UNITED STATES OF AMERICA
NUCLEAR REGULATORY COMISSION

BEFORE THE ATOMIC SAFETY AND LICENSING BOARD

In the Matter of
LOUISIANA POWER AND LIGHT COMPANY
(Waterford Steam Electric Station,
Unit 3)

Docket No. 50-382 OL

HEARING MEMORANDUM ON CONTENTION 8/9

Joint Intervenors' proposed Findings of Fact and Conclusions of Law discuss the evidence presented and applicable conclusions. Therefore, Joint Intervenors will not reiterate material contained in its Proposed Findings of Fact and Conclusions of Law. Only matters not discussed therein will be dealt with in Joint Intervenors' Trial Memoradum.

UNDISPUTED FINDINGS OF FACT AND CONCLUSIONS OF LAW

Joint Intervenors have no dispute with Applicant's Findings of Fact No. 3. All other proposed Findings of Fact and Conclusions of Law by Applicant are contested as stated.

THE RECORD

The Board may consider all papers listed or identified in Joint Intervenors' Pleadings. 10 C.F.R. 2.740(a), (b), all documentary evidence "as may be required for full and true disclosure of the facts," 10 C.F.R. 2.743(a) official records of a government agency, 10 C.F.R. 2.743(h), and all matters or facts which fall within the Board's expertise or brought to the Board's attention, 10 C.F.R. 2.743(i); and all facts contained in questions (cont'd next page)



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raised during limited appearer's appearances, 10 C.F.R. Part 2, App.A V,d)(1) and all other matters within the Board's discretionary authority, 10 C.F.R. 2.760(a).

Joint Intervenors, in proposed Findings of Fact and Conclusions of Law, have cited pertinent scientific papers and government studies which the Board may consider in making its recommendations as discussed previously. To refuse to take cognizance of pertinent, reliable evidence concerning the health threat to the people of Louisiana would constitute arbitrary and capricious action on behalf of the Board, and, would constitute a dereliction of the Board's duty to reach its decision only after a "full and true disclosure of the facts," 10 C.F.R. 2.743(a), and to consider whether the issuance of the license will be inimical to the health and safety of the public." 10 C.F.R. Part 2 App. A VIII(b)(b).

Many of the papers and studies referred to are contained in Joint Intervenors' Exhibits 1-27, citations of which were furnished to the Board and all counsel. The Board can and should consider all such exhibits as part of the evidentiary record of the hearings. Although Joint Intervenors' counsel agreed to the withdrawl of some exhibits, he acted without authority, and in disregard of his client's instructions. (See Affidavit attached hereto.) While ordinarily an attorney has discretion in such matters, it is clear from the record that Mr. Jones did not have such authority.

Mr. Jones was instructed that he could stipulate with all other counsel that the Board's ruling on the non-witness-authored SECB report would apply to all documents in the course of the hearings. Jones was not given authority to withdraw, without a ruling, Joint Intervenors' non-witness-authored documents. While decisions made on the part of an attorney regarding the admission of documents or exhibits are normally within counsel's purview, under these circumstances, to allow Mr. Jones' unilateral decision without authorization to prejudice the case of Joint Intervenors and the people of Louisiana whose interests Joint Intervenors are protecting would be a grave injustice and would deprive the court of probative scientific evidence which represents the vanguard of scientific research in this area.

Joint Intervenors' counsel at no time during the course of the hearings informed his clients that he had disregarded their instructions. This failure on counsel's part prevented Joint Intervenors from introducing such documents later on in the hearing because Joint Intervenors' had been led to believe that their exhibits had been excluded by a ruling of the court, thereby protecting their right to appeal on this ground. Joint Intervenors' understanding of their counsel's actions is confirmed by their repeated objections to "non-witness-authored documents" later in the hearings and acting counsel Groesch's objection to the double standard employed by the Board in excluding non-witness-authored exhibits offered by Joint Intervenors while allowing into evidence such documents offered by Staff and Applicant.

Under these circumstances Joint Intervenors are entitled to withdraw from counsel's stipulation and Joint Intervenors' exhibits should be considered by the Board. Staff and Applicant were informed of said exhibits well before trial and therefore would suffer no prejudice. In

the event that the Board does not consider said exhibits part of the evidentiary record and the testimony of Dr. Samuel Epstein, Joint Intervenors move to reopen the synergism hearings and/or hold new hearings on synergism issues in order to bring all probative evidene before the Board, which was excluded by Joint Intervenors' counsel's disregard of his client's instructions or by error committed by the Board.

## LICENSING RECOMMENDATIONS

Joint Intervenors have shown that the operation of Waterford 3 will have disastrous health consequences for the people of Louisiana, but, in the alternative only, if the Board recommends granting the Waterford 3 operating license, Joint Intervenors urge that any Waterford 3 operating license issued to applicant not permit radioactive emissions in each of the following categories: liquid, gaseous, iodine and particulate, to exceed 1/100 of the radioactive emission levels currently allowed by Nuclear Regulatory Commission Regulations contained in 10 C.F.R. 50 App. I.

ATOMIC ENERGY COMMISSION DECISIONS

A.E.C. decisions cited by applicant have no precedential or persuasive value in N. R. C. hearings. The A.E.C. was abolished because it perceived its role as promoting nuclear energy and protecting the nuclear industry rather than protecting the interests of the public. The abuses of public trust and lack of concern for public safety are too well known to require citation. It is inappropriate for the N.R.C. and its licensing boards to consider A.E.C. decisions.

POLITICS AND SCIENCE - THE RADIATION PROTECTION COMMUNITY

Joint Intervenors bring to the Board's attention material pertinent to the above issue recently discovered in Shutdown, The Book Publishing Company (1979) containing transcripts of testimony in Honicker v. Joseph P. Hendrie et. al., No. 78-3371, (M.D. Tenn. Oct. 2, 1978) at which hearing the Nuclear Regulatory Commission had the opportunity to cross-examine said witnesses and the issues involved were similar to those in this hearing. Accordingly, Joint Intervenors move to introduce said testimony of Dr. John Gofman and Dr. Ernest Sternglass at this time as material contained in government records. 10 C.F.R. 2.743(h)

Dr. Gofman , one of the fathers of the atomic bomb , author of 150 scientific articles concerning inter alia the medical effects of ionizing radiation , chromosomes and cancer and the hazards of plutonium and other sources of ionizing radiation, testified inter alia , that the A.E.C. did not look favorably upon scientests whose work showed that radiation was harmful because the thrust of their position was that there is a safe dose of radiation. Dr. Gofman testified that Dr. Arthur Tamplin, his colleague , had twelve of his thirteen staff members

taken away from him after publishing a paper showing that radiation would produce twenty times as many cancers per unit of radiation per unit of radiation as had been previously thought. Dr. Gofman testified that he lost two hundred fifty thousand dollars a year from his cancer chromosome work as a result of his position on the health hazards of ionizing radiation. Dr. Gofman also cited Dr. Thomas Mancuso as an example of the retribution visited by the government on those who expose the dangers of ionizing radiation and nuclear power plants. A former colleague of Gofman's, Dr. Donald Geesamen, who was one of the few persons doing work on the lung cancer hazards of plutonium for the A.E.C. and who felt that plutonium was more hazardous than was commonly accepted by the A.E.C. lost his position . All of the above cases were cases in which Gofman had personal experience and knowledge of.

Dr. Ernest Sternglass, professor and director of Radiological Physics at the University of Pittsburgh since 1967 and author of more than 100 scientific papers in the literature in the field of nuclear physics, radiological sciences, nuclear instrumentation, and biological effects of radiation on man inter alia, testified that Marvin Goldman, who testified before this Board, attempted to discredit his findings appearing in a 1963 edition of Science. In response to questions by N.R.C. counsel Dr. Sternglass testified that Dr. Goldman testified on behalf of utilities at various hearings at which Dr. Sternglass qualified as an expert on behalf of citizens' groups and intervenors. When asked whether he was aware that Goldman received an award from the A.E.C. Dr. Sternglass replied: "That is right, and the Atomic Energy Commission always awards these grants to the people who do its bidding."

Joint Intervenors upon request will supply the Board a copy of Shutdown containing such information and are attempting to secure copies

of said court proceedings for consideration by the Board and other counsel. Joint Intervenors have no objection to the Board or other counsel requesting that said transcript in No. 78-3371 being sent to a district court in Washington D.C.

Luke Fontana

Gary Groesch

For Joint Intervenors

I hereby certify that a copy of the foregoing pleading was served by deposit in the United States Mail, first class, postage prepaid, this 21st day of June, 1982 to the Atomic Safety and Licensing Board and all counsel of record.

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June 21, 1982

UNITED STATES OF AMERICA
NUCLEAR REGULATORY COMMISSION

BEFORE THE ATOMIC SAFETY AND LICENSING BOARD

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| In the Matter of | ) | |
| LOUISIANA POWER AND LIGHT | ) | Docket No. 50-382OL |
| (Waterford Steam Electric Station, | ) | |
| Unit 3) | ) | |

CERTIFICATE OF SERVICE

I hereby certify that copies of the following documents:

(1) JOINT INTERVENORS FINDINGS OF FACT AND CONCLUSIONS OF LAW ON CONTENTION 8/9 INCLUDING APPENDICES 1 THROUGH 7

(2) JOINT INTERVENORS FINDINGS OF FACT AND CONCLUSIONS OF LAW ON CONTENTION 17/26.

(3) MEMO ON JOINT INTERVENORS EXHIBITS WITH AFFIDAVITS

were served by deposit in the United States mail, first class, postage prepaid, this 21st day of June, to parties identified on the attached service list.

Luke Fontana and Gary L. Groesch
Counsel for Joint Intervenors

Dated: June 20, 1982

June 21, 1982

UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

BEFORE THE ATOMIC SAFETY AND LICENSING BOARD

| | | |
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| In the Matter of | ) | |
| | ) | |
| Louisiana Power &Light | ) | |
| | ) | Docket No. 50-382 OL |
| (Waterford Steam Electric Station, | ) | |
| | ) | |
| Unit 3) | ) | |

MEMO ON JOINT INTERVENORS EXHIBITS

Joint Intervenors, Oystershell Alliance and Save Our Wetlands, Inc., as part of the operating license hearings on Waterford 3 did proffer as Exhibits 29 scientific papers and documents relating to the Synergism contention 8/9 of said hearings.

Joint Intervenors also did produce 4 live experts. These experts did author some of these documents and scientific papers. The remainder were non-witness authored documents.

All of these documents were considered important toward the Synergism question which is a scientific question.

On March 27, 1982 Joint Intervenors did meet with their principal attorney, Lyman Jones, of the firm Gillespie and Jones. The purpose of the meeting was to decide the fate of the documents, especially the non-witness authored documents since it was felt they would be challenged by the Applicant and Staff on the following Monday, March 29, 1982, during said hearings.

There was considerable controversy on whether to argue each non-witness authored document on its merit. However, a compromise Jones did not want to argue on a case-by-case basis. position was reached. Counsel Jones would seek a ruling on the non-witness authored document, Joint Intervenors Proposed Exhibit #1, Surveillance, Epidemiology, and End Results. Joint Intervenors would agree to apply this ruling to all other non-witness authored documents.

On March 29 Counsel Jones did enter into stipulation with Applicant Counsel Blake only to surrender all non-witness authored documents if he would agree to withdraw objections to all witness

authored documents.

Staff counsel Turk reserved his right to question the admissibility of the witness authored documents. Regardless, Counsel Jones persisted in agreeing to the half-stipulation with Counsel Blake and agreed to surrender said documents.

Counsel Jones did not inform co-counsel Fontana or other members of the Joint Intervenors that no ruling had been made on non-witness authored documents as per the March 27 understanding.

Joint Intervenors were unaware that no ruling had been made on the admissibility of non-witness authored documents until they reviewed the transcripts of the Hearings (Tr. 1103-1108).

Respectfully Submitted,

Gary L. Groesch
Acting Counsel for Joint
Intervenors

Christine Duncan
Research Coordinator
Joint Intervenors

AFFIDAVIT OF CHRISTINE DUNCAN

BEFORE ME, the undersigned, there did appear, Christine Duncan, who duly being placed on oath deposes and says:

1. That she is a research coordinator for Joint Intervenors.
2. That she resides in Orleans parish in the state of Louisiana.
3. That she is aware of the contents of the 'Memo on Joint Intervenors Exhibits' and attests the information contained therein is true and correct to the best of her personal knowledge and belief.

Christine Duncan

SUBSCRIBED AND SWORN to before me, this 21st day of June, 1982.

NOTARY PUBLIC
MY COMMISSION IS FOR LIFE

AFFIDAVIT OF GARY L. GROESCH

BEFORE ME, the undersigned, there did appear, Gary L. Groesch, who duly being placed on oath deposes and says:

1. That he is the research coordinator and acting counsel for Joint Intervenors.
2. That he resides in Orleans Parish in the State of Louisiana.
3. That he is aware of the contents of the 'Memo on Joint Intervenors Exhibits' and attests the information contained therin is true and correct to the best of his personal knowledge and belief.

Gary L. Groesch

SUBSCRIBED AND SWORN to before me, this 21 st day of June, 1982.

NOTARY PUBLIC
MY COMMISSION IS FOR LIFE

UNITED STATES OF AMERICA
NUCLEAR REGULATORY COMMISSION

BEFORE THE ATOMIC SAFETY AND LICENSING BOARD

In the Matter of
LOUISIANA POWER AND LIGHT COMPANY (Waterford Steam Electric Station, Unit 3)

Docket No. 50-382 OL

Statement of the Case on Synergism

Joint intervenors allege that Applicant has not taken into account the synergistic and/or cumulative effects of ionizing radiation and the multitudes of carcinogens that already exist in the area around Applicants Waterford 3, a 1165 megawatt nuclear power plant located in Taft, Louisiana. This failure will result in excess mortalities and morbidities.

Hearings were held in New Orleans, Louisiana from March 23 through May 12, 1982. The evidence, the testimony, and arguments of counsel, now make the following:

Findings of Fact on Contention 8/9

1.

The Waterford 3 site is located 25 miles upriver from New Orleans at Taft, Louisiana, next to the bank of the Mississippi River. It is 127 miles from the Gulf of Mexico (see Map, Appendix 1). This site is surrounded by petro-chemical industries, chemical manufacturing plants and petroleum refineries. Liquid and airborne effluents from these industries are routinely discharged into the Mississippi River, whose water is used as a water source for over a million and a half people living in parishes along it.

2.

The Harris report (see Appendix II), submitted to New Orleans councilmen in November, 1974, clearly stated that persistent carcinogens (cancer-causing substances) are discharged into the Mississippi River, from the industries that border the river, and also from municipal discharges, accidental spills, and run-off from agricultural and urban areas.

3.

From a 1972 study (see Appendix III), forty-eight (48) organic compounds were identified in raw or treated water supplies at Carville, New Orleans (Carrollton Water Treatment Plant), and Marrero, Louisiana. Included were chloroform, hexachlorobenzene, zylene, ethyl benzene, dimethylsulfoxide, benzene, carbon tetrachloride, and chloromethyl ether. Although some of these chemicals are relatively low levels of exposure, preliminary epidemiologic studies of aggregate populations in Louisiana, Ohio, and New Jersey support the hypothesis that carcinogens in drinking water are related to human cancer. (See also Sworn Statement of Dr. S. S. Epstein, Ques. 13 and 14, Submitted as limited appearance)

4.

Dr. Velma Campbell, in sworn testimony, question 9, cited data taken from the SEER Program (National Cancer Institute), that is, "Cancer Incidence and Mortality in the United States, 1973-77," show high mortality rates for the New Orleans area, compared to the rest of the nation:

(a) Incidence rates (i.e., new cases of a disease in a population over a period of time), show that the average annual age-adjusted incidence

rates in the New Orleans area for the respiratory system (including lung) is 71.1/100,000, while nation-wide it is 52.6/100,000 - the highest in the nation! Females had an incidence rate for respiratory cancer of 30.0/100,000 compared to 24.4/100,000 for the United States. For bladder cancer the incidence rate for males is 27.7/100,000 compared to 25.8/100,000 for the United States. Incidence rates for blacks showed the highest rates in New Orleans for buccal cavity and pharynx (16.3/100,000), the digestive system (95.6/100,000), and the respiratory system (80.1/100,000) than other areas in the study. Black males had the highest rates for stomach cancer (29.0/100,000), and also black females for stomach cancer (13.3/100,000).

(b) Cancer mortality rates (i.e., the number of persons in a given population who die of given cause) also are very high in the New Orleans area compared to the rest of the national; the SEER Report shows these results for average annual age-adjusted mortality rates:
For all races, both sexes, New Orleans had the highest rate for all cancer sites combined (201.1/100,000), compared to the United States (166.5/100,000). Also, New Orleans had the highest rate for the respiratory system (50.8/100,000) compared to 39.7/100,000 nationwide; the highest for breast cancer (16.7/100,000) compared to 15.1/100,000 in the United States, and the highest in the urinary system (8.6/100,000) compared to 7.5/100,000 for the United States. New Orleans tied for highest with Connecticut for rectal cancer (5.4/100,000). Males are

highest in the New Orleans area for respiratory cancer at 94.0/100,000 and second only to Connecticut for colon cancer at 23.3/100,000. Males are also highest in the U.S. for liver cancer at 4.5/100,000. Average annual age-adjusted mortality rates for females, all races, also show the highest rates for all sites combined (152.3/100,000), compared to the other United States areas in the report. Females are second highest (to San Francisco) in pancreatic cancer, second highest (to San Francisco) in lung cancer, and second highest in rectal cancer, next to Connecticut. For Whites overall, both sexes, the New Orleans area is the highest in bladder cancer (5.3/100,000) and in lung cancer (46.1/100,000), and second highest in colon (19.5/100,000) and in rectal cancer (4.9/100,000). Blacks, overall, both sexes, are highest in the New Orleans area in all sites combined (243.9/100,000), in stomach cancer (15.4/100,000), in rectal cancer (6.9/100,000), and in respiratory cancer (58.5/100,000) than the rest of the United States.



Several cancer studies have been published with regard to the southeastern Louisiana area, including the New Orleans metropolitan area, and also parishes bordering the Mississippi River. A study done on lung cancer in Louisiana through death certificate analysis (Gottlieb, Pickle, et.al., JNCI, November, 1979) revealed approximately a two-fold excess risk of lung cancer associated with certain types of industries. Lung cancer

risk was also found among older men who had been employed in the petroleum industry and among male and female residents of towns where the petroleum industry was a major employer. In a study on pancreatic cancer mortality in Louisiana (Pickle, Gottlieb, AJPH, March, 1980), high pancreatic cancer mortality among white males in a cluster of Louisiana parishes was investigated. Excess risk was seen for workers in the oil refining and paper manufacturing industries, and for residents living near refineries. The latest Louisiana study, "Cancer and Drinking Water in Louisiana: Colon and Rectum" was published this year (Gottlieb, Carr, Morris, IJ of E, 1981). This study found a significant risk for rectal cancer associated with drinking water derived from the Mississippi River. A multi-dimensional contingency table analysis found the association between rectal cancer and surface water (Mississippi River water used for drinking water) significant at the 0.0001 level and not dependent on age, race, sex, and diet. Chlorination also associated significantly with rectal cancer. Among those who used river water, the risk increased inversely as the distance from the mouth, with greater risk downstream from the many industries which line the river.

6.

Dr. Velma Campbell in sworn testimony before the Atomic Safety and Licensing Board, did state, (Q.9), that along the Mississippi River

corridor between Baton Rouge and New Orleans, Louisiana, there is a larger burden of chemical exposures through air, drinking water, and occupation than in many other areas of the country. She also stated that rates of cancer for people who live along the lower Mississippi River in Southeast Louisiana are significantly higher than the national average, expecially for respiratory, urinary tract, and pancreatic cancers, and that epidemiologic studies have linked these high cancer rates to such exposures as use of the Mississippi River for drinking water, employment in shipbuilding and chemical industries, and residence near petroleum refineries. Dr. Campbell stated (in the same answer) that the people of this area (i.e., along the Mississippi River "corridor") face a potentially serious public health problem; that they are exposed to a vast array of chemicals from a variety of sources and that they also suffer a burden of cancer incidence greater than the national average, which is demonstrably related to those environmental exposures.

7.

Dr. Campbell, in her sworn testimony, Q.8, defined synergism as "the capacity of two (or more) substances when combined to cause more effect than either would cause acting alone." Dr. Samuel S. Epstein, who has published several papers dealing with synergism, gives a similar definition in his Sworn Statement (Ques. 8, 12) submitted as a limited appearance. The Board may consider the statement of Dr. Epstein pursuant to 10 C.F.R. Part 2, App. A, V (b)(4).

8.

Dr. Campbell stated in Q.9 that chemicals, radiation, and other agents, when found together in the general environment, may behave in ways not predictable by laboratory experiments in which these agents are isolated from each other. She stated that certain chemicals, particularly halogenated hydrocarbons, accumulate in animal and human tissues over time, prolonging and increasing the exposure of body tissues to the offending chemicals, thus increasing the possibility of ill effects, including cancer. Then Dr. Campbell stated(same Q.9) that it is now proposed to add another increment of risk to the already higher than average burden (of cancer incidence). She cited references from the medical literature that include significant research which supports the premise that small doses of radiation increase the development of cancer from exposure to some chemicals. She stated that the logical conclusion is that, to knowingly add radiation, even at low levels, to the chemical exposures confronting the presumably limited capacity of the human immune system is to greatly increase the risk of cancer for each individual who lives in the area, and (Q.12) that small children (less than seven years old) and older people (sixty years and older) are particularly vulnerable to this type of risk. This statement is supported by that of Dr. S.S. Epstein (Ques. 9, 19-21) submitted as limited appearance testimony.

9.

Dr. Carl Johnson, in his sworn testimony, Q.11, defined the term synergism as the action of two or more substances, chemicals, or agents to

achieve an effect of which each is individually incapable. He said that in the general population, one could expect to see this effect after exposure both to carcinogens in drinking water and to low levels of radiation emitted by a nuclear installation, in the exhaust from its smoke stacks and in its liquid effluents.

10.

In Q.13 Dr. Johnson said that exposure to external radiation will be the least important consideration. He stated that inhalation and ingestion of radioactive gases, vapors, and particulates in the air, in the water, or built up in the food chain, i.e., milk, meat, other produce, and grains, will be the most important source of exposure to the plant, and these sources of exposure have been very poorly evaluated.

11.

In Q.14 Dr. Johnson stated that in his study of cancer incidence around the Rocky Flats nuclear plant, he found an excess of leukemia, lymphoma, and myaloma, and cancer of the lungs, thyroid, breast, esophagus, stomach, and colon.

12.

In Q.15 Dr. Johnson said that, in regard to special segments of the

population more likely to demonstrate health effects from living in proximity to a nuclear installation, the fetus is considered about twenty times more sensitive to radiation than the adult, a child about ten times more sensitive to radiation than the adult, and in addition, people with defects in their immune system are considered to be much more prone to injuries from radiation.

13.

Dr. Johnson stated (Q.16) that the effects of radiation are considered to be cumulative. That is, one rem over thirty years will have about the same effect as a single exposure to thirty rems. He said that this has been fairly well demonstrated and accepted in many studies of radiation workers.

14.

Dr. Johnson, in Q.19, when asked about the special risks associated with ground water radionucleide contamination, given the special geographic circumstances of Louisiana, stated that there are special risks associated in ground water contamination with radionucleides, because of the high water table in Louisiana. He also state (Q.20) that we could expect to see a synergistic effect in Louisiana, where people may be exposed to high levels of chemical contamination in the water, along with normal exposure to radionucleides from nuclear plants in the air, water, or food. Dr. Johnson stated (Q.22) that he thinks that the introduction

of additional radiation in South Louisiana resulting from plant operations is unacceptable. Further, he doubts very much that actual exposures will be as small as this, especially considering the biological effects of the 240 radionucleides of importance released by nuclear power plants such as that proposed (see also pp. 1868 of Docket No. 50-382, the Cross-Examination of Dr. Carl Johnson, April 1, 1982). Dr. Johnson stated that many of these radionucleides are isotopes of trace elements and other elements important in nutrition; that they will be concentrated and stored in the body in places where they can do much harm. He said that no one has really done an adequate study of the molecular, cellular, and developmental effects of these 240 radionucleides; that no one really knows what the long-term effects of these radionucleides on the reproduction of man, animals, and plants will be.

15.

Dr. Johnson stated (Cross-Examination, pp. 1902, 1903, 1907, April 1, 1982) that he has seen records of very large releases of radioactive gases and radionucleides in exhaust plumes and liquid emissions from operating nuclear power plants, that releases of five reactors were reported in papers sent to him by the NRC, and in EPA reports. These published releases are considerably higher than the proposed releases of the Waterford 3 plant.

16.

Dr. Hemchandra Pandit, in his sworn testimony, (Q.9), defined synergism as a cooperative action of discrete agents resulting in a total effect which is greater than the sum of effects taken independently. He stated that it is known that synergism operates between chemical agents, such as drugs or environmental pollutants, and physical agents, such as ionizing radiation.

17.

In Q.14, Dr. Pandit stated that the damage due to elements of low-level radiation which get incorporated into the drinking water, the food, and ultimately into the body tissues is slow and cumulative and more dangerous than damage caused by external skin surface exposure, because the skin is much more resistant to the radiation. He stated that since the first phase of respiration is the exchange of gases between the atmosphere and the lungs, the gaseous radioactive materials present in the atmosphere get into the lung very quickly and cause more damage there than they do on the skin. From his studies of the urinary tract, he could say that the bladder would be at high risk for cancer too, since it endures prolonged exposure to carcinogens, including radioactive elements, concentrated in the urine.

18.

In Q.15 Dr. Pandit likened southern Louisiana's environment to the "Love Canal" because both ground water and the major river water are contaminated with chemicals such that all drinking water for the area populations contain some carcinogens. He said that the special risk posed by radionucleide contamination of Louisiana's water is that synergism could cause another Love Canal here.

19.

Dr. Pandit, in Q.17, stated that there was no question in his mind that the addition of nuclear power plant emissions to the Louisiana environment will greatly complicate the existing health problems due to chemical contaminants.

20.

Synergism is defined as "a more-than-additive effect" by Dr. Bross (sworn statement, Q.14). "When two factors jointly have an effect which is greater than additive, that is to say, greater than the sum of the effects of each factor acting separately, the relationship of the two factors is generally considered to be synergistic," (K.J. Rothman, p. 347, Vol. 108, No. 5, AJ of E, 1978). "Synergism has been most frequently regarded as a public health concept reflecting the situation in which joint exposure to two or more factors results in a greater number of cases of disease than exposure to the sum of the separate factors," according to W.S. Blot and N.E. Day, of the National Cancer Institute, in letter to the editor of the American Journal of Epidemiology (p. 99, Vol. 110, No. 1, 1979).

21.

Dr. Bross explicates in detail the mechanism by which radiation and chemicals cause cancer. "The first event in the long evolutionary biological process that ends with death from leukemia or other cancer is the occurrence of a biochemical lesion or break-point in the complex chemical structure of the DNA in the genetic material of a human cell... We know that this genetic degredation is the cause of cancer," (Exhibit 26). This mechanism is also described in response to Questions 20, 43, 44, 45, and 46 of Dr. Bross's sworn statement and in Exhibit 22. Neither Applicant nor NRC Staff witnesses refute or deny Dr. Bross's explanation of the ultimate

cause of cancer as a genetic break-point which can be caused by radiation and chemical agents. C.L. Greenstock and G.W. Ruddock support Bross's explanation of the initiation of cancer with chemical experiments which demonstrate "a mechanistic basis for synergistic effects between toxic chemicals and radiation." See attached Appendix IV, "Radiation Activation of Carcinogens and the Role of OH and $O_2$," for a detailed explanation on the molecular level of how synergism initiates genetic damage.

22.

In response to question 48 of his sworn statement, Dr. Bross states, "Synergism operates at low levels of exposure (and possibly more efficiently at these levels)." Allen Brodsky, in the NRC'c Office of Standards Development, strongly supports Dr. Bross's observations with his most significant preliminary studies of which the Board takes notice pursuant to 50 CFR 2. 743 (h), (i). Brodsky on p. 425 of his presentation, writes "The present stochastic two-sequential stage model does contain features, however, that could account for the sometimes greater carcinogenic response observed for the same dose given at lower dose rates (within a certain range) - both for radiation as well as chemical carcinogens. Lower dose-rates and extended durations of irradiation, would particularly be more effective in situations where radiation was acting primarily as a promoter in the presence of active chemical initiators in the environment." See attached Appendix V.

The earliest adverse effects upon a population exposed to low levels of radiation and chemical agents are manifested upon young children, infants, and fetuses. Effects evident in the two former groups can be due either to direct exposure, or to in utero exposure, or to preconception parental exposure. Effects on the fetus, obviously, are due either to exposure of the pregnant mother or to exposure of either or both parents prior to conception. Children, infants, and fetuses, being the first affected by cumulative and/or synergistic risk factors is due to the fact that they are among the most sensitive members of any population in terms of immune defense systems and genetic vulnerability. "The studies of childhood cancers caused by X-rays during pregnancy suggest that the infant is 5 to 10 times as sensitive as an adult," (R. Wilson, p. 47, Vol. 51 of Yale Journal of Biology and Medicine, 1978). "Radiation received in utero is probably about five times as likely to produce leukemia per rad as in the adult," (N. Stannard, p. 98, Nuclear Power and the Public, ed. H. Foreman, 1971). "The absolute excess of leukemia and other cancers per rad is higher following prenatal irradiation than following postnatal irradiation... susceptibility to the induction of thyroid cancer is higher in those irradiated during childhood than in those irradiated during adult life," (A.C. Upton, p. 484, Origins of Human Cancer, Book A, Incidence of Cancer in Humans, ed. by Hiatt, Watson, Winston, 1977). Excessive sensitivity to drugs and environmental chemicals is well established in the medical literature

on children, infants, and fetuses. It should be noted that adult members of the population, being less sensitive to genetic damage, may exhibit either similar or different health effects and may exhibit effects only after a longer exposure than younger population members. (Bross sworn statement, Q.38).

