estimated his exposure at less than 2 rem. The plaintiff's injuries were basically benign, consisting of pancreatic carcinoids in 1985, a benign thyroid condition in 1987 and lymphocytosis in 1989, as well as parathyroid tumors and

the appearance of benign adrenal nodules. All of the plaintiff's conditions were benign and his thyroid had been surgically removed.

The jury awarded a total of \$1,250,000 to the plaintiff: \$830,000 in punitive damages; and \$415,000 in compensatory damages. Of the compensatory award, \$180,000 was for anticipated future medical expenses. The only testimony on further health costs, however, was presented by the plaintiff's treating physician, which identified the need for continual checkups and patient surveillance.

In radiation injury litigation there are problems not faced in routine cases. One such problem is the long latency period between exposure and the biological consequences of radiation. Long latency periods tend to obscure the causal relationship between radiation exposure and radiation injury. Other problems are sui generis to nuclear litigation and may, in part, account for the relatively small number of cases that have come to trial.

The relatively few radiation injury cases that have been resolved in court may, in part, be due to (1) the unsettled state of the law relating to Federal preemption, at least until the Supreme Court decided *Silkwood versus Kerr-McGee*, 464 U.S. 238 (1984) and (2) to the problems associated with having to sue the United States under the Federal Torts Claims Act (e.g., the Nevada test site cases; *Prescott versus United States* 1992 WL 54002, F.2d, 9th Cir. 1992).

Due to the limited database involving radiation injuries, it is appropriate to review representative legal cases pertaining to other cancer-causing agents. It is worth noting that over the last 10 to 20 years the law has evolved considerably in this area. Based on emotional distress arising from their risk or their fear of developing cancer, persons exposed to carcinogenic substances may now recover damages more easily than in the past. Older cases required a plaintiff seeking damages for emotional distress to prove: (1) physical harm as a result of the conduct that caused the emotional distress, (2) that the physical harm either caused or was caused by the emotional distress, and (3) that the physical harm had objective symptomatology. Therefore, in the past, risk without any accompanying physical injury was insufficient to recover damages (*Mink versus University of Chicago*, 460 F. Supp. 713 (N.D. Ill. 1978); *Sypert versus United States*, 559 F. Supp. 546 (D.D.C. 1983)).

These strict requirements have been relaxed in many jurisdictions. Some courts have held that the physical harm requirement is satisfied by evidence that a demonstrable physical change in the plaintiff's body has occurred (*Plummer versus United States*, 580 F.2d 72 (3d Cir. 1978)). Other courts have held that the ingestion of a toxic substance is sufficient for a cause of action to accrue, even though a significant physical effect cannot be shown (*Hagerty versus L&L Marine Services, Inc.* 788 F.2d 315 (5th Cir. 1986)). Once a plaintiff satisfies either the demonstrable physical change or ingestion of a toxic substance test, many, if not most, jurisdictions will allow recovery of damages for the fear of a potential future disease (*J. Allison, Evidence Supporting Recoverable Damages for Potential Disease*, XXIV Tort and Ins. L.J. 39 (1988)).

Other courts have also allowed damages for the impairment of quality of life. In those cases, a plaintiff has been allowed to recover damages for those activities, which need not be profit making, that he could enjoy prior to his injury but not afterwards.

One element of damages frequently considered and allowed in tort litigation, but which will not be taken into account in this analysis, is the element of punitive damages. The reason that this will not be considered is that such damages do not bear a direct relationship to the value of life or health. Rather, punitive damages are designed to punish the wrongdoer who has acted in reckless disregard for the health and safety of others. It is not extraordinary for punitive damages in some particularly egregious cases to be 10 or 20 times the amount of the compensatory damages. For this reason, some jurisdictions, either by statute or decisional law, have limited the amount of punitive damages that may be awarded.

Accordingly, listed below are selected cases that reflect what value courts and juries in various jurisdictions have placed on some elements of damages discussed above. Significant among the missing cases is *Silkwood versus Kerr-McGee*, supra. This case is not listed because the issue decided by the Supreme Court involved principally punitive damages (which represented \$10 million of the \$10.5 million originally awarded). The personal injury award, the Court of Appeals decided, should have been decided under state workers' compensation law.

- *Allen versus United States*, 588 F. Supp. 247 (D. Utah 1984): wrongful death and personal injury claims from radioactive fallout from open air testing of nuclear weapons -- eight wrongful death verdicts from \$235,000 to \$625,000 and a personal injury verdict of \$100,000.
- *Kerksieck versus McDermott Inc.*, Louisiana district court, 16th judicial district, St. Mary's Parish, 1991: pre-cancerous thyroid condition and pancreatic carcinoids from gamma radiation -- compensatory damages of \$415,000 (\$180,000 of which was for future medical expenses).
- *In Re: Fernald Litigation*, U.S. District Court, S.D. Ohio, No. C-1-85-0149, filed September 29, 1989: settlement fund of \$73-78 million created by United States for radioactive fallout from Fernald affecting a 14,000-person class. Covered by the fund are medical monitoring, emotional distress, and diminution in property values.
- *Ochiuto versus Johns-Manville Corporation*, 1992 WL 67140, A.2d (Pa. Super. April 7, 1992): \$400,000 to husband and wife for husband's exposure to asbestos resulting in increased risk of cancer (pleural thickening) and resulting emotional distress.

