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*A Methodology for*  
**Environmental  
and Occupational**  
*Cancer Surveys*

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## INTRODUCTION

Environmental cancers are malignant tumors which are usually caused by prolonged exposure to exogenous agents of various types. In a few instances, these environmental cancer-producing factors are well-defined physical or chemical agents; in others they are variable and undetermined mixtures of chemicals; while in a third group the cancerigenic exposure is represented by contacts or conditions of a rather vague nature. The different environmental carcinogens which form a part of our natural or artificial environment are practically the only known causes of cancer in man at the present time, and for this reason have considerable general significance. Exposure to these factors is related to occupational activities, medicines, diets, cosmetics, building material, habits, customs, climate, fauna, contaminants of drinking water, atmospheric air and foodstuffs, and procedures of warfare. Since prevention of cancer depends fundamentally on adequate information as to its etiology, the study of environmental cancers, which may bring vastly increased knowledge as to the causes of all types of cancers, is one of the most important approaches to a future control of cancer. Environmental cancer surveys which are directed at this goal represent, therefore, a basic step in the development and institution of preventive cancer control measures.

### A. THE NATURE OF THE PROBLEM

Investigation into the epidemiology, etiology, and control of environmental cancer depends upon the application of knowledge and approaches peculiar to this special type of hazard. Often these factors may not be adequately considered in the usual studies of toxic industrial health hazards and differ in some respects from those used in epidemiologic investigations of infectious diseases.

For example, some of the environmental carcinogens, such as betanaphthylamine and benzidine, scarcely ever cause toxic manifestations. In most instances, the carcinogenic process elicited by these aromatic amines in the bladder is symptomatically silent during a latent period that lasts from 5 to 25 years. Industrial health surveys limited to the demonstration of acute or chronic toxic reactions and disregarding the peculiar nature of these carcinogenic hazards would fail to disclose the serious danger to exposed persons.

Other environmental carcinogens, such as benzol, ionizing radiations (X-rays or rays from radioactive substances), will produce

severe degenerative and necrotizing reactions in the tissues as the result of brief but intense exposure. This more striking effect can obscure the fact that less severe but more prolonged exposure may produce cancerous responses in the same type of tissue after a long latent period. When these two different types of reaction are seen in members of a surveyed occupational group, their etiologic kinship may not be apparent.

Moreover, the long latent period characteristic of environmental cancer formation tends to hinder the recognition of causal relations between the exposure to carcinogenic agents and the subsequent development of cancer.

This outcome may well appear when the affected individual has long since left the employment in which the effective exposure occurred.

One purpose of environmental cancer surveys is to collect data on the occurrence, incidence, types, and causes of these malignant tumors and their precancerous manifestations, on the routes and types of exposure to the carcinogenic agents involved in their production, and on the physiochemical states and properties of these agents. Only through such information is it possible to establish the principles upon which effective measures for the prevention and control of environmental cancers must be based.

Another purpose of occupational cancer surveys is to determine which persons may be effectively exposed to environmental carcinogens and thus become potential victims of environmental cancer. Since the development of such cancers depends on a number of associated factors, environmental cancer surveys must obtain reliable data for an adequate number of cases on age, sex and race, as well as the degree, nature and duration of exposure, and the length of latent period. Information on the approximate minimal effective exposure to any particular environmental carcinogen and on the expected latent period is essential in establishing standards for precautionary and preventive measures.

A final objective of occupational cancer surveys is the collection of specific technical information needed for the institution of adequate control measures. These data can benefit industry by aiding in the design and introduction of effective technical measures for protection of their personnel. The evidence acquired through such surveys should also provide a sound and appropriate basis for drafting proper and uniform industrial disease codes, food and drug legislation, and workmen's compensation laws covering the varied and complex features of environmental and occupational cancer hazards.

## 1. Occupational Carcinogens

Occupational carcinogens, known or suspected, cover a wide range of inanimate and animate agents. This spectrum, summarized in table

1, includes a great variety of organic chemicals, both aromatic and aliphatic, several inorganic chemicals, various types of physical radiation, and the parasite, *Schistosoma hematobium*, the only generally recognized animate carcinogen, which attacks outdoor workers in Egypt and other tropical countries, inducing a form of bladder cancer.

Table 1. *Recognized and suspected occupational carcinogens*

1. Chemical carcinogens:
  - (a) Organic chemicals:
    - (1) Aromatic chemicals: Beta-naphthylamine, benzidine, aniline (?), benzol, tar, pitch, asphalt, soots (domestic, industrial, and commercial), shale oil, crude paraffin oil, crude anthracene oil, creosote, lubricating and fuel oils and greases, synthetic estrogens (?).
    - (2) Aliphatic chemicals: Isopropyl oil (?).
  - (b) Inorganic chemicals: Arsenicals, chromates, nickel carbonyl (?), asbestos (?), beryllium (?).
2. Physical carcinogens: Nonionizing radiation-ultra violet rays, ionizing radiations-corpuseular radiations (alpha and beta rays) and electronic radiations (gamma and X-rays).
3. Parasitic carcinogens: *Schistosoma hematobium*.

It must be pointed out that the various environmental carcinogens differ considerably in their potency not only from each other but also among members of the same type. The carcinogenic potency of different types of tar varies greatly, gas-house and coke-oven tar being the most potent. Similar variations seem to exist regarding the carcinogenicity of the various types of soot and the different kinds of natural and processed petroloums, many of which are noncarcinogenic. Beta-naphthylamine appears to be much more carcinogenic than benzidine.