24.

Dr. Bross provides evidence for synergistic radiation effects which do not involve joint chemical exposure. Low level radiation to both parents produces health effects on offspring which exceed control group effects by a factor which is larger than the sum of factors by which individually exposed parent groups exceed the control group effects. (Bross sworn statement, Q. 35, 36, 37).

25.

It is an established fact, known to and relied upon by the scientific community, that fractionation of radiation dose does not diminish the carcinogenic effect which would result from a single exposure to the same total dose of radiation. This was documented by the BEIR I Report in 1972 and is supported throughout the independent scientific literature. This observation strongly supports the contention that radiation health effects are cumulative over time in a given population. To the extent

that radiation and chemical carcinogens operate by similar mechanisms upon the genetic material, the observation concerning fractionation of radiation dose indicates that chemical agents and radiation can have a cumulative health effect over time on a given population where chemical "fractions" and radiation "fractions" act interchangeably and thus cumulatively. Dr. Goldman and Dr. Hamilton clearly subscribe to L.J. Cole's and W.A. Foley's conclusions about radiation dose fractionation in the presence of carcinogens which are the "Fractionated X-radiation (50R X 6 given daily) plus urethan (0.2 mg/g) elicited a higher lung tumor frequency than observed in several appropriate control groups... fractionated X-rays yield an over two-fold increase in tumor multiplicity per mouse." This paper is cited as Reference 8 by Dr. Hamilton and as Reference 11 by Dr. Goldman in their Direct Testimonies.

26.

The Board finds that it is well established in the scientific literature that health effects and/or genetic effects caused by exposure to chemicals and radiation are cumulative or additive in an exposed population over time. This is established in Dr. Bross's sworn statement: Q. 17, 23, 24, 25; and in his published report, "Cumulative Damage in Children Exposed to Preconception and Intrauterine Radiation," (Investigative Radiology, Vol. 15, No. 1, p. 52, 1980).

27.

Despite the lack of direct experimental evidence (in human populations) of synergism at low or environmental levels of radiation and chemical agents, circumstances in the U.S.S.R. duplicate those which would be created in South Louisiana, should Waterford 3 operate for 30 - 40 years. (Bross, sworn statement, Q.29 and 30). The health effects experienced by populations in the U.S.S.R. exposed to heavy chemical pollution and at the same time to routine releases from nuclear power plants can reasonably be expected to parallel health effects South Louisianians will experience under the same circumstances (Bross, sworn Statement, Q.31, 33, 34, 47). This observation, which is discussed at length in Dr. Bross's cross-examination, is not refuted by either Applicant's or NRC Staff's witnesses, and is substantiated in the U.S.Dept. of Commerce 1980 publication "Rising Infant Mortality in the U.S.S.R. in the 1970's" (C3.186:P95/74) written by C. Davis and M.Feshbach.

28.

The population in the Love Canal region is and has been exposed simultaneously to radioactive wastes and to hazardous chemical wastes. This population exhibits high incidence rates for certain types of cancer in adults as well as above normal rates for miscarriages and infant health effects. Dr. Bross and Dr. Pandit both express the view that, given the numerous chemical pollutants and resulting high cancer rate in South Louisiana, the simultaneous exposure of this burdened population to radiation in its food, air, and water can be expected to result in health effects in this population similar to those in the Love Canal population. These views were not refuted or denied by witnesses for the Applicant and NRC Staff.

29.

In so far as the NRC functions as a management agency for implementation of peaceful nuclear technology, the adverse health consequences observed as a result of management's (in Russia, the government's) siting policy in the U.S.S.R. serve as a clear example to the Board of what not to do. As a nuclear management agency and as a final decision-making body, the Board can be expected to take notice of and draw conclusions applicable to siting policy from management decisions made by similar decision-making bodies in other nations. As an expert in "metatechnology" and in biomedical technology and as President of the Biomedical Technology Corporation, the Board finds persuasive Dr. Bross's testimony that the U.S.S.R. siting policy is an error and that to site a nuclear power plant on the lower Mississippi River would be duplicating the U.S.S.R. management error - much to the detriment of the public health (Bross, Hearing Transcript, pp. 1366 - 1368, sworn statement, Q.51).

30.

The same logic which is applied to radiation risks in the BEIR I Report (and in FDA evaluations) is applicable to synergism risks; i.e., in the absence of specific data in the lowest dose ranges (for both chemical and radiation doses and/or for any combination of high and low doses of each agent), regulatory agencies must extrapolate from available information in higher dose ranges to risks at lower doses. The absence of specific data

at low chemical dose levels with low radiation dose levels does not preclude a determination that synergism can be expected to operate at these low dose levels. This is logical because synergism is known to operate at higher dose levels of either and both chemical and radioactive agents. Not only do Joint Intervenors' witnesses Drs. Pandit, Johnson, and Bross agree that synergism is a significant biological/medical phenomenon, but also Applicant's and NRC Staff's witnesses do not dispute or refute the fact that synergism is a known phenomenon at certain chemical-plus-radiation dose levels where it can practicably be tested and even quantified. See Hutchison on Hearing Transcript, p. 3437, lines 23-25; Goldman on p.943, line 19, and p. 945 of Hearing Transcript as well as p. 10 of his Direct Testimony; Hamilton, Direct Testimony, pp. 13-14; finally see Exhibit 27.

31.

Research data, statistics, and all other information identified by Joint Intervenors since the initiation of this intervention represent "the state-of-the-art" for the study of synergism between radiation and chemicals at extremely low dose rates in large human populations over extended periods of time. Besides the ethical and complex logistical obstacles to populations at multiple risk, excessive costs and times required for observation of synergism at work among ultra-low levels of various chemical agents in conjunction with low level radiation severely limit the state-of-the-art for synergism research in human populations. (However, data

is available for occupational and accidental exposures to carcinogens at higher levels over relatively short time periods). Similar constraints of time and money limit synergism and ultra-low level exposure studies even in laboratory animals, as noted by Dr. Goldman on p. 988, lines 11 and 18 of the Hearing Transcript. Any uncertainties as to the exact risk factor(s) attributable to introducing additional radiation to an already chemically burdened and cancer prone population represent the limits of current scientific knowledge, rather than any proof that no risk exists. Given the great weight of indirect evidence that synergism between low levels of radiation and chemicals can adversely affect the public health, and given the unlikelihood of any direct experimental evidence becoming available in the foreseeable future, it is reasonable to expect that regulatory decisions will be made based upon the state-of-the-art information and the implications thereof. Especially considering the intractable, painful and most often fatal nature of cancer and other diseases which can result from the synergistic effects under consideration, the limits of scientific knowledge indicate not that "what we don't know won't hurt us," but rather that, like an untested drug, synergistic health effects have not been adequately researched to say that they cannot cause adverse health effects (Bross, sworn statement, Q.51).

Applicant fails to evaluate the health consequences of any synergistic effect operative between existing chemical agents in the south Louisiana environment and routine radioactive releases from Waterford 3 to the extent that Applicant relies on BEIR Committee reports and NRC regulations. This is so because NRC regulations and guidelines (and BEIR reports upon which they are based) do not explicitly and quantitatively account for synergistic, multiplicative, or more-than-additive effects in their risk factor calculations, nor do they in any way account for chemical agents which may enhance the effects of radiation within 50 miles of Waterford 3. This fact is made clear in Dr. Bross's sworn statement in answer to Q.18 and in the Hearing Transcript, p. 1351, lines 10-16, and p. 1448, line 14 through p. 1451, line 7, and p. 1524, lines 20-23, and in Exhibit 25. Exhibit 23 further indicates why Applicant's reliance on federal guidelines does not in any way represent an actual evaluation of health consequences of synergism. H.F. Kraybill of the National Cancer Institute provides supporting evidence of this fact on p. 44 of Environmental Cancer, edited by himself and published by Hemisphere Publishing Corp. in 1977: "Quite frequently, scientific and regulatory decisions are made on the basis of exposure-response relationships relevant to a single stress agent or one route of exposure. In the environment, both humans and animals are exposed to multiple stresses via contaminants or additives in the air, water, and diet in addition to the insults received from drugs, biological agents (viruses, pathogens, parasites), and physical agents (radiation from

gamma rays, X-rays, or ultraviolet rays). The multiple factors involved in human exposures may play either a synergistic or an inhibitory role. Test systems, on the other hand, are developed to detect the responses of specific agents. The role of combined factors in the induction of carcinogenic effects has been studied in too limited a number of cases."

33.

Applicant fails to evaluate the cumulative health effects due to population exposure to both chemical agents existing in the south Louisiana environment and radioactive releases from Waterford 3 to the extent that Applicant relies on NRC regulations and BEIR Committee reports. This is true because the NRC regulations and the BEIR Committee reports in no way evaluate health effects due to chemical agents nor do they evaluate in any way the mechanisms by which chemical risk factors can be cumulative with radiation risk factors in a population over time. This fact is highlighted in the following: Dr. Bross's sworn statement, Q. 18; Hearing Transcript, p. 1375, lines 23-25; p. 1524, lines 20-23, Exhibits 25 and 23; 10 CFR, 50 et. seq.

34.

Applicant fails to identify, much less evaluate, chemical agents within 50 miles of Waterford 3 which can interact cumulatively and/or synergistically with radioactive releases from the plant. Neither Applicant's

witnesses Kenning nor Mauro (the only witnesses presented who were familiar th the actual plant site and environment) offer evaluations of such chemical agents or related factors.

(a) Applicant's witness Kenning ackowledges that in his calculations of background radiation he omits existing radiation exposure from Mississippi River water and from sources in the food chain. He further acknowledges that he has no information about other environmental pollutants in the food, water, and air in the Waterford 3 area which he evaluated. (Hearing Transcript, p. 478, lin 16 through p. 479, line 10).

(b) Applicant's witness Mauro admits that he does not account for environmental chemical pollutants nor for existing cancer rates in South Louisiana in his risk assessment (Hearing Transcript, p. 530, lines 13-24).



Dr. Branagan's response to the line of questioning which begins on Hearing Transcript, p. 879, states that the annual radiation exposure to the maximally exposed individual from Waterford 3 is 23 millirems. He further calculates that this exposure is equal to 27% of background radiation (p. 880, lines 15-20). Since these figures are arrived at by simple addition of exposures estimated for various pathways and nucleides, a similar addition process for exposure estimates of other individuals in the unrestricted area must yield higher doses than generally cited by the Applicant.

36.

Dr. Bross points out that actual exposures are likely to exceed "average" estimated exposures in some individuals because of the methods by which "averages" are derived and because of concentrating and dissipating factors in the environment (Bross, sworn statement, Q.40, Hearing Testimony, pp. 1372-1375). This observation is supported by the Argonne National Laboratory Report, "Plutonium in Drinking Water: Effects of Chlorination on Its Maximum Permissible Concentration" (Science, Vol. 201, p. 1008, 1978) and by J.R. Watts and C.E. Murphy, Jr., who close their abstract with the following statement: "These potential doses show the necessity of considering the interaction of radioactive material with the ecosystem for dose calculation," (Health Physics, Vol. 35, p. 287).

37.

NRC Staff and Applicant proffer Dr. Branagan's testimony as evidence that Staff and Applicant have adequately considered cumulative and/or synergistic effects of routine emissions from Waterford 3 on the Louisiana environment. Their assertions are entirely misplaced. Dr. Branagan's calculations concern only the amount of planned radioactive emissions that Staff estimates Louisianians will be exposed to. Dr. Branagan admits that he knows nothing about chemical carcinogens in the Louisiana environment (Branagan, pp. 844, 846). His calculations (and those of Staff) do not take into account the massive quantity of chemical carcinogens in the Louisiana environment and its high cancer rate (Branagan, pp. 844, 846). Moreover, the competence and credibility of Dr. Branagan and Staff is severely

discredited by Dr. Branagan's numerous and material changes to his sworn testimony (Hearing Transcript, p. 767 et. seq.) and the FES submitted in September 1981. The Board does not need to decide the truthfulness of Dr. Branagan's explanations for these untimely changes occurring at the moment Dr. Branagan took the witness stand and why all significant changes in calculations favored positions advanced by Applicant and Staff to observe that the emissions calculations testified to by Dr. Branagan are contradicted by his March 13, 1982 statement under oath. Whether these eleventh hour changes were the result of fraud or gross incompetence on the part of Staff is immaterial. The erroneous emission estimates (whether in the sworn statement or testimony before the Board) are not trivial errors, especially those pertaining to Neptunium, which decays in a short amount of time into plutonium, the deadliest element known to man, and those involving Iodine 131 which concentrates in the thyroid gland. But for these hearings, Dr. Branagan, Staff, and Staff Attorneys may never have "corrected" what they now allege to be false statements in the sworn testimony of Dr. Branagan and the Staff's FES. Under these circumstances, the Board does not find the testimony of Dr. Branagan or the Staff's FES Appendix J estimates credible or reliable, therefore it does not reach the issue whether the Staff's calculations are "Mickey Mouse arithmetic" (Bross Transcript, p. 1372) or whether the NRC estimates are unreliable because of the Nuclear Regulatory Commission's "notorious industry bias" (Direct Testimony of Dr. Johnson, p. 10).

38.

Dr. Hamilton makes repeated references in this Direct Testimony to the estimated amount of additional radiation from Waterford 3 as "smaller even than the existing variations in natural background radiation" (p. 10) and as "being a tiny fraction of the doses the population already receives annually from natural background radiation" (p. 10) and again as "the tiny incremental addition of low-level doses of radiation" (p. 15). He apparently does not know the exact figures to which he refers as "tiny" and nowhere in his testimony offers a specific amount in rems or a percentage of background radiation. Nevertheless, his defense of Waterford 3 hinges on the assumptions quoted above which are at serious variance with Dr. Branagan's estimation that certain individuals can be exposed to 23 millirems annually or 27% above the natural background radiation level, hardly a "tiny fraction." The vagueness of Dr. Hamilton's assumptions and the fact that they contradict Dr. Branagan's explicit statements call the validity of his argument and even his familiarity with Waterford 3 into such serious question as to make his testimony unreliable.

39.

Dr. Hamilton misses the point of J.A. DiPaolo's report which he cites as Reference 6 on p. 13 of his Direct Testimony. "The lack of transformation by X-irradiation alone" means that, regardless of the actual number of rads used (which Dr. Hamilton sees as the significant point), the DiPaolo experiments constitute a viable model for the environmental situation

at hand. This model is entirely analogous to the situation in which a dose of radiation which alone causes no effects is then shown to significantly enhance the effects of polycyclic hydrocarbon carcinogens. As a model, DiPaolo's experiments fulfil the requirement that circumstances of observed effects parallel those of the greater human environment; i.e., a non-carcinogenic (or non-transforming) dose of radiation, which is no hazard alone, becomes a hazard by causing more cancers (or transformations) than would be expected from a given dose of chemical carcinogen alone. These experiments represent a more-than-additive effect because the radiation effect alone is zero. What Dr. Hamilton overlooks is that it is the experimental response to the radiation dose which makes DiPaolo's work relevant, not the magnitude of the dose.

40.

Dr. Hamilton fails to consider the difference in biological effect between external radiation exposure ("natural background radiation") and internal radiation exposure (such as that of the thyroid gland having concentrated I-131). His position that "... environmental pollutants in the absence of Waterford 3 would already be interacting with natural background radiation to produce the postulated cumulative and/or synergistic effects," (p. 10, Direct Testimony) does not account for the fact that radiation exposure pathways from Waterford 3 include eating, drinking, breathing, and metabolizing into the cell structure radioactive elements. Dr. Carl Johnson states that internal radiation exposure is more dangerous and damaging to tissues than external exposure (sworn statement Q. 12; p. 1869, Hearing Transcript). Dr. Pandit confirms this view, which is not directly refuted by Applicant or NRC Staff (sworn statement, Q. 14).

Therefore his comparison of synergistic and/or cumulative effects operating in the presence of background radiation with those which will come into play as a result of Waterford 3 emissions is inappropriate and partial at best. The same is true of this unsupported argument repeated at the bottom of p. 14 in his Direct Testimony.

41.

Dr. Hamilton's reference to various experiments and reports on synergism (pp. 13-14 of his Direct Testimony) indicate his knowledge of synergism as an accepted medical phenomenon. He offers no direct statement or conclusions on the possibility of simple additive or cumulative health effects. He indicates no knowledge whatsoever of the types, sources, or concentrations of chemical agents to which the population is exposed which can act cumulatively and/or synergistically with Waterford 3's radioactive emissions.

42.

Dr. Hamilton's objectivity in advocating Applicant's position on the plant licensing is called into question by the fact that he testifies regularly for utility companies and has never testified at the request of the NRC, and ASLB, or any Congressional Committee. His selectively bad memory in recalling just whom he had testified on behalf of at various NRC hearings had to be prompted by the Board before these facts were acknowledged (Hearing Transcript, pp. 540-544).

Applicant relies entirely on Dr. Hamilton's assumptions concerning linear dose-effect curves for the ultimate satisfaction of issues raised in contention 8/9, after acknowledging that "neither Applicant nor N.R.C. Staff explicitly took synergism into account" (Applicant's Findings of Fact, pg. 65). Dr. Hamilton makes three basic assumptions which are in no way supported and which the Board questions as sufficient scientific support for Applicant's position. The first assumption is that the linear-linear dose-effect curve derived from scientific observation of responses to <u>radiation alone</u> will automatically reflect multiplicative effects in responses to radiation-plus-chemicals. There is no evidence for this assumption whatsoever, as pointed out in the exchange between Judge Foreman and Dr. Hamilton (Hearing Transcript, pg. 717 top). It is reasonable to assume that synergistic effects observed at relatively high levels of exposure will continue to occur at lower levels. However, it is <u>not</u> reasonable to assume that effects which are multiplicative in nature and which are dependant upon doses of two or more agents (as well as time intervals between administration of the agents in some experiments cited) will be simply linear over a range of radiation doses. Despite evidence in the medical literature that synergism is optimized at certain doses of

radiation and even disappears at higher or lower doses, Dr. Hamilton's second unsupported assumption is that "I would expect the results of addition to be directly proportional to the additional dose of radiation" (Hearing Transceipt, pg. 717, lines 18-19). And further based on his assertion "the dose we're talking about is zero, less than 0.01 millirem a year" (pg. 716), Dr. Hamilton concludes that the synergistic effects "proportional" (calculated presumably using some constant factor, as yet unknown) to such a small additional dose above background radiation will be negligibly small. However, if the Board applies Dr. Hamilton's assumption to Dr. Branagan's calculated total annual radiation dose to the maximally exposed individual of 23 millirems, or 27% of the background radiation dose (Hearing Transcript, pg. 880, lines 15-20), the resulting anticipated health effect of 27% more cancer deaths is absolutely unacceptable, and, it is hoped, unreliable and inaccurate. The third unsupported basic assumption upon which Applicant's presumed compliance with Contention 8/9 hinges is that "the ability to place an upper bound on the effect" (Applicant's Opinion, pg. 24) is bestowed by the linear-linear dose-effect curve developed in the B.E.I.R. I Report for radiation doses alone. However, even the B.E.I.R. Committee makes no assertion that the linear curve represents an upper limit of risk, but frankly states that "because there is greater killing of susceptible cells at high doses and high dose rates,

extrapolation based on effects observed under these exposure conditions may be postulated to underestimate the risks of irradiation at low doses and dose rates" (B.E.I.R. I, Chapt. VIII, Sec. Iv). The B.E.I.R. I Report goes on to define the linear hypothesis as "the only workable approach to numerical risk estimation ...since there is no means at present of determining the value of the dose-effect slope in the low-dose region" (same as above, Sec. VI) and to emphasize that "it is clear that these estimates are subject to great uncertainty" (B.E.I.R. I, Chapt. V, Sec. I). These statements clearly contradict Dr. Hamilton's declaration, "But as we use only the linear-linear relationship - and as I know that exaggerates or gives an upper limit to risk, I feel confident..." (Hearting Transcript, pg. 719, lines 14-16). Nowherein his testimony does Dr. Hamilton, or Dr. Hutchinson, who was a member of the B.E.I.R. Committee, offer evidence or support for this upper limit definition within the linear hypothesis, or even make reference to it. Furthermore, it is not common practice, nor is it logical to draw a straight line through mean points defined by two axes, where the actual points occurs both above and below the line, and then to conclude that the line represents an upper limit in areas where there are no points. Dr. Hamilton's basic assumptions simply assume too much to provide meaningful evidence that synergistic and/or cummulative effects are properly evaluated by Applicant.

44.

Dr. Hamilton's claim to have published "150 scientific papers, including many assessing the hazards of various energy sources" (p. 5, Personal Qualifications) is not substantiated by an attached bibiliography such as is submitted by each of the other witnesses whose works are published. Over the last ten years the Index Medicus cites only one scientific paper under the name Leonard D. Hamilton (as second author) and the topic is not remotely related to energy or public safety. There is no evidence that Dr. Hamilton's scientific papers are published in the general medical literature nor that they have been subject to peer review.

45.

Dr. Goldman agrees that synergism is a valid medical principle (Hearing Testimony, p. 943, line 19, and p. 945, and p. 10 of Direct Testimony). He also cites in his Direct Testimony References 7, 8, and 10 which demonstrate greater than additive effects in vivo and in vitro. Dr. Goldman acknowledges and discusses additive or cumulative effects of radiation with various chemical agents in his Direct Testimony and gives supporting References 9, 11 and 12. The latter Reference also cites "more lymphatic disorders... than expected from the sum of the effects of the two agents separately in Collip rats" in its abstract. Dr. Goldman's reference 11, in addition to demonstrating simple additive effects, also proves that several small radiation doses in conjunction with a chemical agent have "an over two-fold increase in tumor multiplicity" above that produced by a single radiation exposure delivering the same total dose.

These observations on fractionation of radiation dose along with those stated in the Discussion of Dr. Goldman's Reference, indicate not only that multiple low doses of radiation over a period of time may represent a greater health hazard than a single large dose (same total dose), but that the two types of dose delivery, or dosage rates, are not comparable. Dr. Goldman's Direct Testimony, pp. 10-13 and his choice of References 7-12 not only do not refute contention 8/9, but in principle support the underlying concepts of synergistic and cumulative, or additive effects from radiation and chemical agents. Indeed, his choice of references indicates that no published medical reports clearly refute or disprove these principles.

46.

In his discussion of "quantification of the effects of mixtures of radiation with chemicals" (p. 11, Direct Testimony), Dr. Goldman explains that due to cell killing, experimental results probably indicate less transformation/neoplasia than would result at lower doses; i.e., lower doses would produce more cancers and fewer individual cell deaths. His quotation from Cole and Foley (Reference 11) supports this position, as do his References 8, 9, and 12 relevant to fractionation of dose where a large single dose kills cells which otherwise would/do transform. Dr. Goldman's Reference 7 (also cited by Dr. Hamilton)states on p. 441, "TPA most effectively enhanced transformation at low doses of X-Radiation." Therefore, it is clear that the difficulty in quantification of synergistic and additive

effects remarked upon by Dr. Goldman [pp. 11 and 12 (bottom),Direct Testimony] lie chiefly in determining how much greater the effects will be at lower levels and dosage rates than have been experimentally practicable. A conservative public health decision would anticipate more neoplasia at lower doses and dosage rates than at those presently reported on.

47.

Dr. Goldman's credibility and his ability to interpret scientific reports are severely compromised by his gross misrepresentation of the A.R. Kennedy, et.al., (Reference 7) studies. On p. 10 of his Direct Testimony, Dr. Goldman attempts to minimize the magnitude of the observed enhancement: "However, under the most ideal of conditions, using relatively high radiation doses (20 mrem or more) the maximum enhancement was a factor of about eight or nine" (p. 10, Direct Testimony). Nowhere in the Kennedy report are the factors "eight or nine" mentioned. The report actually states (on p. 440): "X-irradiation (100 rads) with subsequent TPA treatment resulted in a transformation frequency of about $1.4 \pm 0.1$ (S.E.) $\times 10^{-3}$ (average of Groups 3 to 5 in Table 1), a 19-fold enhancement in transformation over 100 rads alone... TPA worked most effectively in enhancing X-ray transformation at doses of radiation that yielded very low levels of transformation by themselves." When confronted with this serious discrepancy under cross-examination, Dr. Goldman was unable to explain his interpretation of the Kennedy data, nor did he indicate that an error was made in his original testimony offered under oath (Hearing Transcript, pp. 946, line 19, through

949, line 18). Further evidence of Dr. Goldman's incompetence in interpreting and drawing conclusions from the scientific literature - even those he relies on in his testimony - lies in his discussion of the DiPaolo studies, one of which he cites as Reference 8 (as "DiPaoli, J.A."). He mistakenly focuses on the quantity of enhancement or the size of the enhancement factor as the significnat point in DiPaolo's work. The real relevance of these experiments to low-level radiation-mediated synergism is that a non-transforming dose level of radiation enhances "transformation ordinarily associated with the chemical" and that "the lack of transformation with irradiation alone argues against the selection of a special radiation-sensitive cell." (Goldman's Reference 8, Abstract) Despite this and the introductory statement in this paper, "Under the conditions of these experiments, no transformation was identified as a result of the X-irradiation only," Dr. Goldman insists under cross-examination that "little in the way of transformation" occurred with radiation alone (Hearing Transcript, p. 970). Any astute expert cannot miss the consistent feature of DiPaolo's often described experimental model: the radiation dose utilized is a sub-effective dose level when used alone, thus presenting a valid model for low dose or other sub-effective dose situations. Dr. Goldman's inexplicable misrepresentation of the Kennedy studies and his failure to note the conspicuous feature of the DiPaolo model - both being references with which he claims familiarity - make it impossible for the Board to accept his interpretations of and conclusions from his reading of the literature on the topic of synergism.

Despite any other expertise Dr. Goldman might have, his highly questionable credibility and competance, as well as his mistaken observations on synergism disqualify him in the Board's eyes as an expert on this subject. Thus, his assessments of the health risk due to synergism and the adequacy of Applicant's consideration thereof are given little weight by the Board. Furthermore, Dr. Goldman acknowledges that he has no knowledge of the environmental carcinogens or the cancer incidence rate in Louisiana and that he did not address genetic damage as a possible health effect from operation of Waterford 3 (Hearing Transcript, p. 980, lines 1-12).



The fact that carcinogens acting alone (i.e. without being enhanced by radiation cause concern in the South Louisiana population is irrefutable evidence that cancer causing chemicals (pollutants) exist "in quantities sufficient to support synergism with radiation from Waterford 3" (Applicant Findings of Fact, pg. 63; Opinion, pg. 23). Since the definition of synergism presupposes that relatively ineffective levels of carcinogens (physical or chemical types) become more effective due to interaction, any lack of quantitative evidence of specific carcinogens is adequately compensated for by the self-evident fact that existing carcinogens are present in quanties great enough to cause cancer alone and thus also to interact with radiation from Waterford 3.

Drs. Fabrikant and Hutchison express a certain optimism concerning the peer review process in their statements that Dr. Bross is wrong in his estimation of the "radiation protection community" and its role in the peer review process. (Bross, Hearing Transcript pgs. 1632-56; 1405 line 21-1406; 1613-19) Dr. Fabrikant says, "Neither situation exists; the 'radiation protection community' that Bross describes does not exist" (pgs 13-14, Rebuttal Testimony). Dr. Hutchinson finds it "hard for me to conceive of a system that would effectively block publication of scientific work because of undesired findings" (pg. 28, Rebuttal Testimony). But on cross examination, Dr. Hutchinson acknowledges participation in a Congressional Committee Hearing on a matter of peer review which resulted in Committee Hearing Chairman Representative Paul G. Rogers' conclusion, "It's the most disordered, unstructured mess that I have looked into in some time. If our research programs are being carried on in this manner ...we may also ask the Department of Justice to look into the whole matter." (Hearing Transcript, specifically 3391-2, also 3352-3398, Hutchinson.) Dr. Bross' position that the peer review process as applied to research funding is subject to pressure is confirmed in the New York Times, June 13, 1982, edition which reports, "What worries scientists is political intrusion into decisions on what constitutes good and bad science and on which projects should be funded." Cases of outside pressure being applied

to individuals and peer review panel choices include the National Bureau of Standards, the U. S. Department of Agriculture, and the U. S. Food and Drug Administration. National Academy of Science friends hint that "the Administration might be unhappy with the scientific truth about a politically volatile subject." And the Director of A.A.A.S., which published a related article in Science, on May 7, 1982, calls for a halt to the "spread of the infection of political interference." Clearly, Dr. Bross and Dr. Johnson are not alone in their critical views of certain private and government peer review processes and panels. The Board acknowledges that the highly controversial nature of nuclear power well might focus certain pressures on those identified as the "radioation protection community" and that Dr. Bross' observations reflect a valuable insight into some non-scientific methods and sources which give rise to certain types of data on one side of a controversial topic and tend to understate the importance of conflicting data. See attached Appendises VI and VII .