- Ward versus Terminix, 1991 WL 87336 (Tenn. Ct. App. May 29, 1991): In this case, a chemical (ostensibly a fungicide) was applied to portions of a house occupied by a mother and two daughters. The chemical had been inadvertently mixed with another that caused plaintiffs to suffer physical symptoms, e.g., dizziness, memory lapses. The mother was awarded compensatory damages of \$1 million and each of two daughters were awarded compensatory damages of \$500,000 each. The daughters' verdicts were subsequently reduced by the trial judge to \$100,000.
- Moran versus G. & W.H. Corson, Inc., 402 Pa. Super. 101, 586 A.2d 416 (1991): wrongful death action based on decedent's exposure to asbestos and contracting mesothelioma. Three defendant's settled for a total of \$500,000.
- Potter versus Firestone Tire and Rubber Co., 232 Cal. App. 3d 1114, 274 Cal Rptr. 885 (Ct. App. 1990): Defendant put carcinogens in water supply, which plaintiffs drank. Although there were no physical manifestations or any other evidence showing that cancer was likely to occur, each property owner was entitled to \$200,000 for fear of getting cancer.
- Eagle-Picher Industries versus Balbos, 84 Md. App. 10, 578 A.2d 228 (Ct. Spec. App. 1990): Defendant survived husband by 17 months. Husband died from occupational exposure to asbestos. Decedent's estate was awarded \$750,000 essentially for decedent's emotional suffering, inasmuch as there was little proof of other damages.
- Novelli versus Johns-Manville, 395 Pa. Super. 144, 576 A.2d 1085 (1990): Decedent's estate received \$700,000 in compensatory damages for his death from mesothelioma and widow received an additional \$150,000 for loss of consortium.
- Nussbaum versus Gibstein, 531 N.Y.S. 2d 276 (N.Y.A.D. 1988): Jury awarded \$500,00 for pain and suffering and loss of enjoyment of life. This malpractice suit involved a 35 year-old women's two-year losing battle with breast cancer.

In summary, it appears that society, through the legal system, has shown an increasing willingness to share the burden of illness and injury that befall the individual. This attitude is particularly evident in matters of radiation cancer and injury. Mr. Don Jose, Esquire, legal expert on radiation injury claims, in a personal communication has stated:

" . . . My personal belief is that every radiation case is a million-dollar case even though the person had no cancer or disease (Silkwood = 10.5 million) or had a benign thyroid condition (Kerksieck = 1.245 million). Thus, I would assess a value of around \$750,000 to \$1,250,000 for any thyroid problems resulting from an accident at a nuclear power plant. This number is a market value and the market is the legal system. This number is likely to be what an innocent victim could recover if they sued the owners of the nuclear power plant."

Based on the monetary awards for the radiation and non-radiation injury claims cited, and the opinion expressed by a subject matter expert, the psychological cost component for any radiation-induced thyroid health effect is estimated at \$500,000 and will be applied to the derivation of cost-benefit ratios for KI prophylaxis.

Summation of Thyroid Health Effects Cost

Table D-18 summarizes previously derived values for the direct medical costs, the indirect cost of lost economic opportunities, and the psychological costs attributed to the reduced quality of life for each of the thyroid disorders considered in this report. For all thyroid effects, the direct medical cost for diagnosis, treatment, and follow-up represents the smallest contribution to the total cost. The assigned common value of \$500,000 for psychological costs dominates the total costs of potential thyroid effects.¹

Table D-18. Average Total Cost Per Radiation-Induced Thyroid Effect

Thyroid Effect	Direct (\$)	Indirect (\$)	Psychological (\$)	Total (\$)
Nodule	9,600*	33,300	500,000	542,900
Cancer				
Non-fatal	20,000	38,600	500,000	558,600
Fatal	32,000	629,000	500,000	1,161,000
Hypothyroidism	5,600	38,200	500,000	543,800

* Value represents the mid-point of the range in direct medical cost estimates.

¹ Although the indirect cost of \$629,000 for a fatal thyroid cancer is considerably larger, the low frequency of fatal cancers among thyroid effects (<3.5%) mitigates its impact on the average indirect cost of thyroid disorders.