The data on occurrence and incidence of occupational cancers, as they appear in published reports, are very inadequate. The actual number of cancers which are occupational in origin is undoubtedly much higher than is apparent from the recorded observations. Since it is often difficult to establish the occupational causation of cancer resulting from exposure to known carcinogens (often many years previously), and because the medical profession is to a certain extent insufficiently aware of the existence of occupational cancers, even cancers produced by recognized occupational carcinogens often escape recognition as such. Furthermore, it seems highly probable that many occupational carcinogens are still unknown, and, in view of the fact that new industrial compounds are being synthesized and manufactured every year, the spectrum of industrial carcinogens may be growing even wider.

## 2. Nonoccupational Carcinogens

Occupational cancers belong to the larger group of environmental cancers produced by contact with exogenous agents. Contact with carcinogens may also be related to habits, hobbies, diet, medicinal agents and devices, and other nonoccupational environmental factors.

The known nonoccupational carcinogens are summarized in table 2. They include many agents peculiar to certain cultural and geographic groups not found in the United States (such as the *kangri* and *chutta*) as well as such almost universal agents as solar radiation, soot, and arsenic. As in table 1, the fact is indicated that many of these carcinogens are not yet proved but are only suspected on the basis of limited evidence. Collection of additional evidence in these fields may not only point out hazardous habits or usages, but may also reveal hitherto unsuspected occupational carcinogens. Data provided by occupational cancer surveys are the only source of reliable information on the minimum effective exposure, maximum and minimum lengths of latent period as related to degree of exposure, and on other important aspects of environmental carcinogenesis.

Table 2. *Recognized and suspected sources of nonoccupational environmental cancer*

| <i>Method of exposure and carcinogen</i>                                                                                                                                | <i>Potential sites of cancer</i>        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| <b>HABITS:</b>                                                                                                                                                          |                                         |
| Smoking (tar) (?) or chewing of tobacco (khaini),                                                                                                                       | Lip, tongue, oral cavity, larynx, lung. |
| Betel nut-lime-tobacco quid chewing-----                                                                                                                                | Lip, tongue, oral cavity, cheek.        |
| Chewing of tar, paraffin, etc. (?)-----                                                                                                                                 | Oral cavity.                            |
| <b>CUSTOMS:</b>                                                                                                                                                         |                                         |
| Carrying of special heating devices beneath clothing near abdominal skin (kairo, kangri), or sleeping on hot stoves (kang), causing burns and exposure to tar and soot. | Skin.                                   |
| Smoking of cigars with lighted end in mouth (chutta) (tar and burn injury).                                                                                             | Oral cavity.                            |
| <b>HOBBIES AND HOME ACTIVITIES:</b>                                                                                                                                     |                                         |
| Gardening with exposure to solar rays, and arsenical and other chemical pesticides (soot, etc.).                                                                        | Skin, internal organs.                  |
| Sailing, fishing, golfing and other forms of outdoor sports with exposure to solar radiation.                                                                           | Skin.                                   |
| Home-engineering with contact with mineral oil derivatives (?).                                                                                                         | Do.                                     |
| Use of paints and paint removers containing benzol, chrome pigments, asphalts, carbon blacks (?).                                                                       | Leukemia, lung, skin.                   |

Table 2. *Recognized and suspected sources of nonoccupational environmental cancer—Continued*

| <i>Method of exposure and carcinogen</i>                                                                                                                   | <i>Potential sites of cancer</i>             |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| <b>HOBBIES AND HOME ACTIVITIES—Con.</b>                                                                                                                    |                                              |
| Use of chlorinated aliphatic hydrocarbons in cleaning fluids with hepatotoxic properties modifying metabolism of endogenous and exogenous carcinogens (?). | Liver, internal organs.                      |
| <b>MEDICINES AND MEDICAL DEVICES:</b>                                                                                                                      |                                              |
| Arsenicals.....                                                                                                                                            | Skin, internal organs.                       |
| Tar, impure vaseline and mineral oil.....                                                                                                                  | Do.                                          |
| Hepatotoxic chemicals (chlorinated aliphatic hydrocarbons, cinchophen, etc.) (?).                                                                          | Liver.                                       |
| Hematotoxic chemicals (benzol, sulfonamides (?), aromatic organic chemicals) (?).                                                                          | Leukemia.                                    |
| Ultraviolet radiation.....                                                                                                                                 | Skin.                                        |
| X-rays.....                                                                                                                                                | Skin, bone, leukemia (?).                    |
| Radioactive chemicals (ionizing radiations) ..                                                                                                             | Skin, bone, lung (?) leukemia (?) liver (?). |
| <b>DIETARY FACTORS:</b>                                                                                                                                    |                                              |
| Dietary iodine deficiency.....                                                                                                                             | Thyroid.                                     |
| Dietary protein and vitamin B complex deficiency.                                                                                                          | Liver.                                       |
| Dietary vitamin B complex deficiency.....                                                                                                                  | Laryngopharynx.                              |
| Arsenical contaminants in food, drinking water, air.                                                                                                       | Skin, internal organs.                       |
| Coated mineral oil as fat substitute in baked goods (?).                                                                                                   | Internal organs.                             |
| <b>COSMETIC FACTORS:</b>                                                                                                                                   |                                              |
| X-radiation for depilation.....                                                                                                                            | Skin.                                        |
| Ultraviolet lamp exposure for tanning (?).....                                                                                                             | Do.                                          |
| Arsenicals in hair lotions and tonics (?).....                                                                                                             | Do.                                          |
| Lamp black in eyebrow pencils (tar) (?).....                                                                                                               | Do.                                          |
| Impure vaseline and mineral oils in ointments, creams, etc.                                                                                                | Do.                                          |
| Estrogens in skin creams (?).....                                                                                                                          | Breast.                                      |
| Impure aniline dyes in lipsticks, etc., containing dye intermediates (?).                                                                                  | Bladder.                                     |
| <b>OTHER ENVIRONMENTAL FACTORS:</b>                                                                                                                        |                                              |
| Tar and soot in atmospheric air (?).....                                                                                                                   | Lung, skin (?).                              |
| Dry and sunny climate with excessive solar irradiation.                                                                                                    | Skin.                                        |
| Parasitic infections (schistosomiasis).....                                                                                                                | Bladder, liver, intestine.                   |
| Ionizing radiation in water and air in regions with radioactive ores (?).                                                                                  | Lung, bone, hematopoietic tissue.            |