Joint Intervenors' Contention 8/9 simply states that Applicant fails to properly evaluate synergistic and/or cummulative effects oflow level radiation with environmental pollutants known or suspected to be carcinogens. At every opportunity throughout the hearing, Joint Intervenors clarify two basic points in the contention: (1) the "low level" of radiation refers to the doses and amounts of radiation specified in 10 C.F.R. 50, App. I, and under no circumstances does it refer to any estimated or calculated doses or amounts formulated by Applicant or N.R.C. Staff; (2) by "properly evaluate," Joint Intervenors intend that all available evidence and data on existing carcinogens, low level radiation, and synergism be evaluated by Applicant, and under no circumstances do Joint Intervenors recognize compliance with N.R.C., A.E.C., N.E.P.A. or E.P.A. regulations or design objectives as proper evaluation. The reason for the latter stipulation is that none of the above guidelines explicitly account for risk factors due to synergism. Joint Intervenors' position on these two points was not specifically agreed to by Applicant and N.R.C. Staff, but neither was it debated, refuted or denied by these parties. It is significant that the Board at no time ruled against Joint Intervenors' interpretation of these basic points in Contention 8/9 and so Joint Intervenors' interpretation of meaning for terms in their contention is considered to be the interpretation and definition in force. The Board finds that according to these definitions of the terms of Contention 8/9, Applicant has in fact failed to deal with the provisions set forth in the contention.

CONCLUSIONS OF LAW ON CONTENTION 8/9

1

42 U.S.C. 2232 (a) requires that, in connection with applications to operate nuclear power plants, applicant must demonstrate that the use and specific characteristics of the nuclear facility meet Nuclear Regulatory Commission regulations and that the manner the nuclear facility is operated will provide adequate protection to the health and safety of the public. Congress' command that applicant meet the double burden of showing compliance with N.R.C. rules and that granting the license will not endanger the public health rests upon the sound premise that regulatory agencies too frequently perceive their role as protecting the industry from the public. (The N.R.C. itself was criticized by members of the public on these grounds in the limited appearance portion of the hearings.) This Congressional instruction is reflected in 50 C.F.R. 2.732 and 50 C.F.R. Part 2, App. A (V)(d)(1) which place the burden of proof upon the applicant in licensing hearings.

Applicant and Staff have attempted to show that their predicted estimates of radioactive emissions from Waterford 3 fall within radioactive effluent emissions standards promulgated by the N.R.C. Their efforts are misdirected. They have missed the point of these hearings. Applicant and Staff have failed to counter the probative, reliable, and convincing evidence presented by Joint Intervenors that synergism between pre-existing carcinogens in the Waterford 3 area and allowable releases of radioactive effluents under N.R.C. regulations and/or estimated releases will create a serious threat to the health and lives of thousands of Louisianians living in the cancer corridor stretching from Baton Rouge to the mouth of the Mississippi. Conformance to N.E.P.A., E.P.A., N.R.C. and/or A.E.C. standards will not prevent the cancer deaths of Louisianians who will be killed by the synergistic and/or cumulative interaction of radiation and pre-existing carcinogens in the Louisiana environment because none of the above agencies consider the synergistic and/or cumulative interaction of radiation and other carcinogens, but consider only the effects of individual agents, acting separately.

As the operating license sought by Applicant will permit the exposure of an individual in an unrestricted area to a dose of approximately 10 millirems total body dose from all pathways per year or 80 millirems to any organ, the Board considers this figure rather than the seriously flawed estimated emissions calculations presented by Applicant and Staff to be applicable to this proceeding. This conclusion on our part, of course, would be altered if Applicant were to seek an operating license allowing it to expose individuals in unrestricted areas only to amounts predicted by Applicant and Staff.

4

Accordingly the Board finds as a matter of law that applicant has failed to show that 102 (2)(C),(E) of the National Environmental Policy Act of 1969 and 10 C.F.R. 51 have been complied with in acccordance with 10 C.F.R. Part 2 App. A f(3), 10 C.F.R. Part 2 App. A VIII(6)(7) applicable to operating licenses by operation of 10 C.F.R. Part 2 App. A VIII (a), that it is necessary to deny

applicants license in order to protect envirnmental values, i.e. preventing an aggravation of Louisiana's cancer epidemic, 10 C.F.R. Part 2, App. A (f)(3). The Board further finds that the issuance of applicant's license will be inimical to the health and safety of the public. 10 C.F.R. Part 2 App. A VIII (b), (3), (6), (7).



Accordingly, the Board recommends that applicants license application be denied.

Luke Fontana
Gary Groesch
FOR JOINT INTERVENORS

I hereby certify that a copy of the foregoing pleading was served by deposit in the United States Mail, first class, postage prepaid, this 21st day of June 1982 to the Atomic Safety and Licensing Board and all counsel of record and all others on the service list of said hearing.

June 19, 1982

UNITED STATES OF AMERICA
NUCLEAR REGULATORY COMMISSION

BEFORE THE ATOMIC SAFETY AND LICENSING BOARD

| | | |
|---|---|---|
| In the Matter of | ) | |
| LOUISIANA POWER & LIGHT | ) | Docket No. 50-382 OL |
| (Waterford Steam Electric Station, Unit 3) | ) | |

## I. STATEMENT OF THE CASE

Joint Intervenors allege that evacuation planning around the Waterford Steam Electric Station Unit 3 is inadequate in two major subparts of one contention 17/26. The first subpart has six sub-categories, A through F, which alleges inadequacies in: notifying residents, roads and highways, warning systems, command structure, evacuation drills, and evacuating people in six special categories. The second major subpart alleges inadequacies in the distribution of potassium iodide.

Testimony was heard at the Fifth Circuit Court of Appeals from May 3, 1982 through May 12, 1982.

## II. MEMORANDUM ON CONTENTION 17/26(1) & (2)

### 1. Emergency Planning: Education

Emergency planning around Waterford 3 is ostensibly based on two general principles according to the Applicant. If it is true that "education of those who may be involved in emergency response" and " anticipating events and problems" is one aspect of the first principle, the emergency response personnel-civil defense directors, state and local-should be knowledgeable of the consequences of the severe accidents at nuclear power stations. The President's Commission on the accident at Three Mile Island (The Kemeny Commission) is very clear on this aspect of 'education' in assigning responsibility to the accident at Three Mile Island: (p. 17 of the Kemeny report) "The fact that too many individuals and organizations were not aware of the dimensions of serious accidents at nuclear

power stations accounts for a great deal of the lack of preparedness and the poor quality of the response."

Both NUREG-0654, "Criteria for Preparation and Evaluation of Radiological Emergency Response Plans and Preparedness in Support of Nuclear Power Plants," and NUREG-0396, "Planning Basis for the Development of State and Local Government Radiological Emergency Response Plans in Support of Light Water Nuclear Power Plant," specifically includes core melts in their scenarios of concern. The more important guidance document, NUREG-0654, states: (pp.6-7) "...a planning basis is very large...[including]...the worst possible accident" and (p.7) "...a number of accident descriptions were considered in the development of the guidance, including the core melt accident release category."

Further, (p.6) "FEMA has also concluded that the guidance in NUREG-0396 should be used as the planning basis for emergency preparedness around nuclear power facilities." NUREG-0396 has numerous graphs and extensive texts describing severe accident sequences - including the core melt.

Joint Intervenors were repeatedly denied the right to question key personnel --Azzarello (LP&L), Myers (Louisiana), Madere (St. John) Lucas (St. Charles) -- about their knowledge of the critical end points in the consequences of serious nuclear accidents -- including core melts.

NUREG-0654 (pp. 7-8) also sets down several areas it considers to be of utmost importance to planning officials. The most important of these is the "definition of the area" over which planning is necessary. This is followed by information on "time frames" of accidents. The third category, "knowledge of the kinds of radioactive materials potentially released," was specifically excluded from the cross-examination of Joint Intervenors by ASLB rulings. The key civil defense officials -- Azzarello, Myers, Madere and Lucas -- again were excluded from any testing of their knowledge of the radioactive materials that were released from nuclear power plants during accidents, even though NUREG-0654 considers it important for planning officials to know this material. The Board can now see its error. PF 1

2. Emergency Planning: Paper Plans

The second priciple holds that emergency plans are a continuous activity, a so-called "living document." The Joint Intervenors contend that as no exhaustive plans are available for specific review, the principle is little more than a convenient device to hide oversights, frustrate judicial review and deprive intervenors of their right of due process under the 5th Amendment of the United States Constitution.

More correctly, the "living document" could be seen as a "dead document." A thin skeleton of generalized statements, the emergency plans do not begin to deal adequately with those problems reasonably associated with an orderly evacuation. The plans include: no brochure, no agreements with surrounding parishes for buses, vans or ambulances, no communication systems installed or tested, no implementing procedur no sirens and no evacuation tests.

The Applicant has had nearly 12 years in which to prepare emergency plans (LP&L applied for a construction permit on December 28, 1970) and the result of its work in this regard has produced what can at best be described as a minimal plan.

The Board agrees with Judge Jordan's statement that "there has to be more than paper plans." (tr. 2275-11). This is in response to the suggestion of Staff cousel Turk that "(a)11 that has been raised until now is the adquacy of the emergency plan on paper" (tr. 2273-17&18). Joint Intervenors allege they are interested in more than paper plans. The Board agrees. PF 2

3. Regulations and People

No operating license can be issued unless the Staff can make a favorable finding that the integration of offsite and onsite emergency planning "provides reasonable assurance that adequate protective measure can and will be taken in the event of a radiological emergency"(10 CFR 50.47 (a) (1).

The key words, the verbs "can and will" refer to the elements of the plan itself. In essense, the regulations ask "is it possible to implement listed protective actions effectively?"

The second standard [reasonable assurance that protective action 'will be taken'] implies looking at the individuals involved. There is reasonable doubt that the individuals in key positions 'will'

perform their functions effectively. Joint Intervenors were blocked by ASLB from probing possible conflicts of interest among those officials in the command decision structure. The Parish president in St. Charles parish has potentially severe conflicts of interest with regard to the Applicant -- conflicts that are both familial and financial. Similarly, the civil defense director of St. John the Baptist parish, Bertram Madere, is a full time employee of the E.I. Dupont du Namours in St. John the Baptist Parish. Dupont is the owner of the Savannah River Nuclear Power Station in South Carolina. Madere, as civil defense director, is the chief of staff for the parish president during emergency situations. Thus the health and safety of residents in both parishes is possible threatened by potentially severe questions of conflict of interest.

People - real people - are the essential ingredient in the emergency plans. The NRC takes this into consideration in onsite plans. NRC expert Perrotti: "...I cannot at this time state whether the people are adequate or not, because I have not had a chance to evaluate the individuals involved." (tr. 3920). This conflicts sharply with the Board's rulings against questioning and evaluating the key individual in the offsite plans -- the Parish President: "We're not going to get into incumbents in office. We're talking about command structure." (tr. 2966-15&16). The apex of the command structure is the parish president. Azzarello, et al., at 12-13; Benton and Lookabaugh at 7-8. Thus the Board can question whether there is reasonable assurance that the offsite emergency decisionmaker will respond correctly. PF 3

4. Predictive Findings and Post-Hearing Verification

The concepts of predictive findings or post-hearing verification as a decision-making device in ajudicatory hearings involving members of the public is contrary to the 5th Amendment right of due process under the Constitution of the United States, the Administrative Procedures Act and The Atomic Energy Act. These "verifications" or "findings" are simply convenient devices to deprive legal intervenors the right to question the basis or facts involved in them. It creates an "old boy" network where the real decisions are made between bureaucrats who are out of sight and earshot of the public.

Any predictive findings or post-hearing verification by the NRC or FEMA on subjects delineated in the contentions of Joint Intervenors are illegal. Joint Intervenors contend that their rights can only be

protected by reconvening this tribunal after the substantive parts of the emergency plans have been finalized. The Board agrees. PF 4

5. The Contentions

Joint Intervenors' Contention 17/26(1) (a) asserted that:

> Applicant has failed to adequately make provision, according to the Emergency Plan contained in Chapter 13.3 of the FSAR, for evacuation of individuals located within the 10-mile plume exposure pathway emergency planning zone for the Waterford 3 site in the event of a serious reactor incident, as required by applicable NRC regulations, in that:
>
> A. the provisions for notifying residents of evacuation procedures are inadequate.

The notification of residents is clearly inadequate because no brochure was available to critique (Tr. 2889). The brochure distributed around the Grand Gulf nuclear power plant was produced by Joint Intervenors, but they were barred questioning Azzarello on the general format or nuclear terminology contained therein. (Tr. 2202) It is inconceivable that the key element of the notification system -- the brochure -- was not available for Joint Intervenors to critique. Azzarello testified that plans for notification of the public do not take population increases into account (Tr. 2289&2290). Joint Intervenors object to the post-hearing verification now being planned for the brochure as a violation of their right of due process and of the Administrative Procedures Act. The Board agrees. PF 5

Contention 17/26(1)(b) asserted that:

> B. the roads and highways necessary for such evacuation are inadequate.

Madere testified at length about the need for increased roads and highway in his parish. He said that they were needed to hasten evacuation. Although he has been promised additional roads since 1972, none has been built. (Tr. 2783&2795).

Lucas also testified that he would like to have additional raods built to speed up the evacuatin process. However, neither of these men mentioned the need of prior requests for additional roads to FEMA. As local officials experienced in evacuating their respective parishes, Lucas and Madere should have indicated to FEMA officials their reservations about the existing number of

roads and highways (2875-2877).

The evacuation time estimate (ETE) sponsored by applicant expert Twine also has severe problems. Important categories of individuals were completely excluded. The computer code, GPSS, has never been used at a licensing hearing. The ETE also does not factor the impact of the omission categories under contention F: (a) refusal to evacuate, (b) additional collisions, (c) hysteria, and (d) single mode evacuation.

The Board is aware that NRC and FEMA regulations on the adequacy of the road and highway network are generally weak and vague. In order to protect the health and safety of the people of Louisiana, however, our conclusions can be none other than that Joint Intervenors' contention is correct. PF 6

Contention 17/26(1)(c) asserted that:

C. the evacuation warning system is is inadequate.

The siren system is not in place and, therefore, not tested. Further, no experts were available on the panel to answer questions about the evacuation warning system (Tr. 2341-5). Although FEMA witnesses testified that the warning system was adequate, it was shown that they never visited the proposed siren locations (Tr. 2879).

Madere testified that the outdoor warning system would warn 100% of the population. This would indicate that the hearing impaired of the parish have not been considered (Tr. 2698). The siren warning system would certainly not contact this population segment. In this case, phone calls to the neighbors of the hearing impaired would allegedly be made.

Joint Intervenors were prevented by Board ruling from questioning the adequacy of the phone system in a time of crisis. (Tr. 2820). Because of the overload and breakdown of the phone system aronnd the Three Mile Island facility during the accident, Joint Intervenors believe the phone system around Waterford 3 is inadequate, and therefore provisions for contacting the hearing impaired are also inadequate.

When the public is notified, pre-prepared messages will be used by radio stations to transmit information. The stations will "fill in the blanks" with information supplied by officials at the time of the accident. None of the messages were completed or available, and it is uncertain whether they will provide adequate information to the public.

The Board concludes that Joint Intervenors contentions concerning the inadequacy of the evacuation warning system is valid. PF 7

Contention 17/26(1)(d) asserted that:
D. there is not an adequate command decision structure, including appropriate guidance, for commencing evacuation.

Parts #1 and #3 of this section addressed some of the weaknesses in the offsite command decision structure. These weaknesses dealt primarily with the lack of specific knowledge of the consequences of serious accidents at Waterford 3 -- including core melts. They also addressed the lack of knowledge of the radiological consequences of serious reactor accidents.

Part 3 dealt with the conflicts of interest of the key decision makers in the offsite plan. This includes the parish president of St. Charles parish and the civil defense director of St. John the Baptist parish. There are other, more specific areas on concern which will now be addressed.

Lucas says he will recommend an evacuation order be given by the parish president if the Applicant tells him to evacuate. He says he would so recommend without first contacting the state for an independent accident assessment. (Tr. 2954) FEMA expert Benton says the state can act immediately on information from the licensee, without an independent assessment from other state agencies. (tr.2910-23). Therefore both the parish and FEMA explicitly state that on some occassions, the protective action recommendation of the utility will be all that is necessary to begin an evacuation. Yet FEMA expert Benton states elsewhere in testimony that no confidence can be given to the utility's ability to recommend protective actions. He said the utility has no knowledge of traffic conditions or resources available (Tr. 2913-8).

Independent information available at all times is essential for effective and trustworthy protective action decisionmaking. The fact that the State does not have instant, independently verifiable information on accident parameters to add to parish information on traffic condictions and general state of readiness puts a large cloud over the decisions that might have to be make very quickly. NUREG-0654 guidelines state that a radioactive could have an impact on the surrounding population in one-half hour.

Madere is so unfamiliar with NUREG-0654 that he believes that the people in his parish would get exposure 45 minutes to one hour after a radioactive release because they are five miles away (assuming a three mile per hour wind) (Tr.2676-18ff). Madere apparently does not understnad that the guidance document has subsumed all variables into its calculations. Madere should be planning for a possible exposure to his population in one-half hour. (NUREG-0654 - Table 2).

Madere also indicated grave misgivings about the adequacy of NUREG-0654 (Tr.2570-3&4) thus putting in doubt his use of this guidance document in preparation of plans or in recommending protective actions to the parish president in an emergency. Joint Intervenors were prevented by ASLB ruling from questioning Madere's reservations about NUREG-0654 (Tr. 2572-2).

To allow a utility to offer protective action guides based on data not independently verifiable to a parish constitutes a risky practice. Joint Intervenors showed by cross-examination that the protective action guides that are in the utility and state plans are substantially different concerning specific, high-risk portions of the population -- pregnant women and children. The utility plan offers no special consideration whatsoever to this high-risk group in the categories of whole body dose, one to five rems, and thyroid dose, 5 to 25 rems. It simply uses a child thyroid dose as a category without mentioning pregnant women (Tr. 3107 -- 11 through 13). The state plan, however, does have an option in that dosage category for evacuating pregnant women and children when constraints make general evacuation impossible (Tr. 3141-14).

The Board finds that because of the possible conflicts of interes of the key decisionmakers, the lack of independent accident assessment and the general unfamiliarity of the parish officials with the guidance documents, there is grave doubt that the proper emergency response would be formulated in case of the most severe accidents. PF

Contention 17/26(1)(e) asserted that:

E. the Emergency Plan fails to provide for realistic and comprehensive evacuation drills, in that the provisions for moving individuals are not actually tested.

In their attempt to show that evacuation drill are not necessary, FEMA witnesses testified that they have "observed (evacuation) exercise

in which the public did not choose to participate (Tr. 2883). This conclusion was shown to be misleading because, in fact, they had only observed one exercise.

When the applicant does conduct a drill to test the commitments from resources" and "officials" (Tr. 2614), all but one of these will be announced ahead of time. The only unannounced drill will be conducted after the plant is in operation (Tr. 3097). This schedule does not adequately test the evacuation plans because (a) prior announcement allows time for people to prepare themselves and the resources needed -- time that would not be available in the case of a real accident, and (b), the unannounced drill, as it is scheduled to take place after the beginning of plant operation, will not be of any benefit in the case where an accident were to occur after the opening of the plant and before the scheduled unannounced drill.

These common sense observations were accepted by the Board which concluded that this segment of the plan was inadequate. PF 9

Contention 17/26(1)(f) asserted that:

F. procedures are inadequate for evacuating people who are:

(i) without vehicles;
(ii) school children;
(iii) aged or crippled;
(iv) sick and hospitalized;
(v) imprisonned;
(vi) transient workers.

Part F deals with a number of specific categories of individuals which would be affected by an accident at Waterford 3. Four general considerations were overlooked in the preparation of evacuation plans. These omissions would effect all of the categories listed above in part F. They deal with unforseen drains on resources and poor evacuation routing that could lead to unnecessary and excess doses of radiation. "Dose savings" are the primary consideration for the general population and especially for the population about which Joint Intervenors have raised contentions -- the sick, hospitalized, aged and children.

Omission 1 - Refusal to Evacuate:

Lucas testified that at a recent chemical spill in St. Charles parish that affected nine homes, three of those homes refused to evacuate. Many resources -- human and material -- were used to

extricate these people. Resources were also expended to impound these people's animals (Tr. 2917-19ff). Lucas said that the parish president declared an emergency situation, and then officials physically removed them. (Tr. 2718-6) Joint Intervenors attempted to question Lucas on the amount of resources used to extricate the people -- one-third of the affected population -- but were stopped by ruling of the ASLB (Tr. 2724-18) on objection from Applicant's counsel. This came after the Board had allowed a question concerning the type of police van that would be used to evacuate the people who refused orders to evacuate (Tr. 2723-16). Lucas stated that people who refuse to evacuate during an accident at Waterford 3 could be forcibly evacuated (Tr. 2710-13). This would appear to be logical, as the same emergency situation would doubtlessly be declared by the parish president.

On cross-examiniaion by the Applicant, the Board sustained a reexamination of the question of people who refuse to evacuate (Tr. 3037-3). The Board allowed questions pertaining to resource commitment.

Since the subject of people who refuse to evacuate was not addressed by the Board, Joint Intervenors had no opportunity to re-direct questions at Lucas.

Lucas' assertion that people who refuse to evacuate would not divert resources is without legal basis. If the people threatened by the chemical spill had to be forcibly evacuated because of an executive order by the parish president of a general emergency, people threatened by a serious accident at Waterford 3 deserve the same consideration. They certainly did not create the hazard and therefore do not deserve to be unnucessarily exposed to radiation.

Millions of dollars have been spent by the atomic industry on television, radio, and newspaper advertisements which have had the affect of downplaying the hazards of radiation. In all likelihood, the brochure to be distributed by the utility will contain charts and text stressing the 'extremely low likelihood' of a serious accident. The brochure distributed around the Grand Gulf station contained these leements. It is not unreasonable to assume that the cumulative effect of this information would result in one-third, or more, of the population refusing to evacuate.

The neighboring population should be aware of the massive mortality and morbidity possibilities from a serious nuclear accident. They should not be unduly swayed by hours of television advertisements reassuring them of the safety of the plant and then one day hear sirens go off and be told to run for their lives. Joint Intervenors have been repeatedly stopped from questioning even the evacuation officials on the hazards of a serious accident.

Even attempts by Lucas to downplay the phenomenon of people refusing to evacuate raises many questions. Lucas said: "...through manay, many months that we've had emissions in St. Charles Parish, it (the phenomenon) hasn't been to that extreme. We haven't had that much of it." (Tr. 3036 - 19&20). If one-third of the population refusing to evacuate is considered "extreme", what is the usual percentage? Joint Intervenors were prevented from finding out due to rulings from the Board. PF 10

Omission 2 - Additional Collisions:

Lucas testified that because people would be "enthusiastic" to leave the contaminated area, there would be an increased number of accidents on the evacuation route. Madere concurred. Twine testified that he did not agree, but that he did not want to contradict their experience (Tr. 2840-2843). Twine also testified that when developing ETE, he assumed there would be enough rescue vehicles to clear any accidents (Tr. 3003) However, since he did not count on an increased number of accidents, and in fact, assumed a reduction in accidents, the number of rescue vehicles he assumed would be needed would be below the actual number needed given a greater number of accidents as indicated by Lucas and Madere. This could impede the evacuation by slowing vehicles used on roads and highways. PF 11

Omission 3 - Hysteria:

The question of hysteria as a factor in the emergency plans has had a complex history. The original question on the possibility of hysteria was posed by Joint Intervenors to FEMA expert Benton (Tr. 2886-19ff). Over objection by the Staff, FEMA and Applicant, Benton was instructed to answer. His response was an unequivocal 'no'. On Board examination, Benton said he "personally" did not take it into account - NUREG-0654 does (Tr. 2914).

On further inquiry, Benton said a section in Planning Basis part of NUREG-0654 'implied' hysteria was considered (Tr. 2915-19). Joint Intervenors, on redirect, again affirmed that FEMA witnesses

(Lookabaugh and Benton) did not take hysteria into account (Tr.2918-3) (Tr. 2918-6) nor did hysteria appear in any manner directly in NUREG-0654 (Tr. 2918-16&17).

Then Joint Intervenors attempted to question the witnesses on the relationship of hysteria to the 'evacuation shadow phenomenon", a documented phenomenon related to hysteria seen at Tree Mile Island. Staff, FEMA, and the Applicant objected and the Board sustained. This potentially fruitful line of questioning was ended over objections of Joint Intervenors (Tr. 2920-9).

The vast numbers of people at Three Mile Island who evacuated (nearly 144,000) because of their anxiety contrasts sharply with the actual number (5000) of pregnant women and children who were 'advised' to leave. PF 12

Omission 4 - Single Mode Evacuation:

The relationship between the two parish evacuation plans is strange. In both parishes the plan is to move in a single direction - each opposite from the other - at the same time, with St. John moving west and St. Charles moving east (Tr. 267- - 8&9). Even though there are reasonable mehhods of evacuating St. John parish eastward (Tr. 267 westward is the only alternative now incorporated into the plans. Similarly, despite good methods of evacuating St. Charles parish westaward, the only alternative now available is eastward. This is planned allegedly to "stop the confusion of both parishes evacuating in the same direction." This is in complete noncompliance with NUREG-0654 which says "(T)he overall objective of emergency response planning is to provide dose savings (and in some cases immediate life saving) for a spectrum of accidents that could provide offsite doese." [Read into the record by Judge Wolfe at Tr. 2360ff].

NUREG-0654 also states: "No single specific accident sequence should be isolated as the one for which to plan..." (Tr. 2360-19).

Clearly, flexibility is the key to the NRC/FEMA guidelines. This flexibility of response has been made brittle by the arbitrary nature of the selection of only one method of evacuation when perfectly good alternative routes wre available. This single path was chosen to "avoid confusion" and not for "dose saving." This is unacceptable under NRC/FEMA guidelines. If confusion is possible because

the residents of one parish would have to cross parish lines, then more practice and fuller integration of plans and resources is called for -- not arbitrary segregation of evacuation routes without regard to changing accident circumstances or maximizing dose savings.

This single mode evacuation concept that "avoids confusion" by not crossing parish lines make nonsense of the supposedly longstanding mutual aid agreements between the two parishes which allow them to share resources during times of emergency (Tr. 2989-91). In reality, they appear willing to expose their people to higher doses of radiation than share their resources with people of the other parish. PF 13

F. procedures are inadequate for evacuating people who are:

(i) without vehicles;
(ii) school children;

The primary reality in the plans for evacuating school children and persons without private transportation is the complete lack of agreements to provide for those people in need of evacuation after the parish resources are exhausted.

143 buses are needed for evacuation of residents without vehicles in both parishes (Tr. 2413-20). This is for 5,777 persons without transportation in both risk parishes (Perry, at 3). There are 16,951 students in both parishes requiring 290 buses to evacuate. (Perry at 4

There is a need for 429 buses for total evacuation of both parishes. St. John and St. Charles parish have 138 buses. This leaves a 291 bus shortfall that will, of necessity, have to be obtained from neighboring parishes (Tr. 2545).

No agreements with any neighboring parishes have been reached to provide for this shortfall (Tr. 2536). Madere admits implementing procedures are inadequate and not complete (Tr. 2537). Madere says implementing procedures are never finalized (Tr. 2591).

Madere affirms there is reasonable doubt that bus drivers would drive into St. John and St. Charles parishes from outside the 10 mile EPZ during a major radiological accident at Waterford 3. Somehow volunteer bus drivers would be transported beyond the 10 mile EPZ and allowed to use out-of-parish buses to drive into the contaminated zone (Tr. 2619).

There is no documentation whatsoever that a significant portion

of people without transportation would be given rides by other people during an emergency (Tr. 2755) (Urbanik).

The Board finds that taking into consideration the four omissions listed at the beginning of this section and the massive uncertainties that permeate this plan, it must withhold approval.
PF 14

F. procedures are inadequate for evacuating people who are:
(iii) aged and crippled;
(iv) sick and hospitalized;

There are no agreements whatsoever to provide the aged, crippled sick and hospitalized with transportation - buses, vans or ambulances - from surrounding parishes after the parish resources are exhausted (Tr. 2614).

Lucas says that they cannot get people and wheelchairs into vans (Tr. 2501). Madere says that they do not have sufficient vans and ambulances and that they are in talking stages with support parishes (Tr. 2507).

To evacuate the home bound aged and handicapped calls for 25 vans and 25 ambulances in both parishes (Tr. 2504)(Tr. 2524).

To evacuate the sick and hospitalized in both parishes requires 37 ambulances, 10 buses, and 3 vans. Perry, at 11.

This ia a total number of 62 ambulances, 28 vans and 10 buses to evacuate the aged and crippled needing transportation and the sick and hospitalized in both parishes. The two parishes presently list resources of 11 vans and 7 ambulances. Lookabaugh and Benton, 14 and 16. Thus there is a shortfall of 55 ambulances, 17 vans, and 10 buses needed to evacuate the home bound, infirm and aged needing transportation and the sick and hospitalized.

No arrangements with neighboring parishes to provide for this shortfall have been made in the 12 years that have elapsed since Waterford 3 applied for a construction permit.

The Board finds that the great uncertainties and omissions listed previously leaves no alternative but to withhold approval of the plan to evacuate these population groups. PF 15

(v) imprisoned

Joint Intervenors feel that the four general categories listed under contention F do not result in dose savings to the prison popula-

tion.

The already great strain on resources - policemen, police cars and police vans - during an emergency would make it highly unlikely that sufficient resources would be available to transport prisoners. The prison population is given low priority.