In Utero Cost Estimates. Fetal exposure in utero may also result in thyroid nodules, thyroid cancer, or congenital hypothyroidism. The resultant cost elements are similar to those involving the general population, but are somewhat higher in value to reflect the earlier age at time of first diagnosis. Affected by this shift in time are costs associated with long-term medical care and surveillance, as well as indirect costs. When in utero exposure results in thyroid disorders, the costs are based on the following ages of initial diagnosis:

- hypothyroidism: at time of birth
- thyroid nodule: at age ten
- thyroid cancer: at age five
- for fatal thyroid cancer, the time of death is assumed to occur at age 14.4

The costs of thyroid effects that are the result of in utero exposure are summarized in Table D-19.

Table D-19. Cost Estimates of Thyroid Effects for In Utero Exposure

In Utero Thyroid Effect	Direct (\$)	Indirect (\$)	Psychological (\$)	Total (\$)
Nodule	17,000	53,000	500,000	570,000
Cancer				
Non-fatal	24,000	56,000	500,000	580,000
Fatal	32,000	N/A	500,000	532,000
Hypothyroidism	11,000	79,000	500,000	590,000

An Evaluation of Derived Cost Estimates

The appropriateness of monetary values for thyroid dysfunction and neoplasms derived in this report may be assessed by comparing these values to those that have previously been endorsed by the NRC and other Federal agencies. For example, as part of a study performed by Sandia National Laboratories to estimate the financial consequences of reactor accident health effects (NUREG/CR-2723), cost estimates were determined for on-site emergency workers for five severe accident categories. Health effect "costs" to emergency utility workers were converted to dollar-equivalents using the following conversion: (1) \$1 million per early fatality, and (2) \$100,000 per early injury or latent cancer. These 1983 cost estimates, when adjusted to the current medical costs and market value of the dollar, yield cost estimates that are very comparable to those defined in this report. It may further be argued that cost estimates derived in this report are subject to an adjustment factor, which accounts for the difference in the involuntary non-occupational exposure of a member of the general public and the "voluntary"

exposure conditions of the utility emergency worker. As a rule, it is appropriate to assign a higher compensation value in instances of involuntary participation.

In a more recent value impact analysis involving public exposure to radon, the EPA evaluated the cost effectiveness of radon testing and radon mitigation for five different action levels of residential indoor radon (EPA 1992). Table D-20 provides a summary of the results of EPA's analysis of action levels. The results of this cost-effectiveness analysis show that the EPA's selection of 4 pCi/l, as its recommended action level, would result in a cost of roughly \$700,000 per lung cancer death averted. At this action level, the EPA concluded that ". . . the Radon Program would be as or more cost-effective than many other government programs for personal safety and environmental protection."

Table D-20. Cost Per Life Saved for EPA's Radon Testing and Mitigation Programs

Action Level	Number of Lives Saved Annually	Annualized Cost (1,000s of 1991 \$)	Average Cost per Life Saved (1,000s of 1991 \$)
2 pCi/l	3,100	3,421,000	\$1,110
3 pCi/l	2,600	2,181,000	800
4 pCi/l	2,200	1,504,000	700
8 pCi/l	1,100	501,000	400
20 pCi/l	220	116,000	500

In conclusion, values cited in Tables D-18 and D-19 are in agreement with values cited in other Federal impact analyses and publicly implied valuations of Federal program areas defined in Table D-3.

APPENDIX E

KI EXPERIENCE IN PAST NUCLEAR EMERGENCIES

Although there had been previous reactor accidents, it was the Three Mile Island Accident on March 28, 1979 that initiated major review of existing policies by regulatory agencies and public officials responsible for protecting the public in the event of a nuclear emergency. The TMI Accident demonstrated that (1) when KI prophylaxis is not an integral part of a nuclear emergency plan, and (2) if no readily available stockpile of KI exists, a decision by public officials to mitigate thyroid exposure following the declaration of a nuclear emergency cannot succeed.

The success of KI prophylaxis even if these two conditions are met may be less than optimal. In response to the TMI experience, Tennessee State health officials attempted to provide KI tablets for near-field residents under the simulated conditions of a nuclear emergency drill. Distribution at the time of a nuclear emergency proved too slow to avoid the initial plume inhalation exposure to near-field residents. In recognition of this potential limitation, Tennessee State Health officials in 1981 conducted a pilot project in which KI was predistributed to residents within a five-mile radius of the Sequoyah nuclear facility. Authorities considered predistribution as the preferred option of providing prompt access to the drug for those persons at highest risk and most likely to benefit by its early administration.

The accident at the Soviet Chernobyl nuclear facility on April 26, 1986, which involved massive releases of radioiodine, tested the efficacy of the Soviet emergency plan in providing KI to near-field residents from existing stockpiles. KI was also administered to far-field residents of Poland where fallout of radioiodine resulted in significant air concentrations and contaminated food products.

This appendix briefly describes these three events and identifies salient findings that may be useful in reassessing Federal and State policies regarding KI prophylaxis.

The Three Mile Island Experience.