### 3. Industrial and Public Health Hazards

At the present time, environmental cancer appears primarily an industrial problem, although it extends into many nonindustrial occupations. Fully 90 percent of the known environmental cancers never existed in dangerous concentrations until the development of industrial processes which brought workers into frequent and direct contact with them. As the injurious agents have increased in accordance with the growth of various industries, cancers have developed among exposed workers. Perhaps one of the most striking examples of this pattern is the appearance of bladder cancers among dye workers subsequent to the establishment of aniline dye industries in many countries. Observations in many industries indicate that, although a known occupational carcinogen and the proper conditions of exposure, the appearance of occupational cancers becomes merely a question of time, i. e., of sufficient latent period since the start of the exposure. Clearly such hazards constitute an industrial problem demanding intensive study and control efforts.

Such industrial carcinogens not only provide a serious hazard to the exposed workers but may possibly also affect the health of the general population through various routes of contact. Carcinogenic agents produced or handled in industrial operations, workshops, or laboratories may enter the air, water supply, or soil after being discharged as waste. Persons living or working in the fume or disposal area may thus come into effective contact with the carcinogens. Contaminated clothing worn by workers in carcinogenic occupations may also create a hazard when laundered without proper precautions in the factory, home, or commercial laundry. A possible extension of industrial hazards to the general population is the incorporation of carcinogens into goods for general consumption, either as essential parts or as contaminants. Of course, there are also or similar extrinsic carcinogens which appear as industrial hazards but may also be part of the general artificial or natural environment independent of any industrial operations.

Information and conclusions drawn from occupational cancer surveys, therefore, will have applications that are not restricted to the industrial or occupational field, but may have relevance to the cancer problem as a whole. Since environmental cancers represent a majority of those cancers whose etiology is known, observations in relation to these tumors have positive and immediate value in the study and possible future control of the many types of human cancers whose causes are still unknown.

## B. TYPES OF ENVIRONMENTAL CANCER SURVEY

To attain the objectives discussed above, several approaches may be used in environmental cancer surveys. The first method suggested, analysis of death certificates, provides a preliminary or exploratory approach which may give valuable clues and point to fruitful fields for further investigation. The second approach, occupational history studies of cancer deaths, involves tracking down possible occupational factors in the etiology of individual cancer cases. The third approach, the plant survey, is essential for determining precisely which workers come into dangerous contact with carcinogens, how many may be affected, through which route the exposure takes place, what organ or organs develop cancerous responses, and other important aspects of occupational carcinogenesis.

For the organization of an occupational cancer survey on a State level, it is essential that close cooperation be established between various State agencies (department of health with its divisions of cancer control, industrial hygiene, and vital statistics, and department of labor) and that contacts be made with the State medical society (committees on cancer, industrial medicine, public relations), local tumor registries, and, where necessary and desirable, the State association of clinical pathologists and public health nurses association. The over-all direction of such a survey should be provided by the department of health and the work should be carried out by either the division of cancer control or the division of industrial hygiene, depending upon which one of these two agencies appears best suited and equipped for the work. Since occupational cancer is mainly a biological phenomenon, it appears reasonable to place in charge of the project, a physician experienced in cancer, industrial medicine, or both.

### 1. Analysis of Death Certificates

Working on the premise that certain occupational activities or contact with various occupational or environmental agents result in an abnormally high incidence of total cancer deaths, as well as in an abnormal distribution of cancer as to sites, the effects of such factors on local cancer mortality might be demonstrated through a critical analysis of data recorded in death certificates. If such environmental carcinogenic influences are sufficiently pronounced and specific in a certain area, and the worker population is relatively stable, it might be profitable to plot the local distribution of cancer deaths as to total number and as to sites. Comparison of these data with data from an area having a different environmental and, particularly, occupational carcinogenic spectrum should reveal suggestive relations between these factors and cancer incidence. By comparing the rela-

tive frequency of cancer cases for various sites in the region under study against the normally expected frequency, it may be possible to locate regional foci of carcinogenic exposure—plants, industries or occupations which deserve further investigation and in which protective and preventive measures are needed.

To establish such correlations, not only the residence but also the place of employment must be noted and evaluated. For the purpose of such analysis, the map of the survey area may be divided into regions with more or less well-defined environmental patterns—industrial, agriculture, urban-commercial, maritime.

Within the industrial regions, establishments should be noted which provide known or suspected carcinogenic hazards. Such industries may include tar, pitch, asphalt, and creosote producers and consumers; organic chemical, dye, and pharmaceutical manufacturers; rubber producers and processors; paint manufacturers; distillers and refiners of petroleum products; smelters, refiners, and users of non-ferrous metals such as copper, nickel, zinc, silver, and chromium; producers and users of radioactive substances; glass and pottery manufacturers; makers and users of metallic abrasives; textile makers and dyers; and others. Appendix A provides a more extensive, although by no means complete, listing of occupations in which carcinogenic influences may be suspected.

In addition to name, residence, age, sex, cause of death, and place of death, information on individual cancer cases which may be obtained from death certificates will include occupation, industry or business in which the deceased was employed, and social security number. These data appear as items 1 to 16 on the Occupational Cancer Record blank given as appendix B.