The Board feels that the four omission of contention F are sufficient to withhold approval of the plan to evacuate the prison population. PF 16

(vi) transient workers

The Board feels that the transient worker population will be inadequately protected because of the concerns raised in the four omissions enumerated under Contention F. As noted earlier, the strain on resources, the hysteria, the poor evacuation routing will combine to jeopardize the safety of the transient worker population. For these reasons the Board withholds its approval. PF 17

Joint Intervenors' Contention 17/26 (2) asserted that

> Applicant has failed to adequately make provision, according to the Emergency Plan contained in Chapter 13.3 of the FSAR, for distribution and /or storage of potassium iodide in accordance with accepted public health practice in locations which are readily accessible to affected individuals as protected against thyroid irradiation.

The predistribution of Potassium Iodide (KI) is not included in present NRC or FEMA regulations except for certain restrictive categories (prisons, hospitals etc.). This is not in compliance with NUREG-0654 guidance which specifically lists 'dose savings' as the guiding principle of action.

Joint Intervenors have shown that predistribution of KI reduces of chance of excessive thyroid doses without placing the general population at risk.

The Board concludes that the Atomic Energy Act which places the health and safety of the public as its primary concern must supercede present inadequate regulations. The Board agrees that predistribution of KI to the general population is warranted. PF 18-25

## III. PROPOSED FINDINGS

1.

Emergency planning around Waterford 3 has been guided by two general principles. The first recognizes that effective planning is largely an educational activity. This includes educating themselves and others who may be involved in emergency response and anticipating events and problems(Azzarello et al. pp.1&2). The Kemeny Commission (The President's Commission on the Accident at Three Mile Island) is very clear on this aspect of 'education' in assigning responsibility in the accident at Three Mile Island: "The fact that too many individuals and organizations were not aware of the dimensions of serious accidents at nuclear power stations accounts for a great deal of the lack of preparedness and the poor quality of the response"(p. 17 of Kemeny report read into transcripts at 3130) NRC expert Grimes confirms that individuals involved in emergency planning should be aware of the consequences of a serious nuclear accident (3760-20).

NUREG-0654 includes the most serious reactor accidents in its 'Planning Basis' section. FEMA has also concluded that NUREG-0396 should be used as a 'Planning Basis'(pp. 6&7 of NUREG-0654).

Joint Intervenors were repeatedly denied the right by Board ruling to question the key evacuation officials--Azzarello (LP&L) Myers (State of Louisiana), Madere (St. John the Baptist), and Lucas (St. Charles)-- about their knowledge of the consequences of severe accidents at nuclear power plants and specifically Waterford 3(Tr. 2190-17)(Tr. 2236-15)(Tr.2253-14)(Tr.2253-18)(Tr. 2276-9) (2279-14)(Tr.2279-25) (22-79-10) (Tr.2280-15)(Tr.2280-25)(Tr.2710-12)

NUREG-0654 (pp.7-8) also sets down several areas it considers to be of utmost importance to planning officials. "Knowledge of the kinds of radioactive materials potentially released" is one area in this category. Joint Intervenors were repeatedly denied the right to question the key evacuation officials--Azzarello, Myers, Madere, and Lucas--on their knowledge in this category(all transcript numbers in the preceding paragraph apply and including 2282-16,2237-20, 2237-22).

2

The second principle that the Applicant has used in drafting emergency plans holds that emergency plans are a continuous activity,

a so-called "living document"(Azzarello et al. pp.1&2). In fact, the plans as reviewed by Joint Intervenors have no brochure, no agreements with surrounding parishes for buses, vans, or ambulances, no communication systems installed or tested, no implementing procedures, no sirens, and no evacuation tests. This is after nearly 12 years of preparation. (FEMA "RAC" Review on Waterford Nuclear Power Plant), (Tr. 2537)(2536)(2591)(3955-2&4)(2507-9)(3074).

Joint Intervenors agree with the observation of Judge Jordan: "There has to be more than paper plans"(2275-11).

3

The Board is limited in its power to give approval under 10CFR 50.47(a)(1) which states that onsite and offsite planning "provides reasonable assurance that adequate protective measures can and will be taken in the event of a radiological emergency".

The 'can and will' section is the most important. It implies two standards must be met. The first test (whether adequate protective measures 'can' be taken) is the theoretical plans themselves. Their failures are examined elsewhere in these findings.

The second test (whether adequate protective measures 'will' be taken) denotes examining the individuals in key positions. Joint Intervenors attempted to delineate possible conflicts of interest of individuals in key positions in the offsite planning. The parish president of St. Charles parish has both familial and financial interest in the well-being of the corporation of Louisiana Power & Light. (Tr. 2962-66). The civil defense director of St. John the Baptist Parish, Bertram Madere, is a full time employee of E.I. Dupont. Dupont has a tremendous financial interest in nuclear power in the Savanah River Nuclear Power Plant in South Carolina. (Tr. 2234). The Board prevented Joint Intervenors from pursuing this line of questioning by adverse rulings.

Evaluating personnel involved with onsite planning is a concern of the NRC. NRC expert Perotti: "...I cannot at this time state whether the people are adequate or not, because I have not had a chance to evaluate the individuals involved."(Tr. 3920). This contrasts sharply with the Board"s ruling on questioning the adequacy of the key individual-the parish president- in the offsite plan:"We're not going to get into incumbents in office. We're talking about command structure."(Tr. 2966-15&16)

4

The concepts of predictive findings and post-hearing verification as a decision-making device in ajudicatory hearings involving members of the public is contrary to the 5th Amendment right of due process under the Constitution of the United States, the Administrative Procedures Act, and the Atomic Energy Act. Any predictive findings or post hearing verification by the NRC or FEMA in subjects delineated in the contentions of the Joint Intervenors is clearly illegal. Joint Intervenors contend that their rights can only be protected by reconvening this tribunal after the substantive parts of the emergency plan have been finalized. Joint Intervenors reserved this right in the record. (Tr. 3989-90). However, this right was denied by ruling from the Board.

5

The notification of residents was clearly inadequate because no brochure was available to critique (Tr. 2889). Joint Intervenors were prevented from questioning even a similar brochure (Grand Gulf) on its general foremat or nuclear terminology (Tr. 2202)

6

Madere testified at length about the need for increased roads and highways in his parish. These roads are needed to hasten evacuation from chemical spills. Although he has been promised additional roads since 1972, none has been built (Tr. 2783-2795) Lucas also testified that additional roads built to speed up the evacuation process. However, neither of these men mentioned the prior requests for additional roads to the FEMA experts. (Tr. 2875-77)

7

The siren system is not in place and therefore not tested. (Lookabaugh and Benton, p. 7). Further, no witnesses were present to answer questions about the siren system as an expert (Tr. 2345-5). Although FEMA witnesses testified that the warning system was adequate, they never visited the siren locations (Tr. 2879).

The siren system would not contact the hearing impaired population (Lookabaugh and Benton, p. 7). The siren system would also not contact those individuals who work in an area with high ambient noise (Lookabaugh and Benton, p.6). In the case of the hearing-impaired, officials would attempt to contact the neighbors of these individuals by phone to relay the message.

Joint Intervenors were prevented by Board ruling from questioning the adequacy of the phone system in a time of crisis (Tr. 2820).

The pre-prepared messages that are to be transmitted over the radio are'fill in the blanks' type. No messages were completed or available and it is uncertain whether they will provide adequate information to the public (Tr. 3092).

8

Findings of Fact #1 and #3 deal with command decision structure and they should be subsumed in toto in this finding of fact as written. #1 deals with lack of knowledge of serious nuclear accidents that could contribute to poor response. #3 deals with conflicts of interest and its possible effect on proper response.

Lucas says he would immediately recommend evacuation to the parish president if the utility tells him to evacuate. He would do this without requesting an independent accident assessment from the state(Tr. 2954). FeMA expert Benton says the state can act immediately on information from the licensee without independent assessment from other state agencies (Tr. 2910-23). FEMA expert Benton states elsewhere in his testimony that no confidence can be given to the utility's ability to give protective actions because the utility has no knowledge of traffic conditions or resources (Tr. 2318-8).

Madere shows little knowledge of NUREG-0654 in not knowing that windspeed and distance are all subsumed in guidance calculations that appear in Table 2 of that documents. He does not believe that radiation could reach his populated areas in one-half hour (Tr. 2676-18ff).

Madere also had grave misgiving concerning the NUREG-0654 (Tr. 2570-3&4). Joint Intervenors were prevented by Board ruling from probing Madere's doubts about the document(Tr.2572-2).

The utility and the state have substantial differences in their protective action recommendations concerning pregnant women and children (Tr. 3107--11 thru 13)(3141-14).

9

FEMA witnesses said that evacuation drills are not likely to be well attended if the public was allowed to participate because they had "observed exercises" in which people did not

participate. In fact, they had observed only one exercise (Tr. 2883).

When the Applicant does conduct a drill to test the commitments of resources and officials, all but one will be announced ahead of time. The only unannounced drill will be conducted after the plant will be in operation (Tr. 2614)(Tr. 3097).

10

Lucas testified that at a recent chemical spill in St. Charles parish that affected nine himes, three of those homes refused to evacuate. Many resources--human and material-- were used to extricate these people. Resources were also expended to impound these people's animals (Tr. 2917-19ff). Lucas said that the parish president declared an emergency situation, and then officials physically removed them. (Tr. 2718-6). Joint Intervenors attempted to question Lucas on the amount of resources used to extricate the people-- one third of the affected population-- but were stopped by ruling of the ASLB on objection from Applicant's counsel (Tr. 2724-18).

11

Lucas testified that because people would be'enthusiastic' to leave the contaminated area, there would be an increased njmber of accidents on the evacuation route. Madere concurred. Twine testified that he did not agree, but that he did not want to contradict their experience (Tr. 2840-2843). Twine testified that when developing the ETE, he assumed there would be enough rescue vehicles to clear any accident (Tr. 3003).

12

FEMA expert Benton said he personally did not take hysteria into account (Tr. 2914) but NUREG-0654 does. On further inquiry, Benton said a section in the 'Planning Basis' part of NUREG-0654 'implied' hysteria was considered (Tr. 2915-19). Joint Intervenors, on redirect, again affirmed that FEMA witnesses (Lookabaugh and Benton) did not take hysteria into account (Tr. 2918-3)(Tr. 2918-6) nor did hysteria appear in any manner directly in NUREG-0654(Tr. 2918-16&17).

Then Joint Intervenors attempted to question tee witnesses on the relationship of hysteria to the'evacuation shadow phenomenon', a documented phenomenon related to hysteria seen at Three Mile Island. Staff, FEMA, and the Applicant objected and the Board sustained. This potentially fruitful line of questioning was ended over objections of Joint Intervenors (Tr. 2920-9)

13

The relationship between the two parish evacuation plans is strange. In both parishes the plan is to move in a single direction - each opposite from the other - at the same time, with St. John moving west and St. Charles moving east (Tr. 2671- 8&9). Even though there are reasonable methods of evacuating St. Charles Parish eastward (Tr. 2673-2), westward is the only alternative now incorporated into the plans. Similarly, despite good methods of evacuating St. Charles parish westward, the only alternative now available is eastward. This is planned allegedly to "stop the confusion of both parishes evacuating in the same direction".

NUREG-0654 says this about the primary objective of emergency planning: "The overall objective of emergency response planning is to provide dose savings (and in some cases immediate life saving) for a spectrum of accidents that could provide offsite doses"... No single specific accident sequence should be isolated as the one for which to plan..." [Read into the record by Judge Wolfe at Tr. 2360ff]

14

The primary reality in the plans for evacuating school children and persons without private transportation is the complete lack of agreements to provide for those people in need of evacuation after the parish resources are exhausted.

143 buses are needed for evacuation of residents without vehicles in both parishes (Tr. 2413-20). This is for 5,777 persons without transportation in both parishes. St. John and St. Charles parish have 138 buses. This leaves a 291 bus shortfall that will, of necessity, have to be obtained from neighboring parishes (Tr. 2545).

No agreements with any neighboring parishes have been reached to provide for this shortfall (Tr. 2536).
Madere admits implementing procedures are inadequate and not complete (Tr. 2537). Madere says implementing procedures are never finalized (Tr. 2591).

Madere affirms there is reasonable doubt that bus drivers would drive into St. John and St. Charles parishes from outside the 10 mile EPZ during a major radiological accident at Waterford 3. Somehow volunteer bus drivers would be transported beyoun the 10 mile

EPZ and allowed to use out-of-parish buses to drive into the contaminated zone (Tr. 2619).

15

There are no agreements whatsoever to provide the aged, crippled sick and hospitalized with transportation - buses, vans or ambulances - from surrounding parishes after the parish resources are exhausted (Tr. 2614).

Lucas says that they cannot get people and wheelchairs into vans (Tr. 2501). Madere says that they do not have sufficient vans and ambulances and that they are in talking stages with support parishes (Tr. 2507).

To evacuate the gome bound aged and handicapped calls for 25 vans and 25 ambulances in both parishes (Tr. 2504)(Tr. 2524).

To evacuate the sick and hospitalized in both parishes requires 37 ambulances, 10 buses, and 3 vans. Perry, at 11.

This is a total number of 62 ambulances, 28 vans, and 10 buses to evacuate the aged and crippled needing transportation and the sick and hospitalized in both parishes. The two parishes presently list resources of 11 vans and 7 ambulances. Lookabaugh and Benton, 14 & 16. Thus there is a shortfall of 55 ambulances, 17 vans, and 10 buses needed to evacuate the home bound, infirm and aged needing transportation and the sick and hospitalized.

16

Findings of facts 10, 11, 12, and 13 are all that is necessary to demonstrate bad planning and unexpected drains on resources. Great strains on resources - policemen, police cars, and police vans - during a crisis makes it unlikely that the prison population would receive high priority.

The prison population would receive unnecessary and excess doses of radiation during an evacuation because of this bad planning and unexpected resource drains. Therefore Joint Intervenors believe the plan is inadequate.

17

The bad planning and unexpected resource drains listed in Findings of Fact 10, 11, 12, and 13 will result in unnecessary and excess doses of radiation to the transient worker population during an evacuation.

18.

The human thyroid gland has an active iodide transport system which enables it to concentrate iodide so that the ratio of thyroid to plasma (blood) iodide concentrations is usually between 20-to-1 and 50-to-1. Iodine is essential for the production of thyroid hormones which regulate the metabolic rate of the body and are necessary for full body growth and normal function. (Mauro, ff. Tr. 3138; U.S. Food and Drug Administration, Bureau of Radiological Health Background Material for the Development of the Food and Drug Administration's Recommendations on Thyroid-Blocking with Potassium Iodide. HHS Publication FDA 81-8158, p.1)

19.

The ability to concentrate iodide is not limited to the thyroid gland but is found to a lesser degree in other organs, including the salivary glands, parts of the gastrointestinal tract, mammary glands, and placenta. The latter two have special significance for pregnant women, the fetus, and nursing infants. (HHS Publication FDA 81-8158, p.1 and p.11)

20.

A significant percentage of the long-lived radioactivity in the core of an operating nuclear reactor is radioactive iodine. These radioiodides would make up an even larger percentage of the radioactive gases driven off by an overheated reactor core, because the chemical forms of the radioiodides in a reactor core are relatively volatile. (Von Hipple, statement

on March 5, 1982 before the Subcommittee on Oversight and Investigations of the House Committee on Interior and Insular Affairs)

21.

The principal radioactive isotope released in a reactor accident is Iodine-131 along with other radioiodines. The primary route of exposure is inhalation of contaminated air. Ingestion of contaminated foods, water, and milk can persist as a means of exposure for days, weeks, or months after an accident. These radioiodines tend to accumulate and concentrate in the thyroid where they cause radiation damage which results in many thyroid disorders including benign tumors and malignant cancers. (Mauro at 2; Mauro ff. Tr. 3141; Van Hipple, March 5, 1982, Statement before the Subcommittee on Oversight and Investigations of the House Committee on Interior and Insular Affairs. HHS Publication FDA 81-8158, p. 7)

22.

While only some persons may actually die as a result of thyroid cancers induced by radioiodines many will require surgery, experience pain and suffering, and be forced to take thyroid hormones for the rest of their lives if a major accident occurs at a nuclear reactor. (Mauro, ff. Tr. 3141-42; Von Hipple, March 5, 1982, Statement before the Subcommittee on Oversight and Investigations of the House Committee on Interior and Insular Affairs)

23.

It is possible to achieve up to 90% blockage of absorption of radioiodines into the thyroid by administering 130 mg of potassium iodide to an adult (65 mg to a child one year or less) prior to exposure. The benefit drops to 50% blockage if potassium iodide is administered three to four hours after a release and little benefit can be expected after 10 to 12 hours for a single exposure. In case of prolonged exposure to radioiodines potassium iodide will be of some benefit because it will reduce further accumulation. However the most efficient use of potassium iodide can only be achieved if it is administered prior to exposure. (Mauro, at 2; Myers, ff. Tr. 3198; HHS Publication FDA 81-8158, pp. 2-4)

24.

Due to the airborne nature of radioiodine releases, and the inhalation pathway of exposures to the thyroid a number of analyses have concluded that, out to a distance of ten miles from a release point at least, the only way to ensure that potassium iodide would be available to the population in time would be to predistribute it. It is difficult to discern how the drug can be made available to persons in the "high risk" area soon enough to allow for effective thyroid blocking unless each household is provided in advance with a supply sufficient for all residents of the household. (Myers ff. Tr. 3191-94; Von Hipple and Galwin, March 5, 1982, Statement to the Subcommittee on Oversight and Investigations of the House Committee on Interior and Insular Affairs; HHS Publication FDA 81-8158, p. 13)

25.

Potassium iodide in dosage levels sufficient to provide protection to the thyroid gland (130 mg for adults and children over one year and 65 mg for children less than 1 year) has been found so safe by the U.S. Food and Drug Administration that the Federal legend has been removed and it may be sold without a prescription. Potassium iodide in large doses (300-1200 mg daily) and on a long-term basis has been widely used for years in the management of bronchial asthma and other pulmonary disorders. In eleven years (1969-1980) the Division of Drug Experience of the FDA has only 160 adverse reaction reported. Known allergy to iodide would appear to be the only contraindication to its use in a radiation emergency. (Mauro, ff. Tr. 3156; HHS Publication FDA 81-8158, p.4; Villforth, March 15, 1982, Statement before the Subcommittee on Oversight and Investigations of the House Committee on Interior and Insular Affairs)

26.

Potassium Iodide U.S.P. is an inorganic chemical that is readily available in any pharmacy in small quantities for compounding in whatever dose is necessary either as a liquid or capsule by a pharmacist or physician. It is a common practice for pharmaceutical manufacturers to temporarily cease production of their products until current supplies are depleted to minimum levels before producing additional supplies. (Perratti ff. Tr. 3260; Perrotti, ff. Tr. 3891-93, Perrotti ff. Tr. 3923)

## IV. CONCLUSIONS OF LAW

The Board has considered all of the evidence submitted by the parties and the entire record of this proceeding. Based on the Findings of Fact set forth herin, which are supported by reliable, probative and substantial evidence in the record, this Board, having dedided all matters in controversy, concludes that, pursuant to 10 CFR 2.760a, the Director of Nuclear Reactor Regulation should be authorized to deny to the Applicant a license authorizing operation of the Waterford Steam Electric Station, Unit 3.

## V. ORDER

IT IS HEREBY ORDERED, pursuant to the Atomic Energy Act of 1954 and the Commission's rules and regulations, based on the Findings of Fact and Conclusions of Law set forth in this Initial Decision, the Director of Nuclear Reactor Regulation is authorized under 10 CFR 2.760a to deny to the Applicant Louisiana Power & Light Company a license to operate at any temperature.

Respectfully submitted

_____

Luke Fontana and Gary Groesch
Counsel for Joint Intervenors

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# THE IMPLICATION OF CANCER-CAUSING SUBSTANCES IN MISSISSIPPI RIVER WATER

A Report Submitted To

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Councilman-at-Large
New Orleans, Louisiana

by

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November 6, 1974

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# THE IMPLICATION OF CANCER-CAUSING SUBSTANCES IN MISSISSIPPI RIVER WATER


## Abstract

The Mississippi River rises in Minnesota and flows southward 2350 miles to the Gulf of Mexico, draining over 40% of the United States and part of Canada. Including its numerous tributaries, such as the Ohio River, it is the receptacle for a wide variety of municipal and industrial wastes. Many of the industries, including the petroleum, organic chemical, and coal-products industries, are known to discharge persistent carcinogens into the Mississippi River. In addition, chlorination of water during treatment increases the carcinogenic burden. Consequently, these carcinogens are imbibed by millions of Americans, as has been documented recently by the Environmental Protection Agency during studies on eight cities that receive drinking water from the Mississippi River system. In Louisiana alone, over one million people are served water from the lower Mississippi River or its distributaries. Presumptive epidemiological evidence accumulated by the Environmental Defense Fund with the aid of a computer-assisted statistical model suggests a significant relationship between cancer mortality among white males and drinking water obtained from the Mississippi River. Neither the Environmental Protection Agency nor state and local regulatory agencies have to date developed adequate programs of pollution abatement or drinking water treatment to address these problems, despite the Environmental Protection Agency's strong recommendations to the contrary in 1972, and despite the availability of inexpensive and effective remedial measures.


## Presence of Cancer-Causing Chemicals in Water

There is little question that industrial wastes contain a variety of potentially toxic substances which are routinely

discharged into our nation's waters despite the recent enactment of laws (e.g., Federal Water Pollution Control Act Amendments of 1972, PL 92-500) which are supposed to prevent these discharges. Over a decade ago, Dr. W. C. Heuper, of the National Cancer Institute, outlined the sources of certain of these chemical substances (carcinogens) which can cause cancer (1). Some of these are as follows:

1. Petroleum Products -- Petroleum refinery wastes containing polycyclic aromatic hydrocarbons, fuel oil, lubricating oils and cutting oils are being introduced into lakes and rivers from garages, service stations, petrochemical plants, metalworking plants, and ships. Contamination of public water supplies may also result from the use of kerosene, methylated naphthalenes and similar petroleum products used as vehicles of insecticide sprays, or enter water from rain contaminated with air pollutants or from tarred or asphalted roads.

2. Coal Tar -- Effluents from gas plants, coke oven operations, tar distilleries, tar-paper plants, and wood pickling plants all contain carcinogens. Coal tar, pitch, creosote, and anthracene oil are known human carcinogens.

3. Aromatic Amino- and Nitro- Compounds -- Amino compounds such as beta-naphthylamine, benzidine, and 4-aminodiphenyl are known to be human carcinogens from results of occupational exposure of workers in dye and rubber industries. These compounds along with their nitro-analogues are released by dye and rubber manufacturing, pharmaceutical factories, textile dying plants, plastic production, and others.

4. Pesticide, Herbicide, and Soil Sterilants -- Compounds such as DDT, Dieldrin, Aramite, carbon tetrachloride, acetamide, thioacetamide, thiourea, thiouracil, aminotriazole, several urethane derivatives, isopropyl chlorophenyl carbamate, and beta-propiolactone are capable of eliciting benign and/or malignant tumors in various organs of experimental animals.

In addition to industrial wastes, discharges from domestic sewage treatment plants may also be responsible for a variety of carcinogenic substances found in water. In a recent study by Jolley (2), for example, over 50 chlorinated hydrocarbons were identified in chlorinated domestic sewage effluents. Consequently, Jolley estimated that over 1,000 tons of chlorinated organic compounds are discharged by sewage treatment plants into the nation's waterways annually.

(EPA) laboratories in Cincinnati has confirmed these results. From analyses of five communities receiving water either from the Ohio or Mississippi Rivers, chloroform concentrations were observed to range from 37 to 152 ppb (parts per billion parts of water). Communities receiving well water, which is generally less polluted with organic matter than is surface water, were observed to have less than 1/10th the concentration of chloroform in their drinking water when compared to communities receiving polluted Ohio or Mississippi River water.

From these studies, therefore, it can be concluded that public drinking water supplies are routinely contaminated with carcinogenic substances from industrial and municipal discharges, accidental spills, runoff from agricultural and urban areas, and from the chlorination process at water treatment plants. From analyses of tap water samples at Nitro, West Virginia (5), Evansville, Ind. (6), Ames, Iowa (7), and several Nebraska communities (8), it is evident that carcinogens and other potentially toxic organic chemicals are not removed by standard water treatment processes and are continual contaminants of tap water.

## The 1972 EPA Study of the Lower Mississippi River

In 1967, the Federal government initiated field studies to investigate the causes for the severe taste and odor problems present in the municipal drinking water supplies and the off-

flavors of fish caught in the lower Mississippi River in Louisiana. Much of this problem was assumed to be due to the rapid growth of the petrochemical industry since the mid-1950's. The survey included analysis of river water, treated drinking water, industrial wastes, and fish exposed to the river from St. Francisville to Venice, approximately 250 river miles.

In 1972, the Environmental Protection Agency released the results of this survey. Heavy metals such as mercury, arsenic, lead, copper, chromium, cadmium, and zinc were found in waste discharges in addition to phenols, cyanides, and a wide array of organic compounds. Although time did not permit identification of all chemicals, 48 organic chemicals were identified in the raw or treated water supplies from three plants -- the U. S. Public Health Service Hospital at Carville, the Carrollton Water Treatment Plant of the city of New Orleans, and the Jefferson Parish No. 2 Water Plant at Marrero. Five of these chemicals found in finished water supplies (chloroform, hexachlorobenzene, zylene, ethyl benzene, dimethylsulfoxide) were listed as having induced histopathological changes during chronic toxicity studies on animals. Three compounds (chloroform, benzene, and carbon tetrachloride) were listed as carcinogens.

From the results of this survey, the EPA concluded that the industrial discharges were the principal cause of the persistent "oily-petrochemical" odor in the public water

supplies downstream from Baton Rouge. And on a more ominous note, the EPA concluded that:

> The trace organics in the Mississippi River drinking water supplies are a potential threat to the health of the 1.5 million people who consume this water, particularly the elderly, those that are ill, and children. (9)

In addition, the EPA offered rather strong recommendations for corrective action and for epidemiological investigations to determine the long-term effects on humans of ingesting contaminated water from the Mississippi River:

> It is clear that society must weigh carefully the expenditures for corrective action, both industrial and municipal, against the costs it may have to pay in terms of present or future health impairment of its people stemming from man-made hazards. (9)

* * * * * * * *

> It is mandatory to single out potentially harmful substances and prevent them from entering those bodies of waters that will be used for drinking or food sources until it is clearly demonstrated that they pose no threat to human health or aquatic life. (9)

* * * * * * * *

> Municipal water treatment plants [should] install treatment facilities designed to (a) obtain optimum removal of organic contaminants and heavy metals and to (b) provide increased protection of the water supplies from accidental spills of chemicals and oil upstream from the municipality's raw water supply intake structure. (9)

Although the EPA did not elaborate further on corrective actions, they did suggest that "continuous use of activated carbon would probably be required to remove the trace organics in the water supplies" (9). Despite these warnings and

recommendations, there has in general been no effort by communities along the lower Mississippi River to take corrective action and relatively little effort by the industrial dischargers to abate pollution from toxic and carcinogenic substances.

## The New Orleans Carrollton Water Treatment Plant

The Carrollton Water Treatment Plant in New Orleans is typical of most municipal water treatment facilities in the United States. It was designed and constructed in the early 1900's, employing latter 19th Century and early 20th Century technology. At the time of its construction, the major problems facing the water treatment industry were waterborne diseases such as typhoid fever and cholera. Consequently, a treatment objective was developed that has remained essentially unchanged over the past six decades; Carrollton remains today a facility whose primary function is to prevent the spread of waterborne diseases. The treatment processes at Carrollton were not designed to remove carcinogenic and other toxic substances.

The present treatment process at Carrollton includes permanganate treatment for partial taste and odor control, lime addition for softening, coagulation/sedimentation/filtration for removal of suspended particles, and chlorination for disinfection. Although the average water quality leaving the plant technically meets the U. S. PHS 1962 drinking water standards and is approved by the EPA as an interstate carrier supply, the PHS standards can only be enforced to protect against the spread of communicable diseases, and not to protect against toxic chemicals. For these reasons, the United States Congress is considering corrective legislation and the EPA is currently revising the standards to eliminate the inadequacies of the 1962

Public Health Service standards. Therefore, compliance with the 1962 Public Health Service standards can in no sense be taken as a guarantee of safety.

From an examination of the operation of the Carrollton plant and its operating records, the following can be concluded:

(1) Current treatment practices are inadequate for the proper control of toxic organic compounds which enter the water through municipal and industrial discharges, runoff from agricultural regions, and chemical spills and accidents on the river.

(2) Despite EPA recommendations to the contrary made in 1972, monitoring is still inadequate for toxic organic chemicals and heavy metals. Both would be expected to vary daily, and samples should be taken at least weekly at the consumer's tap.

(3) The sodium concentration in the finished water frequently exceeds the recommended levels set by the American Heart Association for patients on a restricted-salt diet.

(4) The present practice of reducing hardness is probably not beneficial, and in fact there is strong evidence that it may be detrimental to the consumer's health. A number of studies in Canada, Great Britain, Sweden, The Netherlands, South America,

Japan, and in this country have suggested that the softer the water the higher the incidence of diseases of the heart and circulatory system.

(5) By reducing hardness with lime addition, the pH of the water delivered to the consumer generally exceeds 10. This pH is exceptionally high compared to most community drinking water supplies in the United States, although there are no known health effects associated with this condition. However, a pH-value as high as 10 would lower the efficiency of the treatment process for removing viruses and bacterial pathogens.

(6) Storage capacity is inadequate to offer the maximum in fire protection and to guard against toxic spills in the Mississippi River. Adequate storage would permit the bypass of spills in the river.