In the early morning hours of March 28, 1979, the Unit-2 reactor at the Three Mile Island Nuclear Station located in south central Pennsylvania experienced a loss of feedwater to the steam generators. Because of a combination of design deficiencies, mechanical failures, regulatory policies, training inadequacies and human errors, the initial loss of feedwater progressed to the point of severe fuel core damage and the atmospheric release of radioactivity.

Following the accident, extensive investigations were conducted (NUREG-0588; NUREG-0600; NUREG-0637). It was concluded that 30% of the core inventory of iodines was released from the damaged fuel into the primary coolant. However, the majority of iodine was chemically absorbed by the coolant, which was enhanced by increasing the alkalinity through the deliberate injection of sodium hydroxide. The general reducing environment created by a hydrogen-rich

mixture of steam, water, and hydrogen in which little or no free oxygen was present promoted the formation of metallic iodides. The majority of the iodine released in the partial core melt at TMI was found to have been converted to cesium iodide, a highly water soluble and relatively nonvolatile compound. Thus, the cesium iodide was largely retained in the water that leaked from the primary containment structure or was retained within the reactor's primary system. Although the containment building was not completely isolated, there was no structural failure of the reactor containment building at TMI. The release of radioactivity occurred through penetrations in the secondary systems of the auxiliary building. Of a total inventory of 64,000,000 Ci of I-131, only about 17 Ci were released to the environment, yielding a release fraction of 2.7×10^{-7} .

The average thyroid dose from internal exposure to the released radioiodine to the near-field population has been estimated at less than 0.001 rad with an upper limit individual exposure of about 0.02 rad.

While in retrospect these small quantities of released radioiodine and the resultant insignificant thyroid exposure did not warrant the prophylactic use of potassium iodide, the potential did exist for release of large quantities of radioiodine. The ability to implement KI prophylaxis was compromised because there were no commercially available preparations of potassium iodide in suitable form and quantity for timely public distribution.

Only months earlier, the FDA had solicited sponsors for new drug applications (NDAs) for KI as a non-prescription drug in oral dosage form for use as a thyroid-blocking agent in a radiation emergency (43 FR 58798, December 15, 1978). At the time of the TMI Accident, no NDAs had been received. The FDA's concern for high thyroid exposure on March 29th prompted its Bureau of Drugs to petition on an emergency basis drug manufacturers and pharmaceutical suppliers for the needed potassium iodide. It was estimated that the equivalent of 7,500 kg of KI was needed in a saturated solution (SSKI). FDA's request could not be met: companies had neither the quantity of KI and containers, nor the facilities to manufacture SSKI within the needed time frame.

A chemical manufacturer, Mallinckrodt Company, had the necessary quantity of KI and mobilized a workforce on an emergency basis. Joined by Parke-Davis Company, SSKI was delivered to Harrisburg as quickly as it was being manufactured over a period of several days, with the first shipment of 11,000 bottles arriving at 11:00 p.m. on March 31st (Halperin 1989). Over the next four days, six more shipments totaling 225,033 bottles arrived in Harrisburg with the last shipment arriving at 9:00 a.m. on April 4, 1979.

Under these emergency conditions, the manufacturers experienced problems with labels and erroneously included droppers not calibrated to deliver the 65 mg of KI per drop for a two-drop dose. By the time the various problems had been resolved and a decision was made to provide SSKI to area residents of the TMI facility, the risk of radioiodine release had declined considerably and the State decided not to use the drug.

The Tennessee Experience

Following the Three Mile Island Accident and the failure to provide KI to the public in a timely manner, an attempt was made to simulate distribution of KI to area residents as part of a nuclear emergency drill at the Sequoyah Plant operated by the Tennessee Valley Authority. On two separate occasions, the simulated distribution of KI to downwind residents was considered "too slow" with respect to plume arrival time in order to protect residents effectively (Fowinckle 1983).

As a result, Tennessee public health officials decided to predistribute KI to residents within a 5-mile radius of the power station. A significant consideration was the anticipated degree of public acceptance and anxiety induced by the predistribution of KI tablets. While TVA officials expressed concern and recommended that predistribution not be undertaken, State health officials, nevertheless, proceeded on the premise that open communications and proper explanations can achieve public acceptance. The method for predistribution included the following:

- (1) A letter from the Tennessee Commissioner of Public Health was mailed to respective households. The letter advised recipients that a member of the local health department would come to their home to deliver a vial of KI tablets and to explain their proper use.
- (2) The field staff selected to make house-to-house deliveries were professional personnel who were experienced in communicating with the public. A total of 38 individuals were given a one-day training session to ensure their ability to provide technical information and respond to potential questions.
- (3) News media reporters were also encouraged to attend the one-day training session, which schooled the home visitors for their tasks. News coverage of the project was extensive and involved local and national television and newspapers. Dr. Fowinckle, Director of Tennessee's State Health Department, stated that ". . . during the week preceding and the first week of distribution, there was intense public interest. Answering questions from the press and the public required almost all the time of two physicians. Thereafter, each Monday and Tuesday produced a large number of inquiries during the six-week period when KI was distributed" (Fowinckle 1983).
- (4) Each household was provided a package containing a child-proof capped vial of 14 tablets each containing 130 mg KI. This quantity was considered sufficient to give household members a starter dose for thyroid blocking and yet be insufficient to cause serious consequences if an overdose were taken accidentally or the package instructions were ignored.
- (5) The labeling on the vial and a package insert from the manufacturer provided carefully worded information and instructions that the drug was to be used only for thyroid-blocking in a radiation emergency.