For purposes of analysis, it will be necessary to code this information and transfer it to punch cards. Whenever the nature of the information makes this possible, item 11 (industry or business) should be coded in three ways:

(a) By occupation, according to the Alphabetical Index for Occupations and Industries, 16th Census of the United States, 1940, Bureau of the Census.

(b) By specific occupational carcinogenic hazard, according to the Occupational Hazard Code, appendix C.

(c) By place (community or region) of occupational activity.

Since information recorded in death certificates is known to be often unreliable, and because death certificates do not give any data on length of residence, length of employment in last occupation, or previous occupational employments, any conclusions drawn from a statistical analysis of this nature must be merely suggestive. In some instances, they may even prove misleading, and any report based on such an analysis should emphasize the limitations of the technique.

If proper consideration is given to these limitations, however, biostatistical studies of this type may yield valuable clues that can be followed up by other types of epidemiologic investigations, as, for example, those described below.

## 2. Occupational History Study of Cancer Deaths

Using as a basis the information obtained from death certificates, it is possible to study the occupational histories of selected cancer cases in order to discover possible causal factors.

The available evidence indicates that at least some of the cancers involving certain organs (skin, lung, nasal sinuses, bladder, bone, bone marrow) are caused by occupational or environmental carcinogens. Less conclusive evidence, such as geographical, topographical, age, and sex distribution, implicates environmental and possibly occupational factors in the production of cancer in other organ systems (gastrointestinal, nervous). By tracing back the environmental and occupational histories, and, where possible, discovering other exogenous agents to which the cancer patient was exposed, it may be possible to substantiate further these findings, discover hitherto unknown carcinogens, and determine the incidence of various types of cancer in different occupations and industries.

In planning such a study, proper consideration must be given to the fact that these tumors usually result from extended exposure and appear only after long latent periods, the latter ranging ordinarily from 5 to 25 years. It is necessary, therefore, to ascertain the occupational and nonoccupational exposures for as long as possible a period preceding death. Such information should include, in addition to the names and locations of the various employers, detailed information as to the type or types of operations in which the individual was employed, the physical or chemical agents to which the individual was exposed, and the length of employment in the various occupations. Whenever possible, information on injuries and diseases sustained during the survey period should also be collected, as these may indicate specific precancerous or pericancerous reactions. (See C-2.) The type of information required appears on the Occupational Cancer Record (appendix B) as items 17 to 30.

Data on the employment history of the deceased may be obtained from a number of sources, including the last attending physician; hospital records; employers and their insurance carriers; institutions such as homes for the aged, sanitariums, mental institutions, infirmaries, etc., in which the deceased may have been an inmate.

After the places of employment have thus been ascertained from one or more of these sources, it is necessary to obtain detailed information as to the type of work performed and the types of occupational and nonoccupational agents with which the deceased came in contact,

whenever available information suggests the possibility of carcinogenic exposure. Data on the duration, intensity, and type of exposure should complete the information required. From a critical evaluation of the information collected for each case, it is usually possible to appraise whether or not one or several occupational factors might have played an essential role in the production of a particular cancer. (See C-3.)

Through this approach it is possible to ascertain not only the extent of known occupational cancer hazards in a given area but to uncover also new industrial carcinogenic agents and foci. The presence of the latter will be indicated by the predominance of certain types of cancers among individuals either engaged in a specific operation or coming in contact with some particular agent present in and common to different operations.

### 3. Industrial Plant Surveys

The individual plant survey is necessary to determine precisely the location and nature of suspected carcinogenic exposures. In order to discover whether such hazards actually exist in a particular plant, their nature and mode of operation, and how they may be controlled, it is necessary to know as accurately as possible the number of persons who have been exposed and the number showing effects, the nature of these effects and the type of the contact.

For the efficient planning and conduct of such plant surveys, it is desirable to start by obtaining some basic information on the individual industrial establishments within the study area. These data should include plant location; duration of operation; type of medical service; names of plant manager, plant physician, and insurance carrier; number of employees; raw materials used and goods produced; and any evidence of suspected or established carcinogenic hazards. The Plant Survey Record form, given as appendix D, shows these data as items 1 to 11.

This preliminary survey need only be approximate and is intended merely to ascertain whether a detailed survey is indicated, how many investigators will be needed, the length of time to be required for the study, the type and degree of assistance and cooperation available from the management, and the availability of employment, medical, and insurance records.

Since several years of contact with the carcinogenic agent are usually required for effective exposure and since the latent period is seldom shorter than 5 years and sometimes more than 25 years, cancer records of industrial operations should be obtained for as long a period as possible, up to 30 years or more. Occupational cancer surveys are never spot surveys but always time surveys.

However, the biological and epidemiologic behavior of occupational

cancers makes it advisable to survey establishments that have been in operation for as little as 3 years. Workers in such plants may have already developed precancerous and pericancerous lesions, especially if the carcinogenic hazards affect the skin, bladder, bone, or hematopoietic tissue. It is unlikely that within such a short period, cancer attributable to occupational exposure will occur in statistically significant numbers, but the timely recognition of these nonmalignant lesions may serve as a warning signal and hasten the introduction of adequate precautionary measures, forestalling the appearance of an epidemic of occupational cancer at some later date.

In surveys of this type, the chief effort should be expended on discovering and analyzing personnel currently or formerly employed in operations with appreciable recognized or suspected carcinogenic hazards. These persons are the actual test subjects which may demonstrate the type and degree of hazard through significantly elevated cancer incidence rates. Only when these studies demonstrate the existence of an occupational carcinogen is it advisable to extend the investigation to groups of workers exposed to a lesser degree so as to determine the wider scope and ramifications of the hazard.