In conclusion, there seems to be little question that Carrollton is an antiquated water treatment plant attempting to cope with 20th-century problems but handicapped with 19th-century technology. In the absence of procedures to remove toxic chemicals and in the absence of disinfection practices which do not produce toxic chemicals, the citizens of New Orleans can be assured of the presence of carcinogenic chemicals in their drinking water indefinitely, or until procedures are taken to both clean up the river and to remove the remaining toxic chemicals at the water treatment plant.

## Likely Fluctuations in Types and Quantities Of Carcinogens in Mississippi River Water

It can be expected that both the types and quantities of carcinogens in the Mississippi River would vary, probably on a daily basis. For example, many industrial processes are seasonal, others are batch operations, and both practices would lead to intermittent waste discharges. Coupled with seasonal variations in river flow, runoff from urban areas, runoff from agricultural regions during the growing season, and spills and industrial accidents on the river, these intermittent operations practically guarantee that there will be wide variation in the concentration of chemical contaminants in the river at New Orleans.

## Inadequacies of Current EPA Testing Program

In the 1972 EPA testing program, the procedures used to measure organic chemicals in the drinking water employed the "mega" sampler, which uses activated carbon to remove and concentrate the organics, followed by extraction and analysis using GLC-Mass spectroscopy. The New Orleans drinking water supply was first sampled in January of 1970. The current EPA testing program sampled in July-August of 1974. In addition to using the "mega" sampler for this most recent sampling program, the EPA has indicated (10) that additional samples will be obtained and analyzed using both a liquid/liquid

extraction procedure and a reverse osmosis extraction procedure.

The several shortcomings of both of these EPA testing programs can be summarized as follows:

(1) They represent essentially a "grab sample" and therefore are not indicative of the long-term exposure of consumers to carcinogens in their drinking water. Variations in the kinds and quantities (discussed above) of carcinogens in the river will not be measured. Therefore, it will be impossible from the results of these testing programs to determine an average body burden of these carcinogens for New Orleans residents. However, even if precise quantitative and time-dependent data were made available by these testing programs, it is unlikely that definitive conclusions could be reached regarding the cancer hazard (this will be discussed further in later sections).

(2) The activated carbon (mega sampler) procedures have been outdated and should not be used as an analytical procedure for determining carcinogens in water. Activated carbon may not trap every carcinogen that is present and those carcinogens

which are trapped may not be removed and analyzed during the extraction procedures which follow. Therefore, although activated carbon procedures will measure many compounds, they are likely to miss others.

(3) There is incomplete information on the sensitivity and extraction efficiency for all of the compounds that are likely to be present in Mississippi River water.

(4) Certain classes of carcinogens, in particular polynuclear aromatic hydrocarbons (PAH) will probably be missed by the analytical procedures employed by the EPA. PAH are potent carcinogens and their ubiquitous presence in polluted drinking water supplies has lead the World Health Organization to establish standards on 6 of these compounds (11).

when administered to animals or humans, increase the probability of tumor induction. Carcinogens may act at the site of initial contact, at the site of selective organ localization or accumulation, at the site of excretion, or at the site of metabolism. Some carcinogens act at single sites only; others act at multiple sites.

Low Levels of Carcinogens in the Environment

There is now growing recognition that the majority of human cancers are due to chemical carcinogens in the environment, and, therefore, as concluded by the World Health Organization (WHO) are "...potentially preventable." Estimates by the WHO, the National Cancer Institute (NCI) and various cancer specialists suggest that somewhere between 60 and 90% of human cancers are environmental in origin. The basis for these estimates largely derives from epidemiological studies, in large community populations over extended periods, which have revealed wide geographic variations in the incidence of cancer of various organs (Appendix B). Although less certainty exists of the role of most environmental contaminants in human cancer than say cigarette smoking, drugs, and occupational airborne particles, a recent presidential panel concluded that:

> Cancer incitements by so far unrecognized chemicals combine to form a threat to health, that may well be of at least the same general size as the three major threats just described [i.e., cigarette smoking, alcohol abuse and choice of dietary composition]. These chemicals may be natural or synthetic.

Although most of the evidence for the effect of environmental carcinogens on man has come with industrial exposure to high levels of these carcinogens, most cancer experts insist that the low levels of carcinogens to which the general population is exposed are responsible for the majority of human cancers. Although others would argue that the levels of these chemicals in the environment are too small to be of significance to the general population, the scientific evidence simply does not support this viewpoint. For example, the chemical "aflatoxin" is known to cause cancer in man, and in experiments on trout, it was shown to produce liver tumors when present in feed in concentrations as low as 400 parts per trillion; even at this low level, its carcinogenic effect was enhanced by addition of various non-carcinogenic oils to the diet (Appendix B). Similarly, dieldrin (a chlorinated hydrocarbon) has been found to be carcinogenic in the lowest concentrations tested, 100 parts per billion. Therefore, lacking scientific evidence that a threshold existed for any chemical carcinogen, the ad hoc Committee on the Evaluation of Low Levels of Environmental Chemical Carcinogens reporting to the Surgeon General in 1970 concluded that:

> No level of exposure to a chemical carcinogen should be considered toxicologically insignificant for man. (12)

Carcinogenicity Data on Substances Found in New Orleans Drinking Water

Among those compounds found in the 1972 EPA study on treated drinking water supplies in communities in the lower Mississippi River, carbon tetrachloride, chloroform, bis(2-chloroethyl) ether have been shown to be carcinogenic in oral feeding studies using animals. Although bis(chloromethyl) ether, a known human carcinogen, was also listed, it is suspect since this compound is extremely volatile and it is doubtful whether it could be stable in water. A fifth compound, benzene, has been shown to increase the incidence of leukemia and lymphoma among occupationally exposed workers, but has been inadequately tested in oral feeding studies. Five additional compounds are suspected of being carcinogens and have been included in the on-going large-scale carcinogenicity testing programs sponsored by the National Cancer Institute (Appendix C).

Therefore, except for benzene and possible bis(chloromethyl) ether, human carcinogenicity data does not exist for the compounds found in New Orleans drinking water, and it is therefore logical to question the appropriateness of applying data obtained from animal experiments to expected human response. In cases like this, determining whether a carcinogen causes cancer to humans is difficult, since the lag time between exposure and onset of malignance is usually measured in decades.

not possible to predict safe levels of carcinogens based on data from animal experiments. As HEW Secretary Fleming stated some 14 years ago, "Scientifically, there is no way to determine a safe level for a substance known to produce cancer in animals" (Appendix B).

Cancer Mortality in Louisiana and Its Relation to Drinking Water

Considering the incidence of human cancer in the United States, there is little question that wide geographical variations exist as well as variations among ethnic and socio-economic groups. For example, bladder cancer mortality rates are higher in the northeast and lower in the south (Louisiana is a notable exception). Bladder cancer death rates are also higher in Protestants and in lower or middle socio-economic groups and there is an increased risk in cigarette smokers.

Using data collected for the period 1949-51, the U. S. Public Health Service Report on "Comparative Mortality Among Metropolitan Areas of the United States" listed New Orleans as the third highest of 163 metropolitan areas for mortality from kidney cancer, 6th highest for cancer of the bladder and urinary organs, 9th highest for cancer of unspecified digestive organs, and 11th highest for benign and unspecified other kinds of cancer. New Orleans was also listed as having 2.6 times the

national average mortality rate for tongue cancer and 3.5 times the national average of cancer of other parts of the mouth.

The last comprehensive survey of cancer incidence in New Orleans and other major cities in the United States was prepared from data collected for the period 1948-49 (14). Compared with 9 other major cities in the United States, New Orleans ranked second in incidence of all cancers, 25% higher than the average for the 10 cities studied. Dallas had the highest incidence of cancer, largely due to the extremely high incidence of skin cancer. Compared with the three other southern cities (Atlanta, Birmingham and Dallas) included in this survey, the incidence of cancer of the digestive system was 42% higher in New Orleans, while the incidence of cancer of the urinary organs was over twice as high in New Orleans (bladder cancer rate was 3 times higher in New Orleans). Compared to the other 9 cities, New Orleans had a higher incidence of practically every type of cancer except cancer of the digestive system and cancer of the brain and nervous system, as well as a few rare cancers.

Recently, the U. S. Department of Health, Education and Welfare has published a comprehensive study on cancer mortality titled "U. S. Cancer Mortality by County: 1950-1969" (13). As can be seen in Table 2, ranking counties by cancer mortality among white males, nine Louisiana counties are among the top

45 counties in the United States. Comparing Louisiana and New Orleans with average U. S. mortality rates (Table 3) it can be seen that New Orleans, the third highest county for cancer mortality in the United States (230/100,000), has a 32% higher total cancer mortality rate than the national average (174/100,000). Similarly, New Orleans is seen to have a 69% higher respiratory cancer rate, a 35% higher rate of cancer of the urinary organs, a 32% higher rate for cancer of the pancreas, and a 53% higher rate of cancer at unspecified sites. The average cancer mortality for Louisiana as a state is also significantly higher than the U. S. average.

Considering the earlier data on the incidence of cancer in New Orleans, and the more recent data on cancer mortality by parish (county) in Louisiana, there seems to be little question but that certain locations in Louisiana represent "hot spots" for cancer mortality. In view of the debate over whether or not carcinogens in Mississippi River water are contributing to this high cancer rate among Louisiana residents, the Environmental Defense Fund, in cooperation with Dr. Talbot Page of Resources for the Future, Inc. (a Washington-based non-profit research organization) has conducted an epidemiological investigation of the causes of cancer mortality in Louisiana, with particular attention to the importance of drinking water as a causative factor.

It has long been recognized by epidemiologists that cancer rates vary according to social, racial, and economic considerations, which undoubtedly reflect differential exposures to carcinogens caused by differences in dietary habits, smoking and drinking habits, occupational exposure to carcinogens, urban air pollution, and others. Provided that there are clear differentials in exposure of the general population to specific chemicals, epidemiologic techniques may then be able to correlate certain cancers with certain chemicals or groups of chemicals. With regard to carcinogens in drinking water, this condition appears to be satisfied in Louisiana (Fig. 1). For the past decade or more, residents of 11 parishes out of a total of 64 parishes in Louisiana have been receiving part or all of their drinking water from the Mississippi River (Table 4). This represents approximately one-third (over one million people)

Table 4 -- Louisiana Parishes and Their Approximate Population Drinking Water from the Mississippi River

| Parish | Population in 1960 | Population Served Water from Miss. R. in 1960 | Percent of Pop. in 196 Served Wate from Miss. (W) |
|---|---|---|---|
| Ascension | 27,927 | 7,750 | 28% |
| Assumption | 17,991 | 15,000 | 83 |
| Jefferson | 208,769 | 208,769 | 100 |
| Lafourche | 55,381 | 53,135 | 96 |
| Orleans | 627,525 | 627,525 | 100 |
| Plaquemines | 22,545 | 22,545 | 100 |
| St. Bernard | 32,186 | 32,186 | 100 |
| St. Charles | 21,219 | 21,219 | 100 |
| St. James | 18,369 | 14,220 | 77 |
| St. John Baptist | 18,439 | 14,930 | 81 |
| St. Mary | 48,833 | 29,850 | 61 |
| | Total | 1,047,129 | |

than mortality data as more sensitive indicators of the possible effects of drinking water, if such data could be obtained or developed in the future.

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7. "1972 County and City Data Book," U. S. Dept. of Commerce.

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For example, a significant relationship was found over the 64 parishes in Louisiana between total cancer mortality and urbanization, income and drinking water from the Mississippi River. An interpretation of the results would suggest, for example, that if New Orleans, which obtains all of its drinking water from the Mississippi River, were to either treat its water to remove the carcinogens or switch to local ground water free of carcinogens, in the long run over 50 premature deaths from cancer among white males alone would be averted annually. This would represent a reduction of approximately 15% in the cancer mortality rate among white males in New Orleans.

Similarly, extending this analysis to consideration of cancer mortality rates by site, significant relationships were found in the following:

(1) between mortality from cancer of the urinary organs (bladder, kidney, etc.) and drinking water from the Mississippi River, urbanization, and occupation in the organic and inorganic chemicals industry.

(2) between mortality from cancer of the gastro-intestinal tract (stomach, large intestine and rectum) and drinking water from the Mississippi River, urbanization, income, and employment in the organic and inorganic chemicals industry.

(3) between mortality from cancer of the respiratory system (lung, etc.) and urbanization, but not for drinking water from the Mississippi River or occupational exposures (although the petroleum and coal products industry variables were almost significant).

(4) but not between mortality from cancer of the liver and any of the exposure variables, including drinking water from the Mississippi River.

In conclusion, although EDF's statistical analysis is a modest, small-scale study, its results raise serious questions about the safety of drinking water. It is known that there are carcinogens and suspected carcinogens in drinking water; it is known that most of these substances slip through the treatment process unaffected; it has recently been learned that some of them react with chlorine in the treatment process to become more toxic. The remaining question is whether or not these substances, singly or in combination, are in sufficient concentration to produce a detectable increase in the risk of cancer. It would hardly be surprising to find that the answer is yes. The EDF study does not prove that even the most industrialized water is carcinogenic to humans--not even the most massive statistical studies could do that. What statistical, epidemiological studies can do is become more convincing as

they pile up. It is suspected that further studies will be able to refine the data, modify the interpretations, and add to the evidence one way or another. What seems to have been clearly demonstrated, however, is that it is no longer possible to take for granted the safety of drinking water which has been obtained from polluted sources.

procedures (accidental spills, agricultural runoff, etc. will still threaten water supplies), municipal drinking water treatment plants in Louisiana must install technology designed to remove carcinogens. Certain treatment procedures, such as filtration through activated carbon have been demonstrated to be effective (17-21) in removing a wide variety of potentially toxic chemicals and have been shown to be inexpensive in the more than 40 municipal water supply plants (including the City of Houma, La.) that have adopted this procedure. These general principals have been endorsed recently by Frank M. Middleton, Deputy Director, National Environmental Research Center, Environmental Protection Agency, Cincinnati, Ohio. Speaking before the 15th Water Quality Conference at the University of Illinois (22), Mr. Middleton suggested that:

> While identifying and assessing the health effects of organics must be continued and accelerated our treatment and control procedures for organics should be the best possible. The municipal water treatment plant is the last barrier between the consumer and pollution and every possible means must be taken to assure a safe and palatable water . . . Considering the quality of waters in use for drinking water sources, one can be uneasy about the safety of the final product . . . One can well ask the question: Should any public water supply derived from polluted sources be vended without being treated with activated carbon? Although carbon is not a universal panacea, it does have a high capability for adsorbing those organics that are of greatest concern. The token application of a few parts per million of carbon is not necessarily sufficient. Good technology exists for the use of carbon in beds and columns along with reactivation and reuse.

In view of the health hazards which exist from present levels of carcinogens in Mississippi River water, and considering the availability of inexpensive and relatively effective procedures of reducing the levels of hazardous chemicals at industrial outfalls and at municipal water treatment plants, the following are recommended as a prudent action program:

(1) Public Health officials in Louisiana should immediately issue a warning to every community receiving its drinking water supply from the Mississippi River or its distributaries that a health hazard exists from the chemical carcinogens present in the River and from chlorination procedures which produce additional carcinogenic compounds.

(2) Communities receiving drinking water from the Mississippi River should determine the availability of and monitor for the quality of alternative sources of drinking water (including commercial bottled water) and report these results to the public.

(3) These communities should further institute programs to assist lower socio-economic groups in obtaining water from higher quality alternative sources until treatment procedures are installed or

alternative sources of water are found for the community at large.

(4) The State of Louisiana in cooperation with the Environmental Protection Agency should initiate an accelerated program (less than a year) to determine the best available treatment technology economically achievable for reducing the levels of cancer-causing organic chemicals found in the Mississippi River or formed during treatment. Since it is not possible to determine threshold levels for carcinogens, the principle of "zero tolerance" should be adopted, and treatment processes should be prescribed that reduce the levels of carcinogens to the maximum extent feasible.

(5) The State of Louisiana in cooperation with the Environmental Protection Agency should review State and Federal Water Quality Criteria in order to determine their adequacy in light of this new information, and they should review discharge permits for all industries in the lower Mississippi River system for purposes of determining compliance with EPA policies and regulations for implementation of §307 of the Federal Water Pollution Control Act

Amendment of 1972 (Toxic Pollutant Section). Furthermore, the EPA should develop a list of carcinogens and suspected carcinogens under §307, and establish zero tolerances for their discharge to water.

(6) The EPA must begin developing a regulatory strategy for the control of industrial and municipal discharges of carcinogens to water that places the burden of proof on the polluter, rather than on the EPA. Otherwise, it will be impossible for the EPA to keep track of the hundreds of new chemicals developed annually by industry, let alone the thousands already in production.

# APPENDIX A

# Statistical Analysis of Cancer Mortality in Louisiana

By

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November 6, 1974

# APPENDIX C

## Carcinogenicity

## Of

## Organic Compounds

## Identified in Mississippi River Water

By

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## I. Compounds Investigated for Carcinogenicity With At Least One Positive Result

### BENZENE

#### Carcinogenicity of Benzene in Humans

The evidence for benzene as a human carcinogen consists of retrospective epidemiological reports of leukemia and lymphoma incidence among patients previously exposed to benzene at work, or of reports of leukemia cases in individuals exposed to benzene. Most of these reports do not involve either a large number of subjects or a carefully matched control group. However, the incidence of leukemia and lymphoma among workers exposed to benzene appears to be unusually high.

#### Epidemiological Investigations

Cases of leukemia associated with benzene exposure in two Italian provinces have been reviewed by Vigliani and Saita (1964). In the period between 1942 - 1963, 47 patients with blood disorders attributed to benzene were seen in the Clinica de Lavoro of Milan, and 6 of the 47 developed similar hemocytoblastic, undifferentiated stem cell leukemias.

The concentration of benzene in air to which the patients were exposed was reported only for one patient at 0.60-2.10 mg/l. Figures were also given from the Institute of Occupational Health in Pavia. Forty-one cases identified as chronic benzene

## BIS(2-CHLOROETHYL)ETHER

Bis(2-chloroethyl)ether (also known as 2,2-dichloroethyl ether) belongs to a family of compounds, the chloro-ethers, which includes several alkylating agent carcinogens. The chlorine atoms in bis(2-chloroethyl)ether are situated 2 carbon atoms distant from the ether group, in the 2- or "beta" position. Related 1-chloro or alpha-chloro ethers, which have chlorine atoms on the carbon adjacent to the ether group, are the most chemically reactive and carcinogenic compounds in the family. Bis(chloromethyl)ether is carcinogenic to mice and rats (Van Duuren, et al. 1972, 1969) and probably to humans (ICAR Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. 4). However, the relatively high chemical reactivity of 1-chloro ethers leads them to decompose rapidly in water. The 2-chloro compound bis(2-chloroethyl)ether, although a weaker alkylating agent and possibly a weaker carcinogen than its relatives, persists in water and has been reported to be present in finished water from several communities in this country and abroad.

### Experimental Carcinogenicity

#### Oral Administration

A survey of the oral carcinogenicity of 120 pesticides and industrial chemicals in mice found bis(2-chloroethyl)ether to

## CHLOROFORM

In the opinion of the ICAR working group on the evaluation of the carcinogenic risk of chemicals to man (ICAR Monographs, Vol. I, 1972), the carcinogenic potential of chloroform has been inadequately evaluated and no extrapolation of the carcinogenic risk posed by chloroform to man could be made in 1970. The carcinogenicity of chloroform has been investigated only in mice, in experiments involving a small number of animals. Nevertheless among these the frequency of liver tumors was high, in one case with all surviving animals affected.

### Experimental Carcinogenicity of Chloroform

#### Oral Administration

The only two papers located which describe the effects of orally administered chloroform report the formation of liver tumors or hepatomas in mice. In a dose-response study by Eschenbrenner and Miller (1945), groups of 10 mice were given 30 oral doses of 0.1, 0.2, 0.4, 0.8 and 1.6 ml/kg of body wt. of chloroform at 4-day intervals. All mice receiving the highest dose died before termination of the experiment 150 days after first injection, but all the mice surviving the next highest doses of 0.8 and 0.4 mls/kg (4 and 3 females respectively) developed hepatomas. No hepatomas were observed at the two lowest dose levels or in the controls.

mentioned here; at the time of writing either no citations had yet been found for them in the Survey volumes, or, only rather inadequate studies (e.g., experiments with very few animals or lasting only a few months) had yet been found cited. This does not mean that no other work has been done on these compounds.

The following compounds have been contracted out for large-scale carcinogenicity testing, according to Dr. S. Siegel of the National Cancer Institute. No results were available to us in the form of "final reports."

| Compound | Projected Dates of Study |
|---|---|
| Bis(2-chloroethyl)ether | 2/4/69 - 2/4/71 (?) |
| Bis(chloromethyl)ether | 3/72 - |
| Chloroform | 3/72 - 2/74 |
| 1-2-Dichloroethane | 4/72 - 5/74 |
| Tetrachloroethylene | 6/72 - 9/74 |
| Toluene | |
| 1,1,2-Trichloroethane | 5/72 - 9/74 |
| Styrene | 1/73 - 3/75 |

## ACETONE

Consultation of the Survey of Compounds Which Have Been Tested for Carcinogenicity through 1971 reveals that acetone is

FROM: ORIGINS OF HUMAN CANCER - 1977
CONTENTION 8/9 - APPENDIX III

# Carcinogenic Hazards of Organic Chemicals in Drinking Water

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Although there has been considerable interest in the roles of air and food in environmental carcinogenesis, relatively little attention has been directed to carcinogens in drinking water. Recent concern stems from discoveries of widespread contamination of drinking water by chemical carcinogens. Preliminary epidemiologic studies have also suggested that polluted water may be associated with elevated cancer mortality rates. In an effort to review these studies and to assess their implications, the following will be discussed: (1) the occurrence of organic carcinogens in drinking water; (2) approaches to assessing the potential health consequences of these chemicals; (3) recent epidemiologic studies in Ohio and Louisiana; (4) statistical problems in relating exposure to water pollutants to cancer mortality; and (5) the implications of these epidemiologic studies of drinking water in relation to the general problem of assessing the importance of low-level exposure to carcinogens in the environment.

## Carcinogens in Drinking Water

Although most of the scientific studies of organic chemicals in drinking water have been conducted over only the last 5 years, the presence of organic chemical carcinogens in river water and in industrial wastes discharged to water supplies has been known for decades (Middleton and Rosen 1956; Hueper and Conway 1964). In addition to industrial sources of these chemicals, domestic sewage-treatment-plant effluents may also be responsible for a variety of carcinogenic substances found in drinking-water supplies. In a recent study (Jolley 1973), over 50 chlorinated hydrocarbons were identified in chlorinated domestic sewage effluents. The study estimated that over 1000 tons of chlorinated organic compounds are discharged by sewage-treatment plants into the nation's waterways annually.

Discharges from industry and municipal waste-treatment plants represent more or less continuous sources of pollution, but spills and accidents result-

ing from industrial operations, barge traffic, or transportation accidents near bodies of water may also contribute significantly to the levels of hazardous substances in public water supplies (Harris 1974). It is therefore not surprising that numerous studies have demonstrated the presence of chemical carcinogens in river water (Dostal et al. 1965; Anon. 1970; Friloux 1971; Hites and Biemann 1972; Svec et al. 1973) and in treated municipal drinking water (Hueper and Payne 1963; Schafer et al. 1969; Andleman and Suess 1970; EPA 1972; Kleopfer and Fairless 1972; Scheiman et al. 1974; Deinzer et al. 1974; Junk and Stanley 1975). Recent studies have also demonstrated that chlorination of drinking water, particularly if the source is heavily polluted with organic chemicals, results in the production of a variety of chlorinated hydrocarbons, some of which are carcinogenic (Rook 1974; Belar et al. 1974; Dowty et al. 1975; EPA 1975b). Furthermore, drinking water may be contaminated by organic chemicals migrating from materials used in conveyance systems. For example, the Environmental Protection Agency (EPA) has recently observed that vinyl chloride contaminates water carried by polyvinyl chloride piping at concentrations up to 55 μg/l when water stands in the piping for long periods of time (Dressman and McFarren 1976).

Additional studies documenting the chemical contamination of drinking-water supplies include a 1970 U. S. Public Health Service survey which found that the levels of organic chemicals in many water supplies exceeded the Public Health Service's recommended limit (McCabe et al. 1970). A 1972 EPA report identified 46 potentially carcinogenic or otherwise toxic organic chemicals in the drinking water of three communities along the lower Mississippi River in Louisiana (EPA 1972). A second EPA study in 1974 identified 66 organic chemicals in the New Orleans drinking water (EPA 1974). These and other similar studies were cited by the EPA as the reasons for initiating the National Organics Reconnaissance Survey (NORS) in November, 1974, to clarify to what extent organics are present in the nation's drinking water (EPA 1975b).

One of the objectives of the NORS study, which included 80 cities representative of the drinking-water quality throughout the United States, was to determine the extent to which chlorination resulted in the formation of chlorinated hydrocarbons. In addition, a more comprehensive analysis was conducted to identify a broad spectrum of organic chemicals present in the drinking water of 10 of the 80 cities.

Results of the NORS study indicated that the presence of four trihalomethanes (chloroform, bromodichloromethane, dibromochloromethane, and bromoform) was due largely to chlorination of the water. In addition, the study showed that the concentration of total organic chemicals which serve as the precursors to the trihalomethanes was positively correlated with the resultant concentration of trihalomethanes. Accordingly, the 16 groundwater supplies studied, which in general contained considerably lower concentrations of total organic chemicals than did surface supplies, had lower concentrations of trihalomethanes (Miami was a notable exception). Chloroform, a known carcinogen (NCI 1976), was found in the drinking water of all 80 cities. Two additional chemicals, carbon tetrachloride (also a known carcinogen) and 1,2-dichloroethane, which were found in 10 and 26 cities, respectively, were

**Table 1**
EPA Analysis of Representative Contaminants in an 80-City Survey

| *Compound* | *Number of cities detected in* | *Range of concentration (μg/l)* |
|---|---|---|
| Chloroform | 80 | <0.1–311 |
| Bromodichloromethane | 78 | 0.3–116 |
| Dibromochloromethane | 72 | <0.4–100 |
| Bromoform | 26 | <0.8–92 |
| Carbon tetrachloride | 10 | <2–3 |
| 1,2-Dichloroethane | 26 | <0.2–6 |

apparently contributed by industrial sources rather than by the chlorination process and were generally absent from groundwater supplies. A summary of the results of the analyses for these six chemicals in the drinking water of the 80 cities surveyed is presented in Table 1.

The more comprehensive analysis of the organic chemical content of the drinking water of 10 of the 80 cities identified a total of 129 organic chemicals (EPA 1975b). Although less than 10% of these chemicals have been adequately tested for carcinogenicity, a list of those chemicals either known or suspected of being carcinogenic was included in a recent report from the International Agency for Research on Cancer to the National Academy of Sciences (IARC 1976). The frequency of occurrence of these known or suspected carcinogens in the 10 cities of the NORS study and in New Orleans is presented in Table 2.

A survey similar to the NORS study and with similar results was conducted by the Region-V office of the EPA (1975b). Collectively, these surveys demonstrate that contamination of the nation's drinking water by organic carcinogens and other potentially toxic organic chemicals is widespread and extensive. A recent summary compiled from 94 technical reports in the scientific literature listed 423 organic chemicals as having been reported in various waters (Junk and Stanley 1975). Of this total, 325 were identified in treated drinking water.

## Assessment of Health Risk

Methods for assessing the health risk of low-level exposure to chemical carcinogens in drinking water are not yet fully developed. At least four approaches are possible: (1) bioassay using whole extracts; (2) extrapolation of dose–response data on individual compounds; (3) aggregate population studies; and (4) disaggregate population studies.