Program Effectiveness:

The KI packages were distributed door to door from November 16 through December 11, 1981. The 38 health department staff members spent 166 person-days visiting 5,591 households. A total of 3,022 households accepted the tablets. If residents were not home, a letter was forwarded which informed residents of their option to pick up KI tablets at one of two local health care centers. An additional 682 household members responded, which brought the total to 3,704 households or 66% of the total households in the area.

Health officials suspected that a significant percent of the 34% of the households where door-to-door distribution was unsuccessful represented summer residents of cottages who, during the time of KI predistribution (November/December), had vacated their residence (Dr. Sarah Sell, 1991 - personal communications).

Additionally, a supply of 450 vials was provided to two schools located within the five-mile radius in order to provide a first dose to the 6,100 students at those schools.

In the fall of 1984, three years after the initial door-to-door predistribution of KI, residents within the same five-mile radius were contacted by mail and advised that their supply of KI had expired its shelf-life and that a new supply of KI was available for pickup at the local health department. Those that received KI previously could exchange their expired KI for a new supply; and those who had either lost or had never accepted any previously could also obtain a new supply.

Thirty-two percent of the eligible households responded by coming to the health department. This response can be compared to the 66% of households that initially accepted the KI distributed door-to-door in 1981. To date, there have been no reports of accidental administration or adverse effects of misuse of predistributed KI (Dr. Sarah Sell 1991 - personal communication).

In summary, the Tennessee State health officials considered the predistribution pilot program a "success," but no official cost-benefit analysis was performed. While it is difficult to argue the benefits of prompt access to KI to near-field residents who would most likely experience the highest thyroid doses with the shortest time interval, predistribution is considerably less efficient than might be expected. The cost of predistribution is considerably higher than that of stockpiling.

For a KI prophylaxis program limited to local stockpiles, the program costs are primarily those of initial purchase and five-year replacement at the estimated price of \$0.70 per vial of 14 tablets. In contrast, predistribution includes the up-front costs associated with predistribution, which are independent of the unlikely occurrence of a major nuclear accident. Based on the Tennessee experience, the collective cost for the predistribution of 3,704 vials to a corresponding

number of households was estimated at \$125,000 (Fowinckle 1983; and Fowinckle 1991 - personal communications). The unit cost of predistribution at about \$30 per vial can, therefore, be estimated to be 42 times the cost of stockpiling.

The Chernobyl Experience

Soviet Union. The accident at the Chernobyl nuclear power station occurred on April 26, 1986, at 1:23 a.m. This facility is located three km from the nearest town of Pripyat and 30 km from the nearest city of Kiev. The phenomena associated with the Chernobyl accident, including release fraction, duration, rate, and pathways for environmental release, were greatly influenced by design features and materials unique to the RBMK-1000 reactor, which differ from those of U.S. commercial power reactors. Thus, the Chernobyl data on radionuclide release are not directly applicable to predicted releases from U.S. reactors.

Moreover, the release of radionuclides from Chernobyl did not occur as a single acute event. Only about 25% of the radio-particulate release to the environment took place in the first 24 hours (Table E-1); the remaining 75% of the activity was released as a protracted process (NUREG-1250). Nevertheless, owing to the high temperature of the molten fuel, the initial explosion and fuel fragmentation disproportionately released volatile radionuclides of radio-iodine, -tellurium, and -cesium. It is estimated that of the 7.3 million curies of I-131 released in total, about 4.5 million curies were released in the first 24 hours (NUREG-1250).

**Table E-1. Daily Releases of Radioactivity into the Atmosphere
(Exclusive of Noble Gases)**

Date	Days After Accident	Quantity of Activity (Mega Curies)
4/26	0	12
4/27	1	4.0
4/28	2	3.4
4/29	3	2.6
4/30	4	2.0
5/1	5	2.0
5/2	6	4.0
5/3	7	5.0
5/4	8	7.0
5/5	9	8.0
5/6	10	0.1
5/9	14	0.01

The radiological conditions in the near-field and far-field were complex and profoundly affected by the release conditions and the changing meteorological conditions prevailing over the ten-day period. In the first hours after the accident, the radioactive release bypassed the town of Pripyat; but later when the effective release height declined substantially along with changes in the wind direction, contamination and gamma dose-rate levels increased to alarming levels. By 7:00 a.m. on April 27, 1986, the gamma dose rate in areas closest to the plant had reached 180 to 600 mrem per hour levels (II' in 1987).