Information on the health and on other occupational exposures of these persons may be obtained through the occupational history studies of cancer deaths, as described above; plant employment records; plant medical records; insurance companies; hospitals; physicians; institutions; and social security records.

To obtain reliable incidence figures, the present health status or cause of death should be determined whenever feasible for all workers currently or formerly employed for an adequate period in operations with carcinogenic hazards.

Since occupational cancers have a latent period that is usually more than 5 years, if the plant has a fairly rapid labor turn-over, it may be found that no workers in apparently carcinogenic operations are suffering from cancer or even from precancerous lesions. Indeed, the medical records of the plant or its insurer may show no occupational cancer throughout the entire period of operation. However, it may be discovered, by following up former employees, that some persons have developed occupational cancers possibly attributable to the carcinogenic agent to which they were exposed from 2 to 30 years earlier. Labor turn-over may, therefore, totally obliterate any evidence of cancerous reactions in persons exposed unless adequate follow-up studies of former employees are made over a period of sufficient length, say 15 to 20 years.

Consideration must be given, moreover, to the fact that employees with occupational cancer or with therapeutically controlled occupational cancer are, in general, not continued in operations with carcinogenic hazards. In some establishments, however, this practice is not

followed as it is held that removal from the hazardous occupation does not improve the ultimate prognosis, and by continuing the employee in the occupation the absolute number of persons so exposed is held at a minimum. This practice, on the other hand, tends to increase primary cancer incidence among exposed workers.

It is usually found that various employee groups are exposed in widely differing degrees to any carcinogenic agent or agents that may be present. Office workers, for example, are not as a rule significantly exposed to industrial carcinogens unless the administrative quarters form an integral or closely related part of the production zone, thereby establishing direct contact; or unless the disposal of carcinogenic wastes, such as fumes, dust, vapors, gases, mist, represents an environmental hazard in the office area. Not infrequently it is found that only relatively small groups of workers have effective contact with carcinogens. In some industries, however, such as chromate operations, practically all production workers are exposed to carcinogenic agents to some degree.

The investigations should be extended not only to individuals regularly employed in hazardous operations or constantly in contact with carcinogenic agents, but also to those entering the hazardous area or coming into contact with carcinogens at irregular intervals. Intermittent, irregular, or rhythmic exposures of varying intensity may be sustained by such workers as watchmen, repairmen, packers, shippers, truckers, supervisors, clerks, control chemists, guards, and yardmen. Consideration should also be given to workers charged with the disposal of wastes and emptied containers of carcinogenic materials as well as to those workers who may become exposed to an appreciable degree through work in noncarcinogenic operations located near the hazardous one, and thereby possibly becoming exposed to carcinogenic gases, vapors, fumes, dusts, etc., originating from the latter.

Through investigations within the plant, exact information should be obtained as to the nature of the suspected carcinogenic agents; type and route of contact to which employees are exposed; and the type and intensity of such hazards and their possible variations during different periods of operation of the plant due to changes in manufacturing methods and in raw materials used.

Moreover, record should be made of any differences in the degree and type of exposure (skin contact, inhalation, ingestion) and the physico-chemical status of the agents (dust, fumes, mist, spray, vapor, gas) in different parts of the same operation and in different parts of the plant. Special attention should be paid to ascertaining the particle size of dust, fumes, mist, etc., as this factor determines to a certain degree the severity of exposure to respiratory cancer hazards. Such distinctions are indicated for chemical as well as physical carcinogenic agents. Differences in this factor affect not only the incidence rate of occupa-

tional cancers among various groups of workers but may also be of distinct influence in determining the site of resulting cancers.

To assay cancer hazards in industry, the plant must be surveyed by a trained observer as only such a person can detect the potential danger points. In carrying out such plant analyses, it may be wise to follow these suggestions.

(a) The investigator should be thoroughly familiar with the production methods and with the materials handled and manufactured in the plant. He should be able to note any irregularities or exceptions from usual procedures and readily detect areas in which carcinogenic hazards may exist.

(b) Studies should be made when the plant is in operation. Conditions of exposure and observance of precautionary measures by workers and management can be properly studied only under working conditions. Moreover, there is an opportunity to study the physical appearance of workers and, with permission of the management, make personal inquiries of foremen and workers in regard to suspected hazards.

(c) Since visits of this sort may be announced well beforehand, there is an opportunity for cleaning up any operation. Such a procedure may result, unintentionally, in the obliteration of important evidence. It is, therefore, advisable that the inspector look closely at the condition of windows, corners, nooks, ledges, surfaces and joints of pipes and ducts, and other machinery for evidence of poor house-keeping. Arrangement and effectiveness of exhaust ventilation should be tested.

(d) Any survey should include the yard and adjacent buildings, packing and shipping facilities, and disposal of wastes and emptied containers. Finally, the study should be extended to the neighborhood of the plant, noting unusual effects on color and surfaces of houses, vegetation and animals, and condition of drinking water in order to discover any possible effects on the environment of carcinogenic agents handled or produced within the plant. Where evidence indicates the environmental spread of an occupational cancer hazard to persons living near the plant, the survey should be extended to the population living or working in the vicinity of the plant and may, if feasible, include an epidemiologic study of cancer among wild and domesticated animals in the area.

(e) Contact should always be made with the plant physician and information obtained as to the type of medical supervision, the type of medical facilities available, and the employment and medical policy observed in connection with workers who have developed precancerous or cancerous lesions.