### *Bioassays Using Whole Extracts*

Studies on the drinking water from the Kanawha River in West Virginia (Hueper and Payne 1963) and from the Mississippi River in Louisiana

Table 2
Distribution of Chemicals in Drinking Water of Selected U. S. Cities as Reviewed by the International Agency for Research on Cancer

| | New Orleans, La. | Miami, Fla. | Seattle, Wash. | Ottumwa, Ia. | Philadelphia, Pa. | Cincinnati, O. | Tucson, Ariz. | New York, N. Y. | Lawrence, Mr. | Grand Forks, N. D. | Terrebonne Parish, La. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Associated with cancer induction in man | | | | | | | | | | | |
| Benzene | x | x | | x | x | x | | | | | |
| | | 0.1 | | 0.1 | 0.2 | 0.3 | | | | | |
| Chloromethyl ether | x | | | | | | | | | | |
| Vinyl chloride* | | x | | | x | | | | | | |
| | | 5.6 | | | 0.3 | | | | | | |
| Carcinogenic in at least one animal species | | | | | | | | | | | |
| Benzopyrene | | | | | | x | | | | | |
| DDE, DDT | x | | | | | x | | | | | |
| Dieldrin | x | x | x | x | | x | | | | | |
| | 0.05 | 0.002 | 0.001 | 0.002 | | 0.001 | | | | | |
| Hexachlorocyclohexane | | | | | | x | | | | | |
| Bis(2-chloroethyl)ether | x | | | | x | | | | | | |
| | | | | | 0.5 | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Carbon tetrachloride | x | x | | x | x | x | | | | | | |
| Pentachlorobiphenyl | | | | | | | | x | x | x | x | |
| Tetrachlorobiphenyl | | | | | | | | 0.13 | 0.1 | 0.1 | | |
| Trichlorobiphenyl | | | | | | x | | | | | | |
| | | | | | | x | | | | | | |
| Metabolized to a compound which is carcinogenic in at least one animal species | | | | | | x | | | | | | |
| Aldrin | | | | | | | | | | | | |
| Carbon disulfide | x | x | | | | | | | | | | |
| Recent studies, not yet published, reveal a carcinogenic effect in at least one animal species | | | | | x | x | | x | | x | | |
| Chlordane | | | | | | | | | | | | |
| Chloroform | x | x | x | x | x | x | x | x | x | x | x | |
| Heptachlor and its epoxide | 133 | 301 | 21 | 1 | 65 | 38 | 0.08 | 44 | 32 | 40 | 130 | |
| 1,1,2-Trichloroethylene | x | x | | x | x | x | | | x | | | |
| | | 0.2 | | 0.1 | 0.5 | 0.1 | | | | | | |
| Compounds currently under test as suspected carcinogens | | | | | | | | | | | | |
| Acetaldehyde | x | x | x | x | x | x | | | | | | |
| Bis(2-chloroisopropyl)ether | x | | 0.1 | | 0.1 | | | | | | | |
| Diphenylhydrazine | 0.18 | | | | | | | | | | | |
| Hexachlorobenzene | x | | | | | | | | | | | |

Table 2 (*continued*)

| | *New Orleans, La.* | *Miami, Fla.* | *Seattle, Wash.* | *Ottumwa, Ia.* | *Philadelphia, Pa.* | *Cincinnati, O.* | *Tucson, Ariz.* | *New York, N. Y.* | *Lawrence, Mass.* | *Grand Forks, N. D.* | *Terrebonne Parish, La.* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| -Tetrachloroethylene | x | x | | x | x | x | x | x | x | x | |
| | | 0.1 | | 0.2 | 0.4 | 0.3 | <0.01 | 0.5 | 0.07 | 0.2 | |
| 2,4,6-Trichlorophenol | | | | | | x | | | | | |
| Vinyl benzene | | | | | | | | x | x | x | |
| Compounds which tests suggest are carcinogenic but which require further testing | | | | | | | | | | | |
| 1,4-Dichlorobenzene | x | x | | | x | x | | | x | | |
| | 0.01 | 0.5 | | | | | | | | | |
| 2,4-Dichlorophenol | | | | | | | | | | | |
| 2,4-Dimethylphenol | | | | | | | | | | | |
| -Endrin | x | | | | | x | | | | | |
| Methyl methacrylate | | | | | | | | | | | |
| Methyl stearate | | | | | | x | | | | | |
| Compounds whose structures suggest are carcinogenic and are found in high concentrations in drinking water | | | | | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Atrazine | x | | | x | | | | | | | |
| | | | | 0.1 | | | | | | | |
| Bromodichloromethane | x | x | x | x | x | x | | x | x | x | x |
| | | 73 | 4 | | 20 | 15 | | 17 | 2 | 3 | 23 |
| Bromoform | x | x | | | x | x | x | x | | | |
| | 0.6 | 1.5 | | | | | 3 | 1.5 | | | |
| Chlorobenzene | x | x | x | x | x | x | | x | x | x | x |
| | | 1.0 | | | 0.1 | 0.5 | | 4.7 | .12 | | 5.6 |
| Crotonaldehyde | | | | | | | | | | | |
| Dibromochloromethane | x | x | x | | x | x | x | x | x | x | x |
| | 1.1 | 32 | 3 | | 5 | 3 | 0.01 | 0.4 | 0.01 | 0.1 | 1.0 |
| 1,2-Dichloroethane | x | x | | | x | x | | | | | |
| Hexachloroethane | x | x | | | | | | | | | |
| | 4.4 | .5 | | | | | | | | | |
| Methylene chloride | x | x | x | x | x | x | | x | x | x | x |
| | | | | | | | | 0.1 | 1.6 | 0.1 | |

X indicates reported presence; numbers are reported concentrations in $\mu g/l$.
* Vinyl chloride, a known human carcinogen, was not included in the IARC study.

(Dunham et al. 1967) have attempted to assess the carcinogenicity of organic extracts from such water. However, these studies were inconclusive primarily because components of the organic extracts were highly toxic, thus limiting the dose that could be administered to animals without resulting in an acutely toxic effect. Despite this limitation, using whole extracts does offer the possible advantage of assessing additive and synergistic effects. Recently, efforts (Tardiff et al. 1976) have been made to determine the mutagenicity of organic extracts from drinking water, although no extrapolation of these data has been carried out to predict carcinogenicity.

*Extrapolation of Dose–Response Data on Individual Compounds*

Human health risk for individual chemical carcinogens can also be predicted by extrapolating dose–response data from animal experiments. The limitations of this approach are discussed by Rall and by Hoel elsewhere in this volume. As applied to drinking water, the most obvious limitation is that a polluted water supply may contain literally hundreds of organic chemicals, most of which have probably never been tested for carcinogenicity and even fewer have probably ever been tested adequately at varying doses. Extrapolation techniques also fail to predict interactive effects, which are likely to be substantial.

A recent effort (EPA 1975a) to extrapolate dose–response data from animal experiments to humans was made by the Ad Hoc Study Group of the EPA's Hazardous Materials Advisory Committee, which was established to assess health risks from selected organic chemicals in drinking water. A comprehensive assessment of health risks was not made, however, since certain contaminants such as pesticides, asbestos, and inorganic chemicals were explicitly excluded from the charge to the study group. Furthermore, as noted in the study group's final report, the chemicals that have been measured in drinking water "account for only a few percent of the total organic content of drinking water." This indicates that other potentially toxic organic compounds may have gone undetected.

Although numerous carcinogens have been identified in drinking water, with the exception of chloroform, the dose–response data have been insufficient to permit extrapolation to predict human risk. In the case of chloroform, although the tenuous nature of the techniques for extrapolating from animal experiments to man was recognized, the study group estimated the risk in the following terms:

> The level of risk, estimated from consideration of the worst case [Miami, 311 ppb] and for the expected cancer site for chloroform (the liver), might be extrapolated to account for up to 40% of the observed liver cancer incidence rate.

*Aggregate Population Studies*

Scattered European studies (Stocks 1947; Tromp 1955) have suggested a possible association between drinking polluted river water and cancer mortality, although the results were inconclusive. Similar studies (Cook and Watson 1966) in the United States have observed that counties in Missouri with high multiple cancer incidence are clustered around the Missouri River. Despite the suggestion that carcinogens in drinking water might have been a

possible explanation for these observations, this hypothesis was not investigated further.

Because of the historical evidence of high cancer rates in New Orleans and the results of EPA tests demonstrating the presence of numerous carcinogens in New Orleans drinking water, two recent studies (Harris 1974; Page et al. 1976), using multivariate regression techniques, have investigated the relationship between drinking-water quality and cancer mortality rates for the period 1950–1969 by parish in Louisiana. Exposure variables were chosen from the epidemiologic literature to reflect those environmental, social, and demographic variables generally associated with human cancer. Included were urbanization, family income, occupation, population density, and source of drinking water. The results of these studies indicated a statistically significant association between cancer mortality rates and populations which received drinking water from the Mississippi River.

In a similar analysis in New Jersey (P. Vasilenko and L. Magno, unpubl.), a statistically significant relationship was observed between drinking water obtained from surface supplies and cancer mortality rates. A subsequent study (Buncher 1975) investigated counties bordering the Ohio River in Ohio and Kentucky. Although the statistical methods differed from those used in the Louisiana analysis, the findings were suggestive of a water effect. Comparisons of persons in counties along the Ohio River who drank from that source with persons who received other water yielded statistically significant results for white females. For white males, the statistical results were borderline, although in the predicted direction. It is possible, however, that this investigation failed to obtain consistently significant results because of the method employed. The implications of this are discussed below.

Other studies have observed a statistical relationship between chloroform concentrations in drinking water and cancer mortality rates. For example, one study (McCabe 1975) of 50 cities in the 80-city NORS study found a statistically significant correlation between the chloroform concentration in drinking water and the age-, sex-, and race-adjusted cancer mortality rates by city for all cancers combined. The 50 cities chosen all had populations greater than 25,000 in 1950, and 70% or more of the populations received water comparable to that sampled by the EPA.

These relationships were confirmed by another study (Buncher 1975), which observed a similar correlation between the chloroform concentrations in 23 cities with populations of 25,000 or more in 1970 and the total cancer mortality rates for white males. This study also reported a statistically significant correlation between chloroform concentrations in 77 cities with available data and pancreatic cancer death rates for white males. This correlation was shown primarily for the 59 surface-water supplies and for cities that accounted for more than 30% of the county population. For cities that accounted for more than 70% of the county population, there was a significant correlation between chloroform concentrations and bladder cancer mortality rates for both white males and white females.

*Disaggregate Population Studies*

Disaggregate, case-control, or cohort epidemiologic studies are presumably more precise than aggregate population studies. Unfortunately, it appears

that such studies have yet to be initiated to investigate the role of drinking-water contaminants in human cancer.

## Aggregate Population Studies in Ohio and Louisiana

Aggregate population studies, which were discussed above, have relied on two statistical multivariate approaches. The Louisiana study (Page et al. 1976) employed multiple regression, in which the explanatory variables were entered symmetrically in each equation. For all the equations, drinking water, urbanization, income, and, in addition, three occupational variables were included in the equations for males. The drinking-water variable was defined as the percentage of the parish (county) consuming Mississippi River water, as opposed to other surface water or groundwater. In a second approach (Buncher 1975), a two-stage analysis was used on Ohio River counties in which cancer mortality was first regressed upon one or more potentially confounding or contributing variables such as population density, proportion rural, and occupation. The residuals were then divided into two groups depending on the water source of each county. At the second stage, t-tests were performed on the two groups of residuals to determine if the means of the residuals were statistically different.

As discussed above, it is possible that the Ohio River study did not obtain consistently significant results (some t-tests were significant, but others were not) because of the method employed. Possible limitations in this method include:

1. The sample size was small for the drinking-water variable. Although mortality was regressed on the potentially confounding variables for all 88 Ohio counties, a drinking-water classification was defined for only 14 counties. At the second stage, only the 14 counties in Ohio bordering the Ohio River were investigated for the effect of their drinking water. Of these, only seven were estimated to receive water from the Ohio River, the others receiving groundwater.
2. The drinking-water variable was treated discontinuously. All seven Ohio River drinking-water counties were treated identically, even though one county had only 13% usage of the Ohio River and another had 93% usage of the Ohio River. It is likely, however, that the effect of the surface/ground drinking-water dichotomy varies linearly with the percentage of the population utilizing surface water. This is because the percentage receiving surface water is a measure of the relative number at risk from exposure to the probable higher levels of carcinogens. In contrast, urbanization was treated as the percentage of the county population in one category (towns over 2500) as compared with a second category (towns less than 2500). It is not clear, therefore, why drinking water should be treated as a zero-one discontinuous variable and urbanization as a continuous variable. Moreover, with only seven Ohio River drinking-water counties in the sample, it would appear undesirable to discard information, which is likely to occur when a continuous variable is treated as a zero-one variable.
3. The Ohio study was limited to an analysis of total aggregated cancer rates and did not investigate mortality by site or by other groups of sites.

4. There are unknown statistical properties of the two-stage method. This method is equivalent to stagewise linear regression, whereby the residuals of the first regression are regressed on a zero-one dummy variable for drinking water. Stagewise regression is biased in both coefficients and in the estimated standard errors. Thus a test for drinking water is of unknown power and unknown size, both depending on the correlations of the entire list of explanatory variables. However, the two stage method may be more powerful than direct regressions for a given size and maintained hypothesis, depending on the actual values of the explanatory variables. This question deserves more attention.

To gain a more direct comparison of the possible etiologic factors in Ohio and Louisiana cancer rates and to see in what ways differences in methodology influence the analysis, a direct regression analysis was applied to Ohio. First, a drinking water variable was constructed for all 88 counties in Ohio. Then the same equations were estimated as in the Louisiana analysis (Page et al. 1976). Finally, a stepwise approach was followed in which drinking water was forced into the equation and other variables were introduced in the order of their contribution. In addition, direct regressions were performed analogous to the Louisiana studies. These results are presented here for comparative purposes. The results were similar for both methods.

Six independent variables were entered in the regression equations: the percentage of persons in each county living in rural ($R$) areas, as defined by the U. S. Bureau of the Census (1960); median family income (Inc) (Anon. 1960); population density ($D$) (Anon. 1960); an index of industrialization (Ind), which was defined as the percentage of persons in a county employed in mining, construction, or manufacturing (Anon. 1960); the percentage of persons in a county who received surface water ($S$), which was derived from the 1963 Public Health Service survey of U. S. Water Supplies (DHEW 1964); and the percentage of persons in a county whose water is treated for control of taste and odor ($T/O$) (DHEW 1964).

Tables 3 and 4 present the regression findings for white males and white females, respectively. Since $S$ was generally a better predictor of cancer mortality than $T/O$, the equations that include $S$ are reported. For males, the coefficient for the water variable is uniformly in the anticipated direction. For females, the sign is negative for kidney, esophagus, and urinary cancer rates. However, the $F$ ratios, which test for the significance of the entire regression equations, are insignificant, and the coefficients of determination ($R^2$) are extremely low.

For both sexes, $S$ was significant for total cancer and stomach cancer rates. Significant water effects for males were also obtained for pancreas, bladder, esophagus, gastrointestinal, and urinary tract cancers. $R$ was a moderately strong predictor in the equations for males, and the industrialization index was significant for several sites among females.

Particularly striking is the differential effect of water on male and female cancer mortality. For all sites except pancreas and liver, the coefficient of determination ($R^2$) was substantially higher for males. The difference in $R^2$ was most pronounced for total cancer, stomach, large intestine, rectum, bladder, and lung cancer. The male-female difference is particularly interesting because of the "relative protection" of white females found in the

Table 3
Regression Coefficients for White Males in Ohio

| Site | Mortality rate (per 100,000) | $R^2$ | $F_{4,83}$ | Surface water | Rural | Pop Inc | Income | Industry |
|---|---|---|---|---|---|---|---|---|
| Total cancer | 178.41 | 0.48 | 19.44[a] | 18.87[b] | −39.66[a] | −0.002 | | 94.29 |
| Stomach | 15.10 | 0.31 | 9.51[a] | 5.99[a] | 1.77 | 0.0003 | | 26.50 |
| Colon | 18.63 | 0.28 | 7.88[a] | 2.48 | −3.87 | 0.0002 | | 12.15 |
| Pancreas | 8.94 | 0.08 | 1.70 | 1.86[b] | 0.73 | 0.0003 | | −5.05 |
| Lung | 38.06 | 0.60 | 30.69[a] | 3.95 | −17.59[a] | 0.001 | | 24.41 |
| Kidney | 4.03 | 0.09 | 2.05 | 0.45 | −0.76 | 0.0001 | | −1.20 |
| Bladder | 6.85 | 0.40 | 13.74[a] | 1.89[a] | −0.25 | 0.0008[a] | | 1.79 |
| Liver | 5.62 | 0.07 | 1.50 | 0.94 | −0.62 | −0.0004 | | −5.09 |
| Rectum | 8.31 | 0.28 | 7.88[a] | 2.48 | −3.87 | 0.0002 | | 12.15 |
| Esophagus | 4.51 | 0.55 | 25.74[a] | 1.16[b] | −1.93[a] | 0.0005[a] | | −4.70 |
| GI | 42.04 | 0.37 | 12.43[a] | 10.94[a] | −5.96 | 0.0007 | | 50.79 |
| Urinary | 10.88 | 0.34 | 10.48[a] | 2.34[b] | −1.01 | 0.0009[b] | | 0.59 |
| Prostate | 18.85 | 0.11 | 2.49 | 1.74 | 1.08 | 0.0004 | | 17.42 |

[a] $p < 0.01$.
[b] $p < 0.05$.

Table 4
Regression Coefficients for White Females in Ohio

| *Site* | *Mortality rate (per 100,000)* | $R^2$ | $F_{4,81}$ | *S* | *R* | *Inc* | *Ind* |
|---|---|---|---|---|---|---|---|
| Total cancer | 136.25 | 0.28 | 8.14[a] | 9.13[b] | −9.95 | −0.002 | 73.15 |
| Stomach | 7.42 | 0.14 | 3.47[b] | 2.05[b] | −0.18 | −0.0005 | 19.78[b] |
| Colon | 17.72 | 0.07 | 1.57 | 0.43 | −0.97 | −0.001 | 32.28[b] |
| Pancreas | 5.47 | 0.10 | 2.39 | 1.01 | 1.12 | 0.0005[b] | −6.75 |
| Lung | 6.46 | 0.09 | 1.93 | 0.83 | 0.25 | 0.0005 | −6.44 |
| Kidney | 2.03 | 0.06 | 1.32 | −0.05 | −0.58 | −0.00007 | 4.09 |
| Bladder | 2.61 | 0.04 | 0.84 | 0.02 | −0.68 | −0.00004 | 0.86 |
| Liver | 6.29 | 0.16 | 4.09[b] | 0.91 | −1.23 | −0.001[a] | 8.28 |
| Rectum | 5.17 | 0.07 | 1.57 | 0.43 | −0.99 | −0.001 | 32.21[b] |
| Esophagus | 0.87 | 0.10 | 2.33 | −0.29 | −0.78[b] | −0.00003 | 0.18 |
| GI | 30.31 | 0.12 | 2.71 | 2.91 | −2.13 | −0.003[b] | 84.25[a] |
| Urinary | 4.64 | 0.08 | 1.74 | −0.02 | −1.26 | −0.0001 | 4.95 |
| Breast | 26.88 | 0.39 | 13.48[a] | 2.51 | 1.75 | 0.002[a] | −0.74 |

[a] $p < 0.01$.
[b] $p < 0.05$.

Louisiana study. However, it would be inappropriate to minimize the possible role of drinking-water constituents in the etiology of cancer simply because the findings are not consistent between sexes. Exposure to carcinogens in water and to relevant cocarcinogens may vary between sexes. Also, males and females may not be equally sensitive to the agent(s) present in water. The model tested may be inappropriately specified for females, thereby masking a true effect.

Compared to the Louisiana study, the pattern of significance for the drinking-water variable is less strong in the Ohio regressions. Nevertheless, a pattern of significance exists for the Ohio study as well as for the Louisiana study, and, taken together, the two reinforce one another. In both studies, gastrointestinal and urinary tract cancers appear prominently in relation to the drinking-water effect.

Moreover, the Ohio and Louisiana regressions taken together shed further light on the role of diet. It was suggested previously (DeRouen and Diem 1975) that there are important north-south differences in diet in Louisiana and that these differences might be the true explanation for the observed drinking-water effect in the Louisiana regressions. The suggested dichotomy was between north and south, without gradations in diet within each region. To test whether or not drinking water is a proxy for diet (all the surface-drinking-water parishes happen to be in the south), the regressions were restricted to the 29 southern parishes in Louisiana alleged to be homogeneous in diet. In the restricted regressions, the drinking-water effect was still observed, thus showing that diet is unlikely to be the explanation for the drinking-water effect. This does not mean that diet may not be an important factor in cancer mortality in Louisiana. There appears to be a north-south effect (possibly diet) as well as a drinking-water effect. It should also be noted that in DeRouen's nonparametric, univariate test for gastrointestinal cancer in the southern parishes, drinking water was significant at the 0.001 level (DeRouen and Diem 1975). Furthermore, if diet were the true explanation for the drinking-water effect, the water variable would not be expected to be significant in Ohio, where there are no clear-cut regional differences in diet that correlate with the surface water-groundwater dichotomy. Thus a positive finding of the drinking water effect in Ohio strengthens the conclusion from the regressions of the 29 southern parishes in Louisiana—diet is not likely to be the explanation for the observed drinking-water effect.

There remains the difference in the positive finding of a drinking-water effect in the Ohio study reported here and the inconclusive one reported by Buncher (1975). The difference appears to be methodological. Buncher et al. (this volume) have performed a second Ohio study with a drinking-water variable defined for a larger number of counties for which the distinction is between surface water and groundwater rather than between Ohio River water and groundwater supply. Site-specific cancer mortality rates were tested in addition to total cancer mortality. Thus Buncher's second Ohio study is closer to our methodology than his first, although it still differs from direct regression. The second Buncher study is an analysis of covariance with a dichotomous variable for drinking water, and the results do not appear to differ greatly from ours.

Aggregate statistical analysis, as discussed above, is to a great extent pre-

liminary and descriptive; however, it can be useful in specifying more precise etiologic hypotheses. Specifically, the consistent findings with respect to gastrointestinal and urinary sites in the two Ohio studies reported in this volume and in the Louisiana study suggest that the water effect, though modest, is probably not the result of spurious correlation.

## Low Numbers and Statistical Power

Results of the regression analyses in Louisiana and Ohio suggest that if there is a drinking-water effect, it is likely to be a modest one, perhaps 4% to 20% of the background cancer rate. The question immediately arises: If there was in fact such a relatively modest effect, to what extent would these statistical tests detect it? As a general rule, statistical power is a function of the size of the effect; the smaller the effect, the less the power. In addition, a given cancer occurring in a given year is a rare event with a probability of the order of $10^{-4}$ to $10^{-3}$. Thus a second question emerges: How does the rarity of a particular cancer affect statistical power? By means of a simple model, this section discusses how rarity and relative size of effect interact to affect the power of statistical testing.

To focus on the role of rarity, a simple model can be constructed in which the only source of variance is from the low numbers typical of cancer rates. In reality, of course, there is considerable variation within each county with respect to urbanization, income, water quality, and other potentially important variables. However, the interaction of rarity and modest effect can be illustrated in a model where all the variation is between counties and none within. This yields a straightforward generalization to take into account variation within counties.

To construct the model for a state with $J$ counties, suppose that the probability of a person in county $j$ dying of a particular cancer in a given year is a linear function of a background effect, determined by both urbanization and income, and a drinking-water effect:

$$p_j = \underbrace{A_0 + A_1 R_j + A_2 I_j}_{\text{background effect}} + \underbrace{A_3 W_j}_{\text{drinking-water effect}}, \tag{1}$$

where $R_j$ is urbanization, $I_j$ is income, and $W_j$ is the percentage of the county drinking surface water, here 0 or 100.

For a county population at risk of $N_j$, we add up $N_j$ Bernoulli trials into a total number of deaths, this number being a binomial random variable. We can express this binomial random variable, deaths $M_j$, as the sum of a mean and an error term:

plus its drinking-water effect), or signal, and different variance of the error term, or noise. It is well known that the signal-to-noise ratio of a binomial random variable declines as $p$ declines. Thus for large $N$, the smaller the $p$, the harder it is to detect a small change in the signal coming from a drinking-water effect.

To convert deaths to mortality rates per hundred thousand, both sides of Equation 2 are multiplied by $10^5/N_j$. The resulting equation is estimable but heteroskedastic; that is, the variance of the error term $(10^{10}p_j\,(1 - p_j)/N_j)$ varies from county to county. The most obvious correction is to weigh the regressions by county population. However, in the Louisiana regression analysis (Page et al. 1976), various heteroskedastic corrections, beyond weighting by parish population, made relatively little difference in the coefficients and t-values for drinking water. Unlike the empirical regression analysis, here there are clearly other sources of error; in this simple binomial model, the error variance is completely specified in terms of the coefficients $A_i$ and the county characteristics $R_j$, $I_j$, and $W_j$.

In the binomial model, the error variance arises entirely from "inherent binomial variance." To the extent that this variance is not too heteroskedastic, we can use a normal test on the regression coefficient to derive statistical power functions. For this approximate normal test we use $\sigma^2 = 10^{10}p(1 - p)$, where $p$ is the statewide average mortality rate for a particular cancer. For a two-tailed test of size 5%, an effect will be observed if

$$\frac{b}{\sigma_b} > 1.96, \tag{3}$$

where $b$ is the regression coefficient for $W$ and $\sigma_b$ is the standard error of $b$. If the drinking-water effect is actually $\beta$, the power of the test can be computed as a function of $\beta$. In this case, $(b - \beta)/\sigma_b$ is a standard normal variable, and the test indicates a drinking-water effect when

$$\frac{b - \beta}{b} > 1.96 - \frac{\beta}{\sigma_b}. \tag{4}$$

(If $(b - \beta)/b < 1.96 - \beta/\sigma_b$, a positive drinking-water effect is not indicated.) By substitution, the test condition becomes

$$\frac{b - \beta}{\sigma_b} > 1.96 - \frac{\beta}{\sqrt{(X'X)_b^{-1}\,\sigma}}, \tag{5}$$

where $(X'X)_b^{-1}$ is the diagonal element corresponding to $W$ on the $(X'X)^{-1}$ matrix of county characteristics $R_j$, $I_j$, and $W_j$.

Three types of effects on the power of the test can be considered. First, for a given size of background effect and a given $\beta$, there may be more or less multicolinearity among $R$, $I$, and $W$. The greater the colinearity, the greater $(X'X)_b^{-1}$, and hence the smaller the size and the more nearly the power approaches the size, here 5%. Second, for a given background effect, the magnitude of the drinking-water effect may vary. An explicit power func-

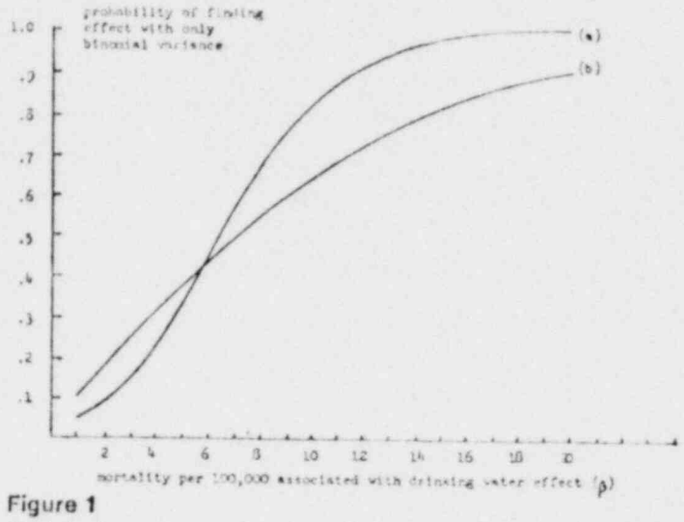


**Figure 1**
Statistical power as a function of the background cancer rate and the drinking-water effect relative to background. (*a*) Background held to a constant 30 per 100,000; only $\beta$ varies. (*b*) Background varies with $\beta$; background is always five times greater than $\beta$.

tion depends upon specific values for $A_j$, $R_j$, $I_j$, and $W_j$. For illustrative purposes, the weighted regression equation for gastrointestinal cancers for white males ($GIWM_j$) in Louisiana can be considered as

$$\underset{\substack{(9.9)\\(t\text{-values in}\\\text{parentheses})}}{GIWM_j = 49} \underset{(-4.4)}{- 12.15R_j} \underset{(-3.8)}{- 1.83I_j} + \underset{(5.0)}{6.24W_j} \qquad (6)$$

For the transformed variables, $\sqrt{(X'X)_{bb}^{-1}} = 1.77 \times 10^{-3}$. For gastrointestinal cancers, the average 20-year (1950–1969) age-adjusted rate is approximately $30 \times 10^{-5}$ cancer deaths per person for the state of Louisiana. Assuming a background rate of $30 \times 10^{-5}$ together with the drinking-water effect, the test cutoff point becomes

$$1.96 - \frac{\beta}{1.77\sqrt{3 + 0.1\beta}}. \qquad (7)$$

For a constant background effect of $30 \times 10^{-5}$, $\beta$ can be varied from $1 \times 10^{-5}$ to $20 \times 10^{-5}$ and the power of the test determined as a function of $\beta$ (Fig. 1, curve a).

Third, the power of the test can be determined when drinking water is a small effect compared to the background and both move up and down together in proportion. For example, suppose that drinking water is a 20% effect compared with the background and that the power is determined for more-or-less rare cancers. Suppose $\beta = 0.2$ (background effect), then the total effect is $6\beta$ and $\sigma^2 = 6\beta \times 10^5$. In this case, the cutoff point is $1.96 - \sqrt{\beta}/1.77\sqrt{0.6}$, and the power of the test is represented by curve b in Figure 1.

Although the drinking-water effect is a constant 20% of the background effect, the drinking-water effect is harder to discover for rarer cancers. This decrease in power with rarer cancers may be called a pure binomial variance effect.

At first glance, the power associated with the numbers of the GIWM equation ($\beta = 6$, GIWM mean = 30) seems very low, a mere 40%; and this is without any other sources of error in the model. However, the model was constructed for illustrative purposes only and is too simple to fit the assumptions of the actual estimated equations. Nevertheless, the model suggests certain questions about the rarity of cancer and the averaging processes underlying the cancer mortality data (Mason and McKay 1974). If the regression analysis is to predict the long-run average impact of environmental factors, cancer rates per decade may be a better definition of rarity than rates per year. The normalization is important because probabilities are pure numbers without dimension. Moreover, the cancer rates carry more information than single-year observations, since the rates are 20-year averages. How the averaging process is taken into account changes the estimated power of the statistical test.

The purpose of developing this simple model was to demonstrate that modest levels of effect and cancer rarity, although representing different concepts, can interact in important ways and may, under certain circumstances, severely restrict the statistical power of a test to detect effects. In certain cases, combining sites may increase the statistical power, and therefore such aggregation may be justified for statistical if not for etiological reasons. Investigation of the power characteristics of various models is important in order to develop expectations as to the consistency of pattern which may be observed in a set of regressions or other tests. Finally, when dealing with modest effects and rare events, the methodology may be close to the edge of statistical capability in finding potentially existing effects. This suggests that the common-sense dictum of searching for the most powerful tests is especially important in the area of assessing modest environmental effects. The process of developing the statistical properties of various estimators and tests in the specific setting of drinking-water research has barely begun.