The Soviet radiation emergency preparedness plans included procedures for stockpiling and distribution of potassium iodide tablets. KI tablets were made available to on-site personnel at 3:00 a.m. on April 26, one-and-a-half hours after the accident. On the assumption that local residents were at home asleep with closed windows (i.e., effectively sheltered) during the first few hours, public notification of the accident was delayed until morning. Door-to-door distribution of KI tablets to the 45,000 residents of the town of Pripyat commenced at 8:00 a.m., or six-and-one-half hours after the accident. It took much longer, from April 28th to the first days in May to complete distribution of KI to an additional 90,000 persons residing in 71 villages within a 30-km radius of the damaged plant.

In light of predictions that the external exposures received by near-field residents might exceed the protective action level used in the Soviet Union, it was also decided to evacuate the inhabitants of Pripyat and several other nearby population centers. The criteria in the Soviet Union for taking protective measures are provided in Table E-2.

**Table E-2. Soviet Criteria* for Taking Protective Actions
(Ref. II'in 1987)**

	Level of Exposure	
	A	B
• External gamma radiation (rad)	25	75
• Thyroid exposure due to intake of radioactive iodine (rad)	25-30	250
• Integrated concentration of iodine-131 in air (micro-curie per day per liter)		
Children	40	400
Adults	70	700
• Total intake of iodine-131 with food (micro-curies)	1.5	15
• Maximum contamination by iodine-131 of fresh milk (micro-curie per liter) or daily food intake (micro-curie per day)	0.1	1
• Initial iodine-131 fallout density on pasture (micro-curie per square meter)	0.7	7

Notes:

If exposure or contamination does not exceed level A, emergency measures that involve the temporary disruption of the normal living routine of the public are not needed. If exposure or contamination exceeds level A but does not reach level B, it is recommended that decisions be taken based on the actual situation and local conditions.

If exposure or contamination reaches or exceeds level B, it is recommended that emergency measures be taken to ensure the radiation protection of the public; the public should immediately seek shelter indoors; time spent outdoors should be restricted; on the basis of the actual situation, rapid evacuation should be organized; prophylactic iodine should be distributed; the use of contaminated products in food should be banned or limited; dairy cattle should be switched to uncontaminated pasture or fodder.

The decision to evacuate the local population was based on a projected external exposure value in excess of the lower level (level A or 25 rem). For internal exposure of the thyroid due to inhalation of radioiodine, the decision to evacuate was based on the upper level B or 250 rads to the thyroid. These selected dose levels of intervention fall within the range of the two levels of intervention cited by the ICRP, WHO, and the IAEA for decisions to evacuate populations at an early stage of an accident (i.e., 5 to 50 rads for whole body exposure and 50 to 500 rads for thyroid exposure).

Orders for the evacuation of the 45,000 residents of Pripjat were announced at 12:00 hours with buses arriving from Kiev at 14:00 hours on April 27 (36 hours after the accident). Evacuation was completed in three hours. Evacuation of the additional 90,000 residents within the 30-km

radius started several days later and was not completed until one week after the accident. Among the 135,000 persons administered KI and subsequently evacuated were about 2,000 pregnant women.

Estimates of Public Exposure

The combined protective actions of sheltering, decontamination efforts, limiting ingestion of contaminated food products, potassium iodide prophylaxis, and evacuation have been credited for reducing exposures among residents living within the 30-km radius of the plant. With the exception of evacuation, which was slowed by the absence of privately owned vehicles, the Soviets were otherwise prepared to enact emergency measures including KI distribution. School children received KI in most instances within six hours of the initial releases. The use of KI by the approximately 135,000 individuals in the immediate area of Chernobyl did not result in any adverse side-effects requiring hospitalization. Among residents of Pripyat and those within a 30-km radius, average exposure to the whole body has been estimated at 3.3 rem and 16 rem, respectively (NUREG-1250). Although a precise measure of the prophylactic value of KI is difficult to ascertain, thousands of thyroid activity measurements of individuals in the exposed population suggest that the observed levels were markedly lower than those that would have been expected had the prophylactic measure not been taken (Table E-3).