(f) Through careful questioning the investigator should discover any changes made in production, handling, and precautionary meas-

ures employed during the period of plant operation. Such changes may have a favorable or adverse effect on the conditions of exposure. The direction of this influence may sometimes be rather unexpected. For example, improved production methods and precautionary measures which may reduce the concentration of carcinogenic dust in the atmosphere may also increase rather than diminish the degree of exposure. In order to obtain better yields in production, the carcinogen may have been more finely powdered, thereby causing a dust which reaches the deeper regions of the bronchial tree. The consequent intensification of the carcinogenic effect causes an increased incidence and a shortened latent period of the resultant cancer of the lung. A corresponding result may follow when a mist hazard is converted into a vapor hazard, or dust hazard into a fume or vapor hazard.

Changes in the physico-chemical status of the carcinogen may result, moreover, in a shift of the site of the ensuing cancers. (See C-1.) Although it is not likely that a carcinogen present in mist form may reach the nasal sinuses (unless these have become abnormally accessible through operative procedures, such as are performed for the relief of chronic sinusitis), cancerous reactions of the sinus lining may be anticipated if the carcinogen appears in the form of a vapor or gas that can enter the sinuses and be trapped, condensed, and retained in the cavity.

In investigating the effects of such changes in production methods, the investigator must constantly bear in mind that, as a rule, effects do not become evident until a lag period of at least 5 years, corresponding to the usual latent period for the type of cancer, has elapsed.

Detailed information should be obtained on the preventive, prophylactic, sanitary, and medical measures taken by plant management for reducing or eliminating the cancer hazard and of the dates upon which such measures were introduced. The type and extent of precautionary measures taken; extent of medical supervision; and follow-up of former workers and of workers shifted from hazardous to nonhazardous operations. Special attention should be paid to the methods employed in the disposal of carcinogenic industrial wastes, since inadequate measures of waste disposal may lead to a perpetuation or reintroduction of cancer hazards into operations which may have been made safe from the standpoint of production.

### C. SPECIAL ASPECTS

The conduct of occupational cancer surveys presents a series of special problems which must be taken into proper consideration to assure results that are reliable, significant and valuable for the con-

duct of cancer research and for the introduction of preventive measures.

## 1. Contact-Site Relations of Carcinogens

Observations in the field of environmental carcinogenesis have shown that the route of contact with these agents, as well as the route and nature of the metabolism and excretion or the site of their deposition plays a definite role in determining the site of the ensuing cancer.

Those observations are summarized in table 3, which indicates the type of contact (direct and primary, depository, excretory) for various carcinogens and the site of resultant cancer.

Table 3. *Contact-site relations of carcinogens*

| Site of cancer               | Type of contact         | Carcinogen                                                                                                                                                                |
|------------------------------|-------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Skin                         | Direct, primary contact | Ultraviolet radiation, X-radiation, radioactive energy, tar, pitch, soot, processed mineral oils, greases, arsenicals.                                                    |
|                              | Depository contact      | Arsenicals.                                                                                                                                                               |
|                              | Excretory contact       | Arsenicals.                                                                                                                                                               |
| Lung, larynx, nasal sinuses. | Direct, primary contact | Radioactive gases and dusts, fumes, dusts, mists, vapors of tar, pitch, processed mineral oils, chromates, nickel carbonyl (?), arsenic, asbestos (?), isopropyl oil (?). |
|                              | Excretory contact       | Radioactive gases.                                                                                                                                                        |
| Bladder, ureter, kidney.     | Excretory contact       | Aromatic amines, tar (?), arsenic (?).                                                                                                                                    |
| Bone and bone marrow.        | Depository contact      | Ionizing radiations (radioactive substances), benzol, beryllium (?).                                                                                                      |
|                              | Direct primary contact  |                                                                                                                                                                           |
|                              |                         | X-radiation.                                                                                                                                                              |

Despite the fact that the tissues of the alimentary and nervous systems are directly or indirectly exposed to a great number of environmental agents—some, such as tar, petroleum derivatives, arsenic and benzol, having definite carcinogenic properties—and although cancers of the alimentary tract exhibit topographical features indicating the causal action of exogenous carcinogens, there exists no definite evidence that specific exogenous and environmental factors are involved in their genesis. Since cancers of the alimentary system constitute almost one-half of all cancers observed in males and since cancer of this organ system, as well as those of the central nervous system, usually have a poor prognosis, it may be hoped that environmental cancer surveys will

provide data indicating the causation of at least some of the cancers affecting these two organ systems, and thereby help open the way to their ultimate control.

## 2. Environmental Cancer Pattern

In studying the medical histories or symptoms of workers exposed to occupational carcinogens, attention should be given not only to cancers, but also to precancerous lesions (proliferative conditions which are sometimes observed preceding and not infrequently leading to cancer), and pericancerous lesions (conditions due to carcinogenic exposure, but are unrelated to the carcinogenic process, yet serving as stigmata of previously sustained specific carcinogenic exposures).

Proper attention should be given to the important fact that exogenous carcinogens not only elicit hyperplastic and benign neoplastic cellular proliferations preceding, preparatory to, or simultaneously with, cancerous reactions. Depending on the quantitative and qualitative conditions of exposure, these carcinogens may also cause degenerative, necrotizing and, in fact, anti-cancerous effects. Such ambivalent responses to exogenous carcinogens appear in many forms and are not infrequently present in individuals with environmental precancerous and cancerous lesions. In fact, whenever such an environmental cancer pattern, including both aplasiogenic and hyperplasiogenic manifestations, can be demonstrated in the same individual or a group of individuals exposed to the same agent, it serves as valuable evidence in support of an exogenous causation of the cancerous responses observed in the population group.