## CONCLUSION

Most of the information that has been accumulated to date on the risk to humans from exposure to chemical carcinogens has been acquired through epidemiologic studies in the work environment. In general, occupational exposures to chemical carcinogens are far greater than exposures to carcinogens through air, water, and food contamination. However, it is evident that the general public is exposed to a wide variety of chemical carcinogens in environments other than that of work. For this reason, it is imperative that epidemiologic studies be undertaken to assess the impact of these general exposures.

In the case of drinking water, contamination from industrial, municipal, and agricultural sources, as well as from chlorination at water-treatment plants, results in the public's exposure to a wide variety of chemical carcinogens. Al-

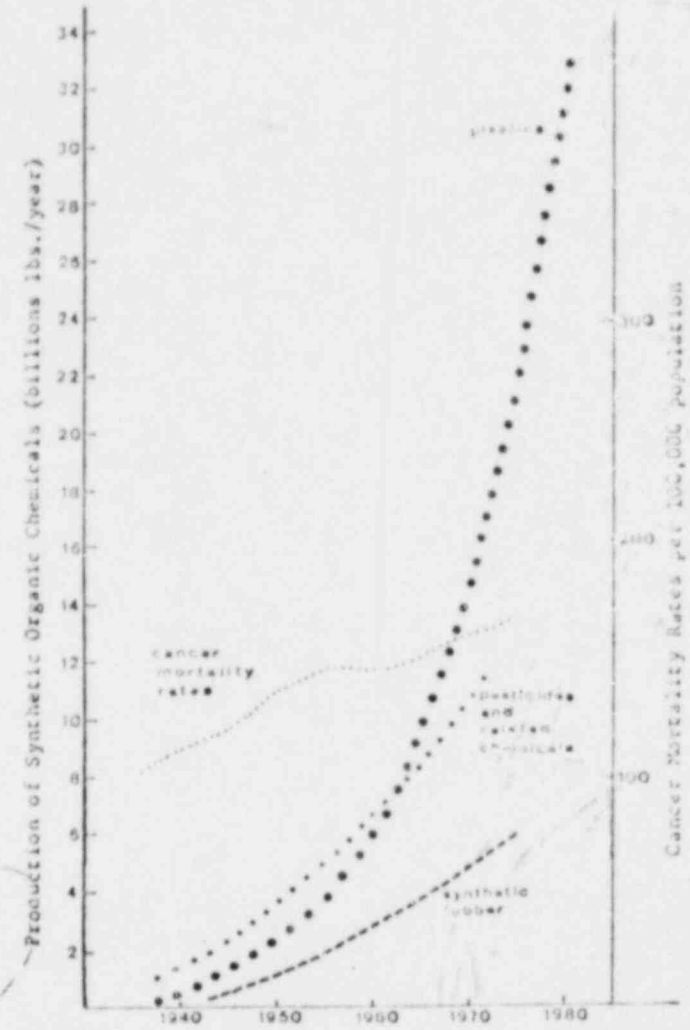


**Figure 2**
Cancer mortality rates and chemical production as a function of time.

though the number of potential carcinogens is large, their concentrations are small in comparison with those typically encountered in the work environment. Although these are relatively low levels of exposure, preliminary epidemiologic studies of aggregate populations in Louisiana, Ohio, and New Jersey support the hypothesis that carcinogens in drinking water are related to human cancer. Although similar organ sites were observed to be affected by drinking-water contamination in these studies, the results are not completely consistent among states. This may be due in part to the low numbers of cancers and the relatively small effect drinking water plays in their etiology. Both rarity and relative size of effect interact to place important constraints on the power of statistical tests.

It is also important to consider that the levels and numbers of chemical car-

cinogens present in drinking water today are likely to be far greater than were present 20 or 30 years ago. Therefore, the modest effects suggested by the epidemiologic studies discussed in this paper, which reflect exposures 20, 30, or more years ago, might logically be translated to larger effects in the future. This is supported by the data presented in Figure 2, which demonstrate that the level of industrial activity contributing many of the chemicals identified in drinking water has increased dramatically over the past 25 years. The effect of this chemical "revolution" would not yet be expected to be reflected in overall cancer rates, considering a probable 20- to 30-year latency for most chemical carcinogens. It is primarily for this reason, i.e., the rapid rise in the level of chemical carcinogens in the environment over the past 20 years, that considerable effort should be devoted to the design and conduct of epidemiologic studies to assess the effect of chemical carcinogens in drinking water.

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Int. J. Radiat. Biol. Vol. 29, pp. 431–440
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CONTENTION 8/9, APPENDIX IV

# RADIATION ACTIVATION OF CARCINOGENS AND THE ROLE OF $^{\cdot}OH$ AND $O_2^{\cdot-}$

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(*Received* 27 *March* 1976; *accepted* 4 *April* 1976)

**Abstract**—Radiation-induced covalent binding of labelled carcinogens to DNA has been investigated under a variety of conditions using ultrafiltration or millipore filtration of TCA precipitable complexes. High yields of carcinogen binding at high DNA concentrations are also observed for a variety of small molecules and are not carcinogen-specific. At high carcinogen concentrations, radiation-induced unstable electrophilic carcinogenic species are produced, and undergo free-radical reactions which simulate cellular redox reactions involved in metabolic carcinogen activation, leading to the formation of covalently bound carcinogen adducts to DNA as a potential target macromolecule. The yields of carcinogen-DNA adducts increase linearly with dose and depend upon carcinogen concentration. The results of scavenger studies indicate that the oxidising species $O_2^{\cdot-}$ and $^{\cdot}OH$ are the principal activating species. Rate constants for the selective radiation-induced oxidation reactions of various chemical carcinogens with superoxide have been measured by a competition kinetic method using pulse radiolysis. The relatively long-lived superoxide radical reacts with carcinogens at a rate which is two orders of magnitude slower than the diffusion-controlled rate for the hydroxyl radical, thus allowing a measure of $O_2^{\cdot-}$ specificity in the presence of competing reactants within the cell.

## INTRODUCTION

Humans are being exposed to ever-increasing levels of a wide variety of physical and chemical pollutants in the environment, including ionizing and non-ionizing radiation and chemical carcinogens. Chronic long-term exposure to these pollutants may lead to cancer (Arcos *et al.*, 1968; Pochin, 1969; Searle, 1976). Although the latent period in both chemical carcinogenesis and radiation carcinogenesis is long, nevertheless, these biological effects are predetermined by chemical events initiated at the time of exposure (Miller, 1970; Miller and Miller, 1966; Heidelberger, 1973).

It was first pointed out by J. A. and E. C. Miller (1953) that chemical carcinogens must be metabolically "activated" *in vivo* before they can react to form covalent bonds with such critical cell components as DNA and proteins. It has been shown that a principal site for this activation is in liver microsomes (Gelboin, 1969; Wang *et al.*, 1975), presumably by inducible mixed function oxidases and hydroxylases. In addition, activation can be achieved chemically (Hoffman *et al.*, 1970; Menger *et al.*, 1976), electrochemically (Adelic and Adams, 1970) or radiation chemically (Carbea *et al.*, 1975; Greenstock and Ruddock, 1976a; Ito and Lu, 1964). It is interesting to note that in all these methods of activation, free radical intermediates, such as superoxide radical anions ($O_2^{\cdot-}$) and hydroxyl radical ($^{\cdot}OH$) are important in initiating free radical redox reactions to simulate metabolic oxidative activation. These species or the products of their subsequent reactions in irradiated solution take part in oxidation, epoxidation (Buxton *et al.*, 1976) and hydroxylation (Cohen and Fridovich, 1972) reactions which are generally thought to be involved in arylamine carcinogen activation *in vivo* (Miller, 1970; Weisburger and Weisburger, 1973). We have used pulse and steady-state radiolysis studies of model chemical systems in aqueous solution to generate free radical species as selective redox reagents to simulate metabolic production of electrophilic carcinogen species including hydroxylation products, and to probe the mechanisms of the underlying chemical reactions involved in carcinogen activation and in the subsequent interaction of carcinogens and their radiation-chemically activated metabolites with potential cellular target nucleophiles (Greenstock and Ruddock, 1976a; Greenstock and Weibe, 1977), according to the hypothesis of Miller and Miller (1953). The role of $O_2^{\cdot-}$ in carcinogen activation and its implication in biochemistry and radiation biology is discussed.

## MATERIALS AND METHODS

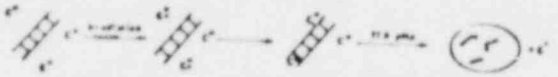
The chemical carcinogens benzidine, benzo[a]pyrene, 3-methylcholanthrene and β-naphthylamine (β-NA) were obtained from Sigma Chemical Company, and 2-acetylaminofluorene from Pfaltz and Bauer, Inc. The $^{14}C$-labelled β-naphthylamine was obtained from Schwartz-Mann. Radiation-induced binding to highly polymerized calf thymus DNA (Sigma Chemical Co.) was determined by precipitation with cold 5% trichloroacetic acid (TCA) and collection by high pressure filtration (60 psi) on glass fibre filters. The filters were digested with Nuclear Chicago tissue solubilizer and counted in a Nuclear Chicago Mark II scintillation counter. The assay for covalent binding is based upon coprecipitation of radioactive carcinogen and DNA, and upon the inability of carcinogen-DNA adducts to pass through these filters which can only retain macromolecules whose mol wt exceeds 10,000.

The pulse radiolysis studies were performed with the

4MV Van de Graaff at Whiteshell Nuclear Research Establishment. Details of the irradiation conditions, design of the experiments, and the associated equipment for the detection of free radicals and their kinetic analysis have been described previously (Greenstock and Ruddock, 1976; Hunt *et al.*, 1972).

## RESULTS

We have studied the radiation-induced incorporation of radioactively labelled carcinogens (C*) into highly polymerized DNA (scheme I):



Scheme I. Radiation-induced carcinogen binding.

When high concentrations of DNA are irradiated in aerated aqueous solution in the presence of low concentrations of the $^{14}$C-labelled precarcinogen $\beta$-Na; the primary water radiolysis species, principally $^{\cdot}OH$ and $O_2^{\cdot-}$ and the secondary products of their self-reactions react predominantly with the DNA. Figure 1 shows how the yield of covalently bound carcinogen incorporated into DNA varies with radiation dose, under a variety of radiation chemical conditions. In all cases, carcinogen binding increases linearly with radiation dose. Maximum binding is observed in nitrous oxide ($N_2O$) saturated solutions where all $e_{aq}^-$ are converted to the oxidizing species $^{\cdot}OH$. In the presence of ethanol, $^{\cdot}OH$ is scavenged to form a mildly oxidizing alcohol radical $CH_3\dot{C}HOH$, whereas in the presence of bromide ions, a very selective weakly oxidizing species $Br_2^{\cdot-}$ is formed. In both these cases, $^{\cdot}OH$ scavenging results in a decrease of DNA–carcinogen binding. In oxygen saturated solution containing *t*-butanol, where $O_2^{\cdot-}$, which does not react appreciably with DNA, is the major species, DNA–carcinogen binding is very low. This type of radiation-induced binding, involves $^{\cdot}OH$ induced DNA radicals and is found for a wide variety of organic molecules (Byfield *et al.*, 1970).

The results obtained when carcinogen is present in high concentration are shown in Fig. 2. Under these conditions, the water radiolysis species react predominantly with the highly mobile carcinogen molecules and these reactions can lead to oxidative activation by generating electrophilic intermediates which subsequently bind to DNA (scheme I). Under these conditions, the highest yield of carcinogen binding is achieved in the presence of the most selective oxidant, $Br_2^{\cdot-}$. The water radiolysis species, $O_2^{\cdot-}$ and $^{\cdot}OH$ are also potent initiators, whereas the reducing radical $CH_3\dot{C}HOH$ produces virtually no binding.

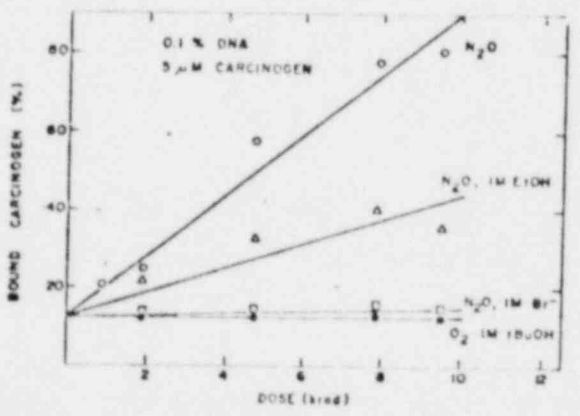



Figure 1. Covalent binding of the carcinogen $\beta$-naphthylamine to DNA as a function of radiation dose, under conditions where the carcinogen reacts with DNA radicals.

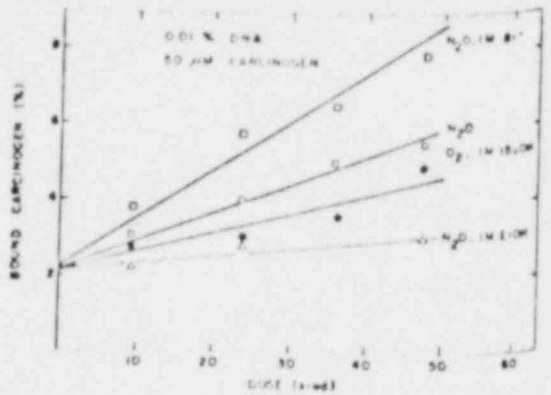



Figure 2. Covalent binding of the carcinogen $\beta$-naphthylamine to DNA as a function of radiation dose, following radiation-induced carcinogen "activation" by the oxidising species $Br_2^{\cdot-}$, $^{\cdot}OH$ and $O_2^{\cdot-}$.

Having established that oxidizing free radical species are capable of activating carcinogens in a simple DNA–carcinogen binding assay, the kinetics of the proposed activation step were studied using pulse radiolysis. In view of the importance of $O_2^{\cdot-}$ as an intermediate in many radiation chemical and biochemical processes (Bors *et al.*, 1974), capable of exhibiting more selective reactivity than $^{\cdot}OH$, a kinetic method (Greenstock and Ruddock, 1976), was used to study the rate constants for the reaction of $O_2^{\cdot-}$ with various carcinogens. Since neither $O_2^{\cdot-}$, nor the activated products in reaction 1, have any appreciable absorption in the wavelength region amenable to pulse radiolysis study, an indirect competition kinetic method was used:

$$O_2^{\cdot-} + C \rightarrow \text{non-absorbing product} \qquad (1)$$

$$O_2^{\cdot-} + p\text{BQ} \rightarrow p\text{BQ}^{\cdot-} + O_2 \qquad (2)$$

$$A/A_0 = 1 + k_1[C]/k_2[p\text{BQ}] \qquad (3)$$

Superoxide radicals, generated in oxygen saturated aqueous solution containing 0.1 *M* *t*-butanol as a hydroxyl radical scavenger, are reacted with a fixed concentration of *p*-benzoquinone (*p*BQ) to form the radical anion $p\text{BQ}^{\cdot-}$ which absorbs strongly at 410 nm. The rate constant $k_2$ obtained by measuring directly the rate of build-up of $p\text{BQ}^{\cdot-}$ absorption as a function of time after the pulse using pulse radiolysis, is $0.95 \times 10^9\ M^{-1}s^{-1}$. If the absorbance of the $p\text{BQ}^{\cdot-}$ species formed after a fixed dose is measured in the absence ($A_0$) and presence (A) of different concentrations of carcinogen C, then Eq. 3 can be used to estimate the unknown rate constant $k_1$ for the reac-

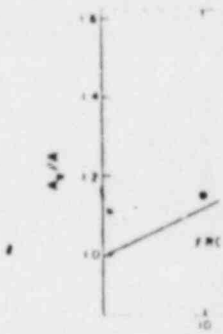


Figure 3. Rate of a
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Pre-carcinogen →

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Table 1. R
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| Carcinoge |
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| 2-Acetylar |
| Benzo[a]p |
| 3-Methylc |
| $\beta$-Naphth |
| Benzidine |

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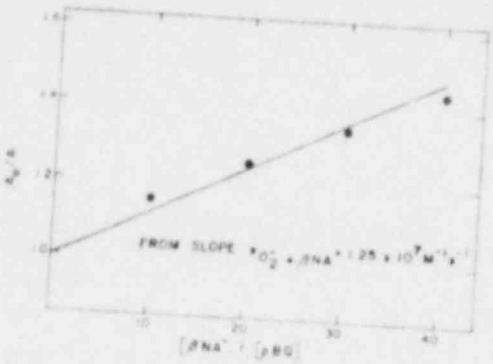


Figure 3. Rate of activation of β-naphthylamine by $O_2^-$ as determined by competition kinetics using pulse radiolysis.

tion of $O_2^-$ with the carcinogen. A typical competition plot is shown for β-NA in Fig. 3. From the slope of the line, a competing rate constant for the reaction of $O_2^-$ with β-NA of $1.25 \times 10^7\ M^{-1}s^{-1}$ is obtained. Superoxide is reactive with a variety of chemical carcinogens. Some of the rate constants, ranging between $10^7$–$10^8\ M^{-1}s^{-1}$, are shown in Table 1.

## DISCUSSION

These experiments indicate that some of the reactive species formed by the indirect action of ionizing radiation on aqueous solutions (reaction 4) react with chemical carcinogen.

$$H_2O \longrightarrow e_{aq}^-, H^\cdot, {}^\cdot OH, O_2^-, H_3O^+, H_2, H_2O_2 \quad (4)$$

In oxygen saturated solution, the principal reactive species, formed in roughly equal yields, are $^\cdot OH$ and $O_2^-$, and in pure water they can further react to form $H_2O_2$. These three radiation-induced reactants may activate pre-carcinogens in solution in an oxidation reaction to generate electrophilic "activated carcinogens" (reactions 5) and such reactions are being used to simulate those chemical reactions which initiate the metabolic activation of chemical carcinogens.

$$\text{Pre-carcinogen} \xrightarrow{\text{Activation}} \begin{cases} \xrightarrow{{}^\cdot OH,\ O_2^-,\ H_2O_2} \text{oxidized carcinogen} \\ \xrightarrow{e_{aq}^-,\ H^\cdot,\ O_2} \text{reduced carcinogen} \end{cases} \quad (5)$$

Previous studies have established that hydroxyl free radicals react at diffusion controlled rates with some

Table 1. Rate constants for $O_2^-$ reactions with carcinogens ($M^{-1}s^{-1} \times 10^{-7}$)

| Carcinogen | $k_{O_2^-}$ |
|---|---|
| 2-Acetylaminofluorene | > 3.5* |
| Benzo(a)pyrene | < 1* |
| 3-Methylcholanthrene | 11* |
| β-Naphthylamine | 1.3 |
| Benzidine | ~25 |

* Solubilized with 0.01 *M* cetyltrimethyl ammonium bromide.

potential carcinogenic substances (Biaglow *et al.*, 1977). These studies confirm that $O_2^-$, while not as reactive as $^\cdot OH$, still reacts very rapidly with a wide variety of chemical carcinogens. From pulse and steady state radiolysis studies, it is apparent that the reactions are oxidation reactions. In previous studies with nitro compounds (Biaglow *et al.*, 1977), it was found that these compounds were toxic following reductive metabolism, which could be simulated by $e_{aq}^-$ attack in pulse irradiated aqueous solution. Some of the reductive metabolites, the nitroso and hydroxylamine derivatives, are believed to be carcinogenic (Weisburger and Weisburger, 1973). These same intermediates are formed following oxidative activation of carcinogenic amines. In light of the strong evidence that the hydroxylated derivatives of many polycyclic hydrocarbons and arylamines are the active carcinogens *in vivo* (Miller, 1970; Weisburger and Weisburger, 1973) it is interesting to note that both $^\cdot OH$ and $O_2^-$ are potent initiators of aromatic hydroxylation reactions (Goscin and Fridovich, 1972; Jerina 1973) as well as epoxidation reactions (Buxton *et al.*, 1976). The $O_2^-$-induced hydroxylations are probably indirect processes either involving catalysed $O_2^-$-induced $^\cdot OH$ production, or secondary reactions of unstable products of $O_2^-$ attack.

In this and previous work (Cardona *et al.*, 1975; Ts'o and Lu, 1964), it has been confirmed that radiation-induced activation leads to the formation of covalently bound chemical adducts between transient carcinogenic electrophilic species and nucleophilic centres in DNA. In the presence of high concentrations of carcinogen to scavenge the water radiolysis species (reaction 5), the yield of carcinogen-DNA binding increases linearly with radiation dose and is highest in solutions containing radiation-induced oxidants such as $^\cdot OH$ and $O_2^-$ and is lowest where these species are scavenged. Although hydroxyl radicals are more reactive towards carcinogens and are therefore better activating agents in a simple model system, in the cell they react indiscriminately and would have a very low probability of seeking out and activating precarcinogens. On the other hand, $O_2^-$ is a very unreactive species with the majority of cellular components (Bors *et al.*, 1974; Greenstock and Ruddock, 1976), being only selectively reactive with protein and non-protein sulfhydryls (Armstrong and Buchanan, this conference) and polyunsaturated fats (Greenstock and Ruddock, 1976). Consequently in the cell, $O_2^-$, generated biochemically or radiation chemically, might exhibit a high probability of activating carcinogens, even those present in low concentration. Intracellular superoxide dismutase may be able to prevent these deleterious effects of non-physiological production of $O_2^-$, but only if the enzyme effectively competes for these superoxide radicals with the cellular target(s) for carcinogenesis.

The results presented represent a simple test of a proposed redox model for chemical carcinogenesis (Fig. 4) in which precarcinogens are activated to elec-

REDOX MODEL FOR CHEMICAL CARCINOGENESIS

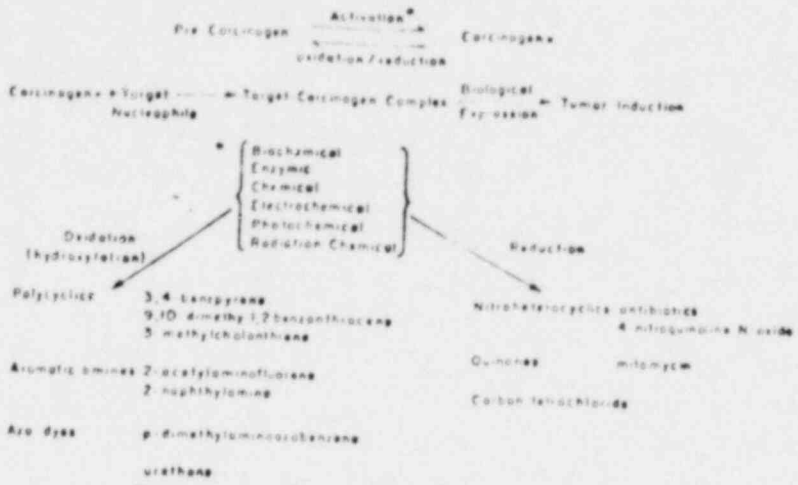


Figure 4. A redox model for chemical carcinogenesis.

trophilic free radical intermediates. These activated carcinogens can subsequently react with target nucleophiles to produce a chemical change, as in the genetic material of the cell, which ultimately may trigger the cell to become neoplastic. We are presently extending our DNA carcinogen binding studies to develop and test the effects of selective scavengers on carcinogen activation in model systems, in order to evaluate the relative efficiencies of the activation step and the target-activated carcinogen interaction step of the proposed model (Fig. 4) under chemically defined conditions.

These studies implicate activated oxygen in the form of $O_2^-$ and $^{\cdot}OH$, not only in radiation carcinogenesis (Pochin, 1969; Yuhas *et al.*, 1976; Khan and Kasha, 1970), but also in carcinogen activation, thereby establishing a mechanistic basis for synergistic effects (Canva and Balny, 1971) between toxic chemicals (Searle, 1976) and radiation, and suggest the important possibilites of carcinogen deactivation or of suppressing carcinogen activation by radiation chemical means.

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CONTENTION 8/9, APPENDIX V



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## A Stochastic Model of Carcinogenesis Incorporating Certain Observations From Chemical And Radiation Dose–Response Data*

(*Received* 14 *July* 1977; *accepted* 21 *November* 1977)

A NUMBER of quantitative models postulating two or more stages of cell transformation before the tumor state is reached have been proposed to describe classes of dose–response data in chemical and radiation carcinogenesis (Bru58; Bu65; Ke71; Bau73; Sh74; Ro74; Wal75; Bo76; Brow76; Je76). However, although these models have been useful in elucidating certain aspects of carcinogenesis, they do not take into account, nor provide theoretical descriptions and adjustable parameters for, certain observed variables and stochastic interactions in experiments at the animal level. The purpose of this note is to introduce a stochastic model of carcinogenesis that incorporates certain phenomena regarding the sequential interactions of co-carcinogens, and to present some preliminary evidence of the consistency of this model with observed quantitative dose–response relationships.

Certain experiments with chemical carcinogens have shown that relatively stable first transitions can be induced by low levels of certain carcinogens, in such a way that later applications of sometimes the same, or sometimes different, substances can produce similar tumor appearance time distributions (Iv53; Po59; Be49). These time distributions seem to be relatively independent of the time between the first and second series of treatments. Also, in some experiments a reversal of the order of application of two substances that previously acted as co-carcinogens would fail to produce any tumors.

These observations (Bro66a, b; Bro67) led to the modification of an earlier stochastic model of chemical carcinogenesis (Iv50; Ar64) to assume that a specific second transition was necessary before a (particular, sensitive) cell could arrive at the "tumor state", where it would then grow by a specified stochastic growth process to a clinically observable tumor. Moreover, since the second transition cannot, according to certain experimental observations, be an event independent of the first transition, a conditional probability for the instantaneous transition to the tumor state was postulated, given a cell previously induced to the intial state (Bro66a, b). The use of a conditional probability for the second transition in deriving this model will be seen to provide a number of qualitative as well as quantitative similarities of the model with observed data. These similarities have been observed for a broad class of carcinogenic phenomena, including cumulative tumor incidence vs dose, average tumor appearance time vs dose, and effects of changing dose-rate—but so far in a limited number of experiments involving carcinogenic chemicals and/or radiation.

It will be useful here to summarize some basic stages in the derivation and mathematical forms of the model, both to discuss ways in which the model can be adapted to radiation carcinogenesis and to indicate some stochastic properties of a model that are necessary in order to be consistent with currently known experimental phenomena. However, before attempting to use or extend the model, the reader should refer to the detailed presentation of the assumptions and limitations of the model (Bro66b).

*This note is a preliminary presentation of some of the author's views and observations on carcinogenesis, and is not intended to represent official views or policies of the NRC.

The conditional probability of a first "excitation" (or transition) of the "cancer control center" within a cell* in $(t, t + dt)$ given it was still unexcited at time $t$ was taken from Iversen and Arley (Iv50) to be

$$p_1(t) = K_1 C\, e^{-At}\, dt, \tag{1}$$

where $K_1$ is the probability of the first transition per unit concentration of carcinogen in tissue (or at the appropriate site in the cell) at $t = 0$, $C(t)$ is the concentration of a given carcinogen, and $A$ is the rate constant for removal of the carcinogen from the tissue. Thus, the probability that a cancer control center, unexcited at $t = 0$, makes its first transition within $(t, t + dt)$ is

$$dF_1 = F_1(t + dt) - F_1(t) = [1 - F_1(t)]\, K_1 C e^{-At}\, dt, \tag{2}$$

where $F_1(t)$ is the cumulative time distribution of the first excitation, the factor in brackets is the probability that the center has not been excited by time $t$, and the remaining factor is the conditional probability of excitation $p_1(t)$ from equation (1). Integration of equation (2) followed by differentiation of $F_1(t)$ yields the probability density function for excitation of a cancer control center to the first excited state

$$\phi_1(t) = \frac{dF_1}{dt} = \left(\exp\left[\frac{-K_1 C}{A}(1 - e^{-At})\right]\right) K_1 C\, e^{-At}. \tag{3}$$

Up to this point, the derivation is equivalent to that in the Iversen–Arley model (Iv50).

Now, a specific second transition, conditioned on a specific first transition having already occurred, is introduced to take into account observations indicating the importance of the sequence of application of two different co-carcinogens, as well as the stability of the first transition (Bro66a). The conditional probability that a cancer control center will be excited to State 2 in time interval $(t, t + dt)$, given that it was previously excited to State 1 in time interval $(t', t' + dt')$, for $t' < t$, is

$$F_{21}(t + dt|t') - F_{21}(t|t') = [1 - F_{21}(t|t')]\, K_2 C\, e^{-At}\, dt. \tag{4}$$

*We are considering probabilities here with respect to a particular, sensitive cell; i.e. the probability of changing this cell to a single cancer cell may become large at certain carcinogen concentrations, but the probability that any cell in the entire volume of tissue exposed will be affected will still be extremely small.

where $K_2$ is the probability that a center in the first excited state at time $t$ will change to the second state within $(t, t + dt)$, per unit concentration $C(t)$ of the same carcinogen, and the mathematical symbols for conditional probabilities are defined as in Parzen (Pa62). By integration of equation (4), the conditional density function $\phi_{21}(t|t')$ was obtained in closed form (Bro66b), and used to obtain the the probability that a given cancer control center will be excited to State 2 in the time interval $(t, t + dt)$ given that the center was in the normal state at $t = 0$:

$$\phi_2(t)\, dt = dt \int_{t'=0}^{t'=t} \phi_{21}(t|t') \cdot \phi_1(t')\, dt' \tag{5}$$

The convolution integral of equation (5) represents the sum over $t'$ of the products of the probability that the first excitation occurred in $(t', t' + dt')$ and the conditional probability that the second occurred in $(t, t + dt)$ given that the first occurred in $(t', t' + dt')$. This type of integration is a necessary step in the development of any quantitative model that can be expected to adequately represent experimental observations regarding the necessity of two sequential transitions to form a tumor cell. The convolution of equation (5) was also integrable in closed form (Bro66b), and gave the following mathematical form for the probability density $\phi_2(t)$ for exciting a cancer control center that is normal at $t = 0$ to State 2 (the "tumor state") in $(t, t + dt)$:

$$\phi_2(t)\, dt = \frac{K_1 K_2 C}{K_1 - K_2}\left[\exp\left(-K_2 C/A - At + \frac{K_2 C}{A} e^{-At}\right) - \exp\left(-K_1 C/A - At + \frac{K_1 C}{A} e^{-At}\right)\right] dt, \tag{6}$$

when $K_1 \neq K_2$, and $A \neq 0$. Equation (6) was found by use of L'Hospital's Rule to appropriately converge to the closed forms obtained by direct derivation for the cases $K_1 = K_2$, and $A = 0$ (Bro66b).