Table E-3. Thyroid Burdens to Near-Field Residents of the Chernobyl Nuclear Facility (Ref.: Linnemann 1987)

Thyroid Burden (μ Ci)	Persons Affected (%)
< 20	87
< 50	94
100 - 150	1.5
> 200	0.5

In August of 1991 (08/03 to 08/17), the World Federation of Ukrainian Medical Association (WFUMA) held its third congressional session which specifically addressed medical consequences including thyroid disorders, to residents of the most highly contaminated regions of the Ukraine. Included were regions well beyond the 30-kilometer radius where KI had not been distributed. On the basis of radioiodine intakes by inhalation and consumption of dairy products as well as measurements performed on populations, thyroid doses were estimated. Using a "realistic" rather than a conservative model, the following thyroid doses among children were estimated (Shandala 1990):

- 56,000 children received thyroid doses of up to 30 rads.
- 29,000 children received thyroid doses between 30 and 200 rads.
- For 7000 children, the thyroid dose is thought to have exceeded 200 rads.
- Based on risk models used by the WFUMA, it was estimated that the collective thyr-o-oncogenic dose of 7,400,000 rads among these children could cause about 300 future thyroid malignancies¹.
- For a significant number of children, the individual thyroid exposures exceeded the threshold dose for hypothyroidism. For the collective 4,200,000 thyroid rads in excess of threshold levels, 418 cases of hypothyroidism were estimated.

The impact of radiation exposure on thyroid endocrinological and auto-immunological status was also evaluated. Measurements among 1,074 exposed pregnant women and 9,560 neonates showed an elevated level of thyrotropin hormone and T₄ (Yakolev 1991; Oliinyk 1991). Children evaluated for their immunological competence showed a generalized weakening of T-cell mediated immunity (Chaban 1991). This evidence may imply an increased risk of auto-immune disease of the thyroid gland in the future.

The Chernobyl Experience: Poland

The effective release height generated by the intense heat of the Chernobyl accident was such that radioactive fallout outside the Soviet Union was sufficiently high to prompt various protective measures including KI prophylaxis. Plume arrival in northeastern Poland was thought to occur some time during the night of April 27 (Linnemann 1987). Analysis of air samples by the Polish Central Laboratory for Radiological Protection verified the presence of radioiodines and other nuclides around noon on April 28. High air concentrations of I-131 in most parts of Poland lasted from April 29 to April 30, reaching a maximum value of 5.4 nCi/m³. In the early hours of April 29, a Polish governmental task group evaluated the radiological situation and established the following protective actions with respect to thyroid exposure (Nauman 1988):

- (1) The committed thyroid dose in persons less than 16 years of age should not exceed 5 rem.
- (2) The committed thyroid dose for persons over the age of 16 years should not exceed 50 rem.

¹ Using the lifetime risk coefficients for I-131 employed in this report, approximately 381 thyroid malignancies would be expected among this highly exposed population of children (i.e., $(31.5 + 71.5)/2$ thyroid cancers per 10^6 thyroid rads = 381 thyroid malignancies).

On the basis of radiological factors and the low dietary content of iodine among Poles, the government at 3:00 p.m. on April 29 approved the prophylactic use of potassium iodide to block further exposure from inhalation and ingestion as well as to minimize the recirculation and reutilization of radioiodine that had already been taken in. The decision initially limited iodide prophylaxis to children and teenagers and recommended the following daily doses of KI:

- less than two years: 30 mg
- two to five years: 50 mg
- five years and older: 70 mg

Initially, the protective administration of potassium iodide was not recommended for adults. It was agreed that the thyroid cancer risk in this group was low and the possibility of adverse side effects was higher in this group than in younger individuals. The government also assumed a neutral position on iodide prophylaxis for pregnant females. The mass media was used to announce and outline the protective guidelines to the public. Potassium iodide was distributed in all kindergartens, schools, public health centers, and pharmacies. Volunteers were used to distribute KI to these centers. On April 30, radiological conditions worsened and government recommendations for iodide prophylaxis became considerably less restrictive.

Follow-up studies were undertaken to assess the effectiveness of KI prophylaxis. The Central Laboratory for Radiological Protection estimated committed thyroid dose equivalents in children and adults in two different parts of Poland where contamination was considered "moderate" and "severe." The results of this study were included in the Government Commission Report (Dziuk 1987) and the WHO Working Group Study (WHO 1986). A summary of their findings is presented in Table E-4 below.

Table E-4. Thyroid Doses for Protected and Unprotected Populations in Poland Following the Chernobyl Accident*

	Dose (rads)			
	<u>Without Protection</u>		<u>With Protection</u>	
	Adults	Children	Adults	Children
<u>Moderate Contamination</u>				
Inhalation	0.12	0.84	0.12	0.75
Ingestion	0.45	6.00	0.15	0.40
Total	0.57	6.84	0.27	1.15
<u>Severe Contamination</u>				
Inhalation	0.36	2.5	0.36	2.30
Ingestion	1.35	18.0	0.45	1.20
Total	1.71	20.5	0.81	3.50

The obvious conclusion cited by the study was that the prophylactic administration of KI was highly effective in reducing radioiodine uptake through ingestion, which contributed the bulk of the thyroid dose among unprotected individuals. Because KI prophylaxis had been delayed and did not commence for several days after the initial plume arrival, it did not significantly reduce thyroid exposure from inhalation.