Among the exogenous carcinogens which produce these ambivalent effects are arsenicals, benzol, ionizing radiations from radioactive chemicals and X-ray tubes, estrogens, urethane, and certain nitrogen mustards. Their anti-cancerous action is utilized in the therapy of malignant tumors, while their carcinogenic action has resulted occasionally in the production of cancers when they have been used medicinally in the treatment of nonmalignant conditions.

These ambivalent precancerous and pericancerous reactions to environmental carcinogens are summarized in table 4. As may be noted, they are found in the entire range of the carcinogenic spectrum and affect the skin, nasal passages, bladder, bone marrow, lungs, and breasts.

A characteristic environmental cancer pattern may be presented by the changes in the blood and hematopoietic tissues following exposure to benzol or ionizing radiations. At one extreme of the scale, heavy exposure is found to bring degenerative, necrotizing and atrophic changes, such as aplastic anemia, leukopenia, thrombocytopenia, macrocytic anemia, and severe atrophy of the hematopoietic tissues. On the opposite end of the reactive range there occur leucoeytotic, hyper-

leucocytotic and leukemoid reactions with the appearance of immature leucocytes, polyglobulia, leukemia associated with metaplastic erythropoietic, myeloid and leukemic proliferations in internal organs, and myeloid and leukemic hyperplasia of the bone marrow.

Table 4. *Precancerous and pericancerous reactions to environmental carcinogens*

| Reactions                                                                                                                                                                                                     | Etiologic Agents                                                                                                                                                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>SKIN</b>                                                                                                                                                                                                   |                                                                                                                                                                                                     |
| Alopecia:<br>Spotty loss of hair.....                                                                                                                                                                         | Arsenic, ionizing radiations (radioactive substances, X-radiation).                                                                                                                                 |
| Atrophy:<br>Skin grossly thinned and glistening in patches, associated with keratotic areas.                                                                                                                  | Pitch, tar, asphalt, petroleum, radioactive substances, X-radiation, ultraviolet radiation, solar rays.                                                                                             |
| Eczema:<br>Dry seborrheic patches on skin.....                                                                                                                                                                | Arsenic, asphalt, pitch, soot, tar.                                                                                                                                                                 |
| Keratosis:<br>Flat, discrete, scaly area on skin with raised pearly borders. Usually on parts of skin exposed to carcinogen, but may occur in unexposed parts, particularly about sweat glands, with arsenic. | Anthracene, arsenic, asphalt, creosote, crude mineral oil, paraffin, pitch, soot, tar, radioactive substances, ultraviolet radiation, X-radiation.                                                  |
| Hyperkeratosis:<br>Rough, fissured keratotic plaques with small, hard, wart-like horns usually on hands and soles. May become nodular and ulcerate.                                                           |                                                                                                                                                                                                     |
| Verrucae:<br>Horn-like hyperkeratosis.....                                                                                                                                                                    |                                                                                                                                                                                                     |
| Ulceration:<br>Breakdown of keratotic lesions.....<br>Chrome holes.....                                                                                                                                       | Araenicals.<br>Chromates, chromic acid.                                                                                                                                                             |
| Leukoderma:<br>Patches of subnormal melanin pigmentation.                                                                                                                                                     | Anthracene, arsenic, asphalt, creosote, crude mineral oil, paraffin, pitch, tar, nonionizing and ionizing radiations (radioactive substances, X-radiation, ultraviolet radiation, solar radiation). |
| Leuko-melanoderma:<br>Patches showing increased pigmentation and patches showing subnormal pigmentation of skin. Most common in areas of highest pigmentation, and may involve oral mucosa.                   |                                                                                                                                                                                                     |
| Melanoderma:<br>Patches of increased pigmentation.....                                                                                                                                                        |                                                                                                                                                                                                     |
| Scleroderma:<br>Dry, scaly, parchment-like skin, with enlarged pores, associated with leuko-melanoderma.                                                                                                      | Crude mineral oil, paraffin oil, ionizing radiations (radioactive substances, X-rays, ultraviolet rays, solar rays).                                                                                |

Table 4. *Precancerous and pericancerous reactions to environmental carcinogens—Continued*

| Reactions                                                                                                                                                                                       | Etiologic Agents                                                                                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| <b>NASAL PASSAGES</b><br>Papillomas and polyps:<br>Growths in antrum, ethmoid cells and turbinates. Nasal septum perforations.                                                                  | Isopropyl oil, nickel carbonyl, chromates, arsenicals.                                            |
| <b>BLADDER</b><br>Hemorrhage, submucosal:<br>Varying size, with telangiectasia. Located mainly in trigone and about ureteral orifices.                                                          | Benzidine, beta-naphthylamine and derivatives.                                                    |
| Papillomas:<br>Polypous or villous, pedunculated or sessile. Often multiple about trigone and ureteral orifices.                                                                                |                                                                                                   |
| <b>EYES</b><br>Papillomas:<br>Pedunculated. Develop mainly on lids, occasionally on eyeball.                                                                                                    | Arsenic, asphalt, creosote, crude mineral oil, pitch, tar, ionizing radiations, ultraviolet rays. |
| <b>BONE</b><br>Chronic periostitis:<br>Thickening of periosteal tissue, necrosis of bone.                                                                                                       | Ionizing radiations (X-rays, radioactive substances).                                             |
| <b>BONE MARROW HYPOPLASIA</b><br>Blood dyscrasias:<br>Hypoplasia and metaplasia, aplastic anemia, thrombocytopenia, leukopenia, monocytosis, erythrocytosis, leucocytosis, leukemoid reactions. | Benzol and derivatives, ionizing radiations (radioactive substances, X-rays).                     |
| <b>LUNGS</b><br>Pneumoconioses and pneumonia:<br>Asbestosis, "lipoid" pneumonia, chronic chemical pneumonia.                                                                                    | Asbestos, arsenic, tar, soot, mineral oil mist, chrome salts, nickel carbonyl.                    |
| <b>BREAST</b><br>Painful, swollen breasts:<br>Glandular hyperplasia.                                                                                                                            | Estrogenic chemicals.                                                                             |

Intermediate degrees of exposure, whether continuous or intermittent, will produce mixed reactions. In general it will be found that increasing exposure will result in increasing effects of both the hyperplastic and atrophic types up to a certain point. From that point, the increasing severity of exposure will cause a preponderantly aplastic effect, overwhelming any hyperplastic reactions and leading, as exposure increases, to death of the organism by destruction of tissues. Thus, a primarily hyperplastic phase may be followed by an aplastic phase, or vice versa, depending upon the degree and rhythm of exposure.