Convolution by numerical computer integration of $\phi_2(t)$ with the Gaussian tumor growth-time distribution of Iversen and Arley (Iv50) then was used to obtain the tumor appearance time distributions $\phi_{app}(t)$ (Bro66b). Double integration gave the cumulative distribution $F_{app}(t)$ of tumor appearance over time, as a function of concentration $C$, as well as the (meaningful) parameters $K_1$, $K_2$ and $A$. For $t$ sufficiently long, or close to the animal lifetime $T$, $F_{app}(T)$ vs $C$ represents the dose–response relationship in terms of percent of animals with tumors vs concentration.

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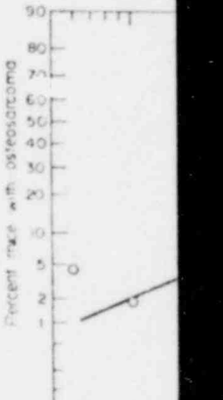


$F_{app}(T)$ vs $C$, although different mathematically from the log-normal function, was found to plot (conveniently) as a straight-line on log-probability paper (Fin62) for a wide range of parameters $K_1$, $K_2$, and $A$, with the slope and position of the line being adjustable by adjustment of these parameters. Experimental dose-response data for a number of single chemical carcinogens was also found to approximate a straight-line on a log-probability paper plot over a wide concentration range (Bro66a, b; Bro67; Dr65), and could be fitted in many cases by the theoretical $F_{app}(t)$ vs $C$.

Sufficient data are now available (from a limited number of experiments with a sufficiently large number of animals) to indicate that dose–response relationships for radiation carcinogenesis may often fit the log-normal shape, or that of this two sequential stage model (see Figs. 1–4). Also, the log-normal shape is sometimes observed for absorbed dose plotted in rad, and sometimes for administered dose in $\mu$Ci or $\mu$Ci/kg—which could produce variable absorbed doses up to tumor appearance times or deaths in individual animals (La63, 64, 70; Sa76).

The two sequential stage model also happens to result in log-normal dose–response shapes for cases involving either short-term ($A$ large) or longterm application of the carcinogen ($A$ close to zero, which might also simulate continuous irradiation, with long-term maintenance of (the probability of) concentrations of particular radiolysis products at particular cell sites). Some of the dose–response data fitting the log-normal shape involve shorter effective half-life nuclides and some involve longer-term irradiation. Irradiations over a longer time span often appear to result in dose–response lines of lower slope (larger standard geometric deviation), other factors being similar (see Figs. 1–3). Single doses of external radiation of low LET produce sharply rising dose–response curves. (See, e.g. Fig. 5 and Shellabarger *et al.*, 1974, which also illustrate the competing risk of animal or cell killing, or other competing effects, at higher dose levels. Any stochastic model describing dose–response relationships in the lower range of dose would require the subtraction or multiplication of an appropriate term that becomes effective only at the higher dose levels, as indicated, e.g. by the data in Figs. 1, 3 and 5.)

In the plot of Fig. 4, lung tumor incidence produced by intratracheal administration of Ce-144 vs beta dose (Ce64), two points are plotted to show the agreement of the Ce-144 data with that from beta irradiation by $^{106}$Ru-$^{106}$Rh implanted in pellets (La63). The pellets were implanted in such a way that the beta dose to sensitive target cells of bronchial mucosa could be accurately calculated. (La63). Furthermore, Laskin *et al.* showed in this paper (La63) that their dose–response curve fitted the log-normal shape all the way to $1.6 \times 10^6$ rad.*

*Of course, calculated doses to certain target cells serve here only as a relative index of dose. From any such conditions of irradiation from a fixed beta source, it should be obvious that there are cells exposed over a wide range of doses and that this situation implies some complex dependence of the parameters of this paper on the probability distribution of "hits" on the appropriate positions of certain cells.

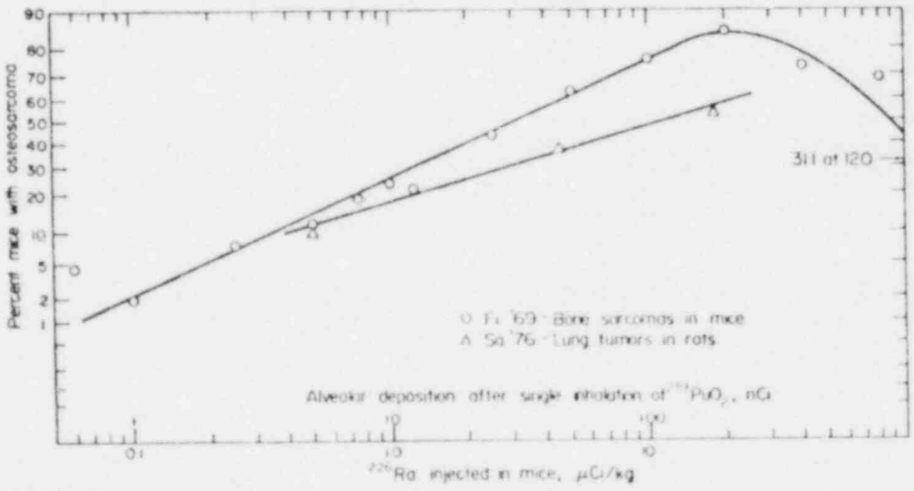
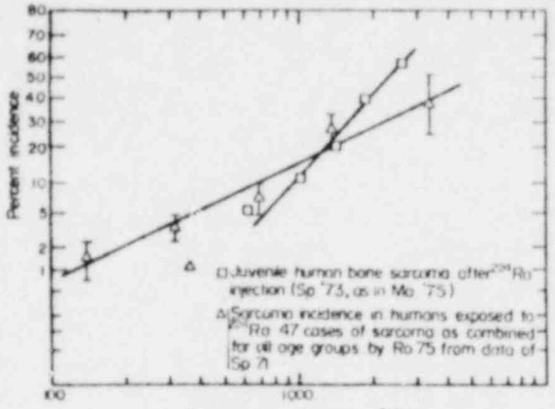



FIG. 1.

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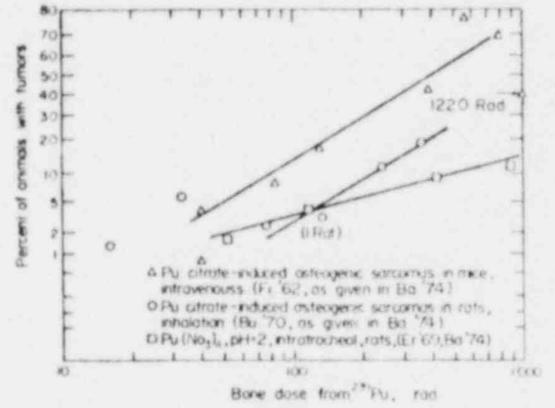
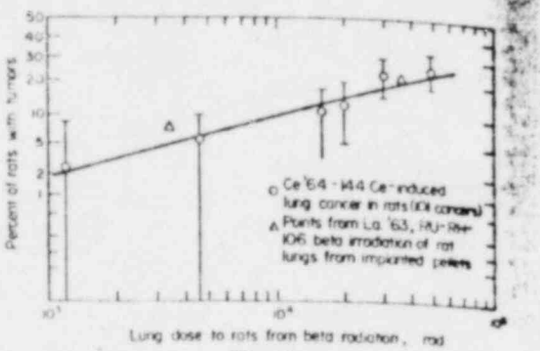



FIG. 3.

(Note that only a small volume of tissue was irradiated.)

Data on tumor appearance time vs radiation dose or administered activity are also presented in a number of the references cited. Tumor appearance time in radiation carcinogenesis generally decreases with increasing radiation dose and increasing tumor incidence in a manner similar to that predicted by the model (Bro66b), and also that observed for applications of single chemical carcinogens (Bro66b). The shape of the tumor appearance time distribution depends of couse on the growth-time parameters assumed for the particular tumor-type and species, although the cumulative lifetime tumor incidence vs dose curves are generally not very seasitive to omission or inclusion of the growth-time distribution in the integration (Bro66b), particularly for animals exposed early in life.

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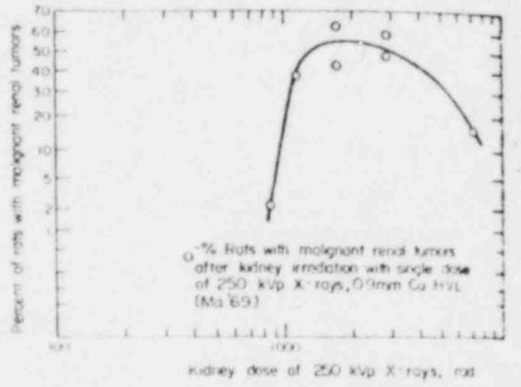
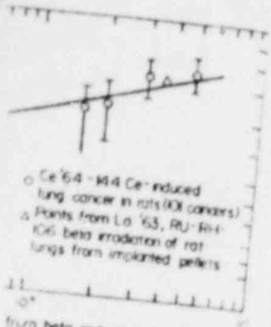



FIG. 5.

Although the model as presented in this note deals only with the probabilities of induction of transitions in a single "cancer control center" (or single cell?), the model may be easily extended logically to any number of postulated cells or sites when a large volume of tissue is exposed to the carcinogen (Bro66b). However, since the necessary specific interactions between carcinogens and the susceptible tissue sites have been shown to be extremely rare events (Mo75, War74), the model established on the basis of the first transformed tumor cell, or not more than a few, may suffice for purposes of setting radiation protection standards at low doses and dose rates.

Although the model has been derived for only a single carcinogen applied in concentration $C$ at $t = 0$, it may be noted from the form of equation (6) that terms containing $C$ within the brackets are either of the products $K_1C$ or $K_2C$. Thus, by adjustment of $K_1$ and $K_2$, it may be possible to empirically simulate experiments where a second co-carcinogen is added in concentration $C_2$ at times on the order of those required for most of the first transitions to occur. Nevertheless, a new

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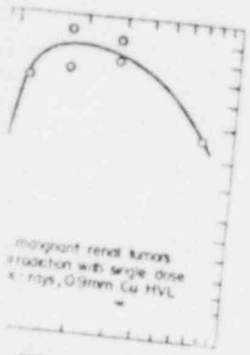


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derivation incorporating steps similar to those of equations (1)–(6) would be needed to represent experiments with two different co-carcinogens, e.g. radiation in sub-optimal amounts enhanced by a chemical "promoter." However, if radiation of a single type were to be administered continuously at any given dose-rate, the single carcinogen model may still turn out to be applicable. Recent evidence (Mo75; Tr76; Se75; War74) indicates that even with radiation, the carcinogenic transitions at the molecular level are more likely initiated indirectly by radiolysis products near the specific DNA locations, particularly for low LET radiations. Since ionizing radiations are carcinogens in their own right, it is possible that the same induced molecular radicals ultimately produce both the first transition with constant $K_1$ and the second transition with constant $K_2$. If this turns out to be the case, then $K_1$ and $K_2$ may be derivable from the rate constants for the chemical reactions that produce the first and second transitions in DNA. Also, $A$ may be adjusted to specific finite values for pulses of radiation, or set equal to 0 for continuous production (and replenisment) of radiolysis products to maintain a continuous concentration $C$.

A sequence of protracted multiple irradiation pulses would, however, require some additional mathematical analysis to represent competing reactions of the active molecular species in either "promoting" to the second stage (tumor state) a first transition already produced by a previous pulse, or initiating a first transition. Radiation, and some chemical carcinogens (Bro66b), are known to be able to act as promotors alone, as well as carcinogens or initiators, in appropriate dose ranges [in exception to the statement that promoters are not generally carcinogens or initiators (Tr76)].

The stochastic model presented here may not only be useful for understanding and predicting carcinogenic effects, but may also turn out to be applicable to other radiobiological and toxicological phenomena involving two sequential stages of mutagenesis. The log-normal dose–response shape has also been observed in experiments on 30-day lethality of mice, produced by 440-MeV and 730-MeV protons and by X-rays (Bra63; Bra64). Also, the dose–response lines on a log-normal plot of the 440-MeV and 730-MeV experiments were each parallel to the respective X-ray response lines, but slopes ("biological variability") were characteristic of the mouse strain used at each laboratory. This result would be interpreted in ordinary toxicological experiments (Fin62) as allowing a single relative potency (RBE) to be assigned to each proton energy, independent of dose level, with the assumption that each type of radiation produces lethality by the same set of mechanisms, but with differing potency. Thus, the two-stage sequential stochastic model may provide an alternative model to the log-normal for interpreting a broad range of radiobiological and toxicological effects. The log-normal model in toxicology has always been a completely empirical model, and can be derived theoretically only under the assumption that the biological end result is produced by a large number of multiplicative factors and events, each differing only slightly from unity (Fin62). Evidence is mounting to show that, during irradiation, the stochastic deposition of variable quantities of energy at microscopic sites (on the order of nanometers in dimension) can induce noncarcinogenic mutations that may result in biological effects other than cancer (Bail75; Ke71; He76; War74).

Data on human carcinogenesis by radiation, although adequate to establish reasonably safe standards for protection of radiation workers [due to early epidemiological initiative (Ev74; Row75; Brow76)], is (fortunately) in the author's opinion not plentiful enough to discriminate between the shapes of various models (Brow76) extending into the lower dose ranges. The present stochastic two-sequential stage model does contain features,* however, that could account for the sometimes greater carcinogenic response observed for the same dose given at lower dose rates (within a certain range)—both for radiation (Brow76) as well as chemical carcinogens (Bro66b). Lower dose-rates and extended durations of irradiation, would particularly be more effective in situations were radiation was acting primarily as a promoter in the presence of active chemical initiators in the environment. Since $F_{app}(t)$ vs $C$ approximates very closely the $S$-shaped curves of the log-normal family, the model could also account for the supra-linearity in the leukemia incidence vs dose data of Hiroshima-Nagasaki as observed by Baum (Bau73)—particularly in consideration of the

*The proper convolution of the conditional probability of the second transition $\phi_{2|1}(t|t')$ with $\phi_1(t')$ as in equation (5), builds into the resulting formula of equation (6) a probability of zero of reaching state 2 before state 1; thus events that in other models would allow the second "hit" to be effective at any time, are "wasted" in this model if they occur too early. This effect could become more striking if the model is extended for application of 2 different co-carcinogens acting in concentrations $C_1$ and $C_2$.

competing risks that obviously were effective at the higher dose levels.

Relatively little additonal human data on radiation carcinogenesis will appear (hopefully) in the near future, under present and evolving standards of radiation protection, particularly with sufficient statistical precision and accuracy in case identification and dose estimation to improve understanding of carcinogenic mechanisms. Thus, more immediate progress in understanding the quantitative nature of dose–response relationships at the mammalian level will depend on animal experiments. Some suggestions to make these experiments more helpful in developing "macroscopic" theories useful in elucidating dose-response phenomena are:

(1) More experiments should be carried out to examine the potential for radiation to act as a co-carcinogen (initiator and/or promoter) with other known chemical agents. Such experiments should include exposures with single doses of radiation, accurately measurable, both before and after application of chemicals known to be carcinogens by themselves as well as those that act only as initiators or promoters (Bro66b, La63, La70). Also, time intervals between applications should be varied for pairs of exposures where sufficient numbers of tumors appear, to test the stability of the initial transition, as well as the time independence of the postulated growth-time distribution. Experiments should also be carried out where a chemical known to act only as an initiator at specific concentrations is applied first, and then graded single doses of gamma radiation are applied at a specific time interval (e.g. one month) following the initiator, in radiation dose groups lower than tumors would be observed by radiation alone and extending to a dose range where up to 50% tumors or more would be observed. Repeated experiments of this kind, varying the time interval between treatments, could help characterize the tumor growth time distribution for a particular species; present experimental methods would not otherwise allow the observation of the moment of transition of a cell to the tumor state *in vivo* in order to obtain direct measurements of growth time distributions.

(2) In addition to other plots that may be of interest, the lifetime incidence of animals with tumors at each dose level should be plotted on a log-probability scale, with probability on the vertical scale as in Figs. 1–5, for ease in intercomparing data of different experiments and for convenience in weighted-regression analysis of the probit versus dose line (Fin62).

(3) In experiments where information on quantitative dose–response relationships is among the objectives, a sufficient number of animals should be included in each dose group of interest so that the variability in estimating the "true" expected proportion of tumors $p$ is not greater than any desired $s_p$ on the vertical probability scale; e.g. $N$ should be large enough so that $\sqrt{(pq/N)} < s_p$, where $q = 1 - p$. Preliminary estimates of $p$ may be made from plots similar to those of Fig. 1–5 of appropriate published data, from experiments that might be expected to provide similar dose-response relationships. Also, when the study of dose–response shape is important, at least 3 animal groups satisfying the preceding inequality should be included. It is suggested that values of $s_p$ not greater than about 0.02 would be helpful in improving current dose–response information.

(4) When an experiment is complete (all animals have died and autopsy results are evaluated), all quantitative data on all animals should be published along with the analysis of results. This data should include: estimated appearance time of first tumor in each animal; number of tumors of each type in each animal at autopsy; times of autopsy and/or death; time(s) and age(s) of administration of each carcinogen; the dose level and mass of tissue exposed for each carcinogen application in appropriate units; the cumulative fraction of animals with one or more tumors integrated over lifespan for each dose group; and estimates of average radiation absorbed dose in rad received by tissues of interest within each dose group up to clinical observation of the first tumor, and up to time of death or sacrifice. In this way, quantitative data of interest on individual animals may be pooled appropriately by future researchers or reviewers to obtain better statistical power for investigating various quantitative aspects of carcinogenesis.

*Acknowledgements*—The excellent work of George Elchin in designing and producing the figure layouts is appreciated. Eileen Haycraft's excellent assistance with manuscripts and correspondence is also appreciated. Charles A. Willis kindly re-programmed the models for use in this paper.

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*Health Physics* Vol. 35 (Aug), pp. 428–430
Pergamon Press Ltd., 1978. Printed in Great Britain


## Comparison of Relative Risk from Radiation Exposure and Other Common Hazards*

(*Received* 21 *November* 1977; *accepted* 30 *January* 1978)

### Introduction

MANY occupationally exposed radiation workers do not have adequate training in the fundamentals of health physics to understand or interpret the meaning of monthly personnel dosimeter reports. One of the most frequently asked questions following a discussion of radiation safety with such workers is "I received 240 (or 60, or 500 etc.); what does this number mean?" It has proven helpful to relate the risk due to health (somatic injury) due to the radiation exposure with other common risks faced by workers today. Statistics are available both for the risk for health from radiation (NAS72) and for the risk from other common hazards (BC76).

It is assumed that there is no recovery from radiation injury and that the effect of 1 rem is the same whether delivered over 1 month, 1 yr or 5 yr. It is also assumed that the latent period for the radiation injury has passed. These simplifying approximations do not alter the basic conclusions and make presentation of the results to untrained groups much more straight forward. Three comparisons have proven useful in placing radiation effects in perspective and in assisting radiation workers in evaluating the relative risk due to radiation exposure. The first is a comparison of the hazards from radiation exposure with hazards from accidents in the United States. The second is a comparison of relative accident rates for various occupations in the United States and the third is a comparison of the health hazards associated with cigarette smoking and radiation. These comparisons are presented in the belief that others will find them useful in discussions of radiation safety to radiation workers and the general public. The results are reported in terms of hazard per one rem exposure, which is taken as a conservative average of occupational exposure (NRC76).

*Supported in part by Grant CA 16127 and CA 14052 and CA 21074 from the National Institute of Health.

CONTENTION 8/9, APPENDIX VI

# Can Science and Politics Safely Mix?

Robert Neubecker

By ROBERT REINHOLD

WASHINGTON — Remember Allen V. Astin? He became the Eisenhower Administration's first big bombshell back in 1953. As director of the National Bureau of Standards, Dr. Astin ran afoul of the political leadership because his agency — which jealously guarded its reputation as a scientific bastion impregnable to political and commercial pressures — had declared a chemical called AD-X2, then sold as a rejuvenator of tired car batteries, useless.

The product's promoter, however, was a friend of Dr. Astin's boss, Sinclair Weeks, the Secretary of Commerce, who promptly fired the Bureau of Standards director. The result was a storm of protest from the scientific community, Mr. Weeks's recanting and Dr. Astin's rehiring. AD-X2 was not heard from again.

As that incident suggests, science cannot always be separated from politics. And as recent events indicate, the fallout is not always so humorous. Last month, for example, Science, the journal of the American Association for the Advancement of Science, disclosed that the Department of Agriculture was using a political litmus test in appointing its peer review panels, which judge the quality of basic research proposals. Department officials said that in choosing among scientists with comparable professional credentials, preference was given to those "philosophically compatible" with the Reagan Administration. In the publicity that followed, Secretary John R. Block reversed the policy.

The Washington Post last week reported that political referrals were being used to fill vacancies in the Food and Drug Administration's advisory panels of experts. Aides to Health and Human Services Secretary Richard S. Schweiker said they were trying to broaden panel membership. Meanwhile, the National Academy of Sciences has been frozen out of Government-supported research on acid rain, with the Administration suggesting that academy studies are biased and the academy's friends hinting the Administration might be unhappy with the scientific truth about a politically volatile subject.

In other matters, the Reagan Administration appears to have respected the independence and integrity of science. It appears not to have interfered, for example, with the two largest Federal science agencies, the National Science Foundation and the National Institutes of Health. The institutes' new director, Dr. James Wyngaarden, is a respected professional, nominally a Democrat, and has expressed views on abortion inconsistent with the Administration's.

So, it remains to be seen whether a consistent pattern is emerging. Reaction in the scientific community, however, is clear: There is widespread unease. "With each political era we find examples where the sensitivity of the scientific system is tested by abuses," said Dr. Donald Fredrickson, who served under three Presidents and five department secretaries as director of the National Institutes of Health. "There is always someone who exerts more zeal than is justified in appointments. Political people come in not understanding scientific method. They must learn."

Dr. Fredrickson does not perceive an organized effort to subvert the integrity of science. Neither does William D. Carey, executive director of the A.A.A.S. But Mr. Carey does argue that Government departments need more guidance from the White House science adviser to prevent spread of the "infection" of political interference.

There seems little hope in that direction. When asked about the problem, the science adviser, Dr. George A. Keyworth 2d, said it was "eminently reasonable" for the President to want scientific panels that share his political philosophy. "There are not very many panels that look at issues that are 100 percent scientific and technological," Dr. Keyworth said, citing birth control, abortion, industrial innovation, agriculture and arms control. What is wanted, he said, are "competent scientists who understand what President Reagan perceives as the role of government." If a panel is to evaluate basic research proposals, he said, no political considerations should enter. But according to Dr. Keyworth, when it comes to evaluating, say, birth control research, anti-abortion activists should be considered.

Asked if a political loyalties test would be used in replacing Dr. John Slaughter, who announced that he would leave this summer as director of the National Science Foundation, Dr. Keyworth said a scientist of "excellence" would be chosen, but "ultimately we will choose a person whose philosophy is compatible with the President."

Clearly, there are posts in government where science and medicine merge into policy and politics, particularly in regulatory agencies. While many may disagree, for example, with the strong views of Surgeon General C. Everett Koop on family life and abortion — he's pro-family and anti-abortion — few would disagree that the President has the right to appoint a doctor who shares his views on such matters, particularly since the Surgeon General has little to do with research. He is mainly the Government's spokesman on health.

What worries scientists is political intrusion into decisions on what constitutes good and bad science and on which projects should be funded. Traditionally, these choices have been guided by nonpartisan panels of working scientists from outside government.

Even politically conservative scientists, such as Herbert I. Fusfeld, a physicist and head of New York University's Center for Science and Technology Policy, are worried. "It's plain stupid to use political criteria in staffing these groups," Dr. Fusfeld said. "From time to time, and for certain purposes, a government representative uses nontechnical criteria. But in almost every case, they distort the purpose of the panel and they mess up the program."

control by the military. These, according to the GAO, for the most part will be large mainframes from International Business Machines (IBM) known as 3033's, which were developed around 1977. These already are two generations old, having been superseded by IBM model 3081 and the recently announced IBM 3083.

What is to be gained by the use of obsolete equipment? For one thing it is cheap. The 3033's are no longer selling well, and IBM recently announced a price cut on some models of up to 17 percent. Perhaps more important is that the old computers will allow the military to use software that already runs on computers at Johnson, a great savings since developing software is often more expensive than buying the computers themselves. The problem is that the software, too, is far from state of the art. Many of the astrophysical algorithms go back to the days of Project Mercury.

At "some point," says Charles E. Rey, a GAO auditor who worked on the report, "you've got to upgrade. You've got to optimize your software.

What the military gains most in this approach is speed—not efficiency, accuracy, or low cost, but speed. And, taking the headlong approach one step further, the Air Force has signed a contract with IBM so that the antiquated setup at the Controlled Mode can be exactly duplicated in Colorado—so the military can further save steps in its mushrooming space program.

Using the Controlled Mode layout is only part of the replication strategy. In order to speed the space effort, the military is also building in Colorado a near

CONTENTION 8/9, APPENDIX VII

# Security Checks on USDA Peer Reviewers

The U.S. Department of Agriculture (USDA), according to a well informed Administration official, has been screening scientists for security risks and political compatibility before inviting them to sit on peer review panels. These panels, composed of people supposedly chosen for their expertise alone, will decide which research proposals deserve to be funded by the USDA's competitive and special grants offices. Spokesmen for the National Science Foundation and the National Institutes of Health say these procedures are unusual; their agencies do not subject peer reviewers to Federal Bureau of Investigation (FBI) or political checks.

The practice of screening scientists for their political views is irregular in itself. But, according to several observers, it has also caused severe problems in scheduling basic research awards this year. Background checks are time consuming. At present, nominations are moving slowly through the bureaucratic maze, and the review system seems threatened with delay.

In the case of the 4-year-old competitive grants program, names of 140 potential reviewers were submitted for approval early this year. As of 23 April, only 15 of the 72 needed to conduct business had been cleared by the Secretary of Agriculture. These reviewers are supposed to meet and give their final decisions on grant applications on 3 May. Many have been reading applications for weeks in preparation.

The person responsible most directly for screening the nominations, Charles Grizzle, confidential assistant to Secretary of Agriculture John Block, says there has been no impropriety in selecting members of peer review committees this year. It is true that nominees for policy or advisory committees are checked for their political coloration. "If two names are submitted to us and one is a Democrat and one is a Republican, we will choose the Republican," he says. Candidates for the scientific panels are not scrutinized as carefully as those for the policy committees, but they are screened.

Grizzle says that nominations to the peer panels are sent to the FBI for a routine name check. Then they undergo a "very cursory check" at the Agriculture Department "to make sure that we've got people in the right slot and that they haven't gotten mixed up somewhere along the line," Grizzle says. "Our principal criterion is scientific qualification." However, if there is a choice between two people and one is "more philosophically attuned" with this Administration, we are going to choose that person." But Grizzle insists that "there is no effort to politicize those panels." Anyone who suggests otherwise, he adds, "must be trying to embarrass the secretary, and we're not too pleased about that."

There are two reasons for the delay in setting up the peer panels for the research programs, according to Grizzle. One is that the department has been required to operate according to the rules of the Federal Advisory Committee Act this year for the first time. The procedures are unfamiliar. Second, the nominations came in late, "private at the end of February. Grizzle says the FBI clearances came through 6 to 8 weeks later, and that he hopes to complete the department's in-house "cursory check" within 4 days. Of the 270 nominations for the various peer review panels, 80 had been cleared by 23 April, according to Grizzle. (A spokesman for the FBI says it takes 10 to 14 days to process a routine name check.) Grizzle says he has been working "rather feverishly" to review all the lists sent over by the FBI. He hopes to have all the names cleared by the night of 26 April.

There was, however, no clear explanation for the delay in hiring the man who was recruited to direct the competitive grants program, David Krogmann, professor of biochemistry at Purdue University. He ran the same program while taking a year's leave from Purdue in 1980. This year he has been asked to run it again, splitting his time between Purdue and the USDA. He recruited his own administrative staff early this year at the USDA's behest. But as of 23 April, he and his recruits still had not been given formal approval to take control of the program. This delay of 5 months in getting started, Krogmann says, "may set a new record for the department."

The first director of the competitive grants program, Joe Key, now a professor in the botany department at the University of Georgia, fears that some USDA officials may be practicing a form of malign neglect. The competitive grants program has never been liked by traditionalists at USDA, Key says. "If the department is not mature enough to handle an open basis, research program, perhaps we should consider moving it somewhere else."

—I. TROY MARSHALL



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