Adverse Reactions to KI

The most likely population groups to manifest intrathyroidal adverse reactions leading to hypothyroidism and hyperthyroidism are neonates whose mothers were administered KI during pregnancy and older adults with underlying thyroid pathologies. Although the exact number of pregnant women who received KI is unknown, a best estimate assumes that approximately 10,000 pregnant females took 70 or 100 mg of iodide in single or repeated daily doses (Nauman 1988). Clinical data for 140,000 newborns delivered in the "severely" contaminated portions of Poland and tested for neonatal hypothyroidism indicate that neither radioiodine nor KI prophylaxis significantly affected the incidence rate of neonatal hypothyroidism (Nauman 1988). Among the approximately eight million adults who were administered KI, no single case of thyroiditis was reported. However, among an unspecified number of individuals with a history of Graves' Disease whom under medical supervision had become euthyroid, relapse was expected to have occurred in some, but this remains undocumented.

For extrathyroidal effects, Nauman (1988) reported the following: (1) Among the 10.5 million teenagers and children given KI, only a few minor to moderate allergic responses were noted and (2) for the eight million adults, severe but non-fatal anaphylactoid reactions were reported for only three individuals. There were, however, reports of nearly 5,000 cases involving mild to moderate reactions.

The adverse reaction incidence rates experienced by Poles are not directly applicable to U.S. populations due to significant differences in dietary levels of iodine.

Conclusions

The ability of stable iodide to block thyroidal uptake of radioiodine with an efficiency approaching 100% is a matter of scientific observation. For programmatic iodide prophylaxis, which is primarily directed to the plume inhalation pathway, the single most limiting factor effecting efficacy is time. For effective prophylaxis, stable iodide must be administered shortly before and no later than exposure to radioiodine. The potentially brief time interval between the initiating events of a serious nuclear accident and the subsequent release of radioactivity into the environment dictates the need for quick decisions and rapid implementation of emergency actions.

During the TMI Accident, the absence of available KI clearly limited its potential use. For any emergency plan with provisions to provide stable iodide to the general public, a readily accessible stockpile and a prompt method for distribution are essential requirements. Even when

these two requirements are met, distribution to residents in the immediate vicinity of a nuclear plant may not be achievable before plume arrival. Under conditions of delayed distribution, the residual prophylactic value would be limited to the balance of plume exposure following the administration of stable iodide. An alternative to the stockpiling option, is a limited predistribution of KI to nearby residents. The pilot project undertaken by the Tennessee State health officials, however, demonstrated the limitations and costs for this option.

To date, the only experience with KI prophylaxis involves the Chernobyl accident. In spite of claims that the Soviets were well prepared for such an emergency, KI distribution to nearby residents was delayed by hours to days following the initial burst of released radioactivity. Similar delays by government officials in Poland to make KI available, reduced or eliminated the efficacy of KI to prevent inhalation thyroid exposures. The bulk of iodide prophylaxis was restricted to the avoidance of thyroid burdens from ingestion of contaminated food products.

The ability to extrapolate the value of iodide prophylaxis based on the Chernobyl experience to a potential future accident in the United States is complicated by a host of differences that may either enhance or diminish its potential benefits or need. The following is a partial list of variables:

- Engineering design features of the Soviet RBMK-1000 reactor versus the typical United States LWR affect the accident scenario including release fraction, release rate, duration of release, etc.
- Housing and population density differences for the near-field populations. Population densities affected by multi-family residents in the Soviet Union have a profound affect on distribution procedures, methods, and distribution efficiency.
- Availability of privately owned vehicles may play a key role in the distribution of KI as well as the prompt and alternative protective measure of evacuation.
- Food distribution system and the degree of dependency on locally obtained food products. For the Soviet Union and eastern bloc countries, total or partial dependency on locally contaminated food products implies prophylactic benefits from the ingestion pathway. For U.S. populations, there is a lack of dependency on localized food products in the event of a nuclear emergency which, therefore, limits the value of iodide prophylaxis to plume inhalation of radioiodine.
- Dietary intake of iodine. A low dietary intake of iodine (i.e., 50-70 μg per day is common among European countries versus 125-700 μg per day in the U.S.) increases the thyroid uptake and thyroid dose for a given exposure condition. The prophylactic benefit of stable iodide is, therefore, enhanced by low dietary intakes. Offsetting this benefit is the adverse intra- and extrathyroidal effects associated with stable iodide that are disproportionately seen among persons with low dietary intakes of iodine.

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A generic difficulty countered in cost-benefit analyses is the quantification of major elements that define the costs and the benefits in commensurate units. In this study, the costs of making KI available for public use, and the avoidance of thyroidal health effects predicted to be realized from the availability of that KI (i.e., the benefits), are defined in the commensurate units of dollars.

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