### 3. Identification of Occupational Cancers

Occupational carcinogenic agents and cancers do not, in themselves, possess any characteristic properties that distinguish them from agents and cancers of nonoccupational nature. The occurrence of cancer in an exposed person of a tumor characteristic for the particular carcinogen and type of exposure is not, therefore, absolute proof that the cancer is of occupational origin; anatomically and histologically identical cancers are found in persons who apparently have had no contact with the occupational carcinogen in question. However, there is often sufficient associated evidence present, which, when critically analyzed, provides adequate and acceptable proof as to the occupational nature of the cancer.

Such evidence is represented by the presence of typical precancerous and pericancerous lesions, such as radiation, tar, oil, paraffin, pitch, solar and arsenic dermatitis; radiation osteitis; and pre-leukemic leukopenias and leukemoid reactions after exposure to benzol and ionizing radiations. Additional supporting evidence is the demonstration of exposure of adequate length and intensity to the carcinogenic agent. However, consideration must be given in this connection to the possibility that effective carcinogenic exposure may be the result of contact with the carcinogen sustained in different employments or for other environmental reasons, or exposure to different carcinogens having additive action. Thus, a critical analysis of the entire occupational history and nonoccupational exposures is indicated for all cases in which the initial evidence shows that the exposure sustained in any single employment appeared insufficient or sufficient to account for the cancer.

Identification of cancers found in a particular survey area or plant may be made by statistical methods when individual cancers cannot be accurately identified as to etiology. This identification will not apply to any specific case, but may provide a strong suggestion of occupational or environmental etiology. These criteria of identification are:

(a) Significant variations in total and organ incidence of cancer in different environmental or occupational subdivisions after the data have been properly adjusted and standardized as to race, age, sex, and other possible factors.

(b) Shift in organ incidence, sex distribution, frequency of multiplicity and age range of cancer during different parts of the survey period, especially if these developments should follow upon the establishment of industries with known or suspected cancer hazards in the area.

(c) Differences in the incidence rate and localization of cancer within one organ system (exposed and unexposed skin, alimentary

tract, etc.), among persons living in various parts of the survey area. Different types of exposure to the same carcinogen, as well as contact with different carcinogens, have a direct influence on the incidence rates and localizations of cancer within one particular organ system.

For a conclusive demonstration of the occupational or environmental nature of cancers suspected on the basis of statistical and epidemiologic evidence, it is usually necessary to reproduce identical cancers in experimental animals by means of the suspected agent. In fact, it is held by many investigators that the actual cause of a particular occupational cancer is not proven until experimental reproduction has been achieved. Conversely, it is not infrequently believed that the demonstration of carcinogenic responses to an exogenous agent in animals is evidence that this agent may exert a similar action in man. On the basis of this assumption, chemicals produced and used in industry and consumed by the general public are screened and tested in experimental animals for potential carcinogenic properties they may possess for man. However, existing facts indicate that neither a successful reproduction of cancer in animals nor the bioassay of chemicals for potential carcinogenicity in man fulfill entirely the requirements that must be placed on such tests.

For instance, under proper conditions of exposure beta-naphthylamine and benzidine elicit bladder cancer in man. Such tumors are produced in 100 percent of the individuals after sufficiently intense and prolonged contact with these chemicals. Age, sex, and heredity do not seem to have any appreciable influence in this respect. The experimental reproduction of these bladder cancers was successfully achieved by feeding male or female dogs beta-naphthylamine. There is controversy as to whether or not rabbits react similarly to the administration of beta-naphthylamine; it is established that rats and mice do not respond with the development of bladder cancer when given this chemical by various routes, although they readily show this response upon the introduction of related aromatic amines (2-acetylaminofluorene) and aromatic azo-compounds (O-aminoazotoluene, o-toluidine). On the other hand, dogs fed benzidine in high and at times toxic doses for a period of more than 5 years did not develop bladder tumors; rats receiving the same treatment respond with the production of cancers of the eustachian tube, hepatocarcinomas, and leukemia. The two aromatic amines found to be carcinogenic to man cause species specific cancerous responses which in the rat are complicated by a shift of the carcinogenic shock organ (i. e., the bladder, in man) to several other tissues (i. e., liver, bone marrow and, probably, eustachian tube).

The chemical analysis of the urinary metabolites of the two aromatic amines when given to different species suggests that variations

in their metabolism characteristic for the species tested seem to be related to the species specific carcinogenic properties observed. It thus was found that beta-naphthylamine is excreted by the dog as 2-amino-1-hydroxynaphthalene conjugated with sulfuric acid, while rats, rabbits, and monkeys given injections of beta-naphthylamine in olive oil eliminate in the urine the base itself, its N-acetyl derivative, its N-acetyl-6-hydroxy-derivative and an unidentified dihydroxyaminonaphthalene. After the administration of benzidine rabbits excrete the free base and a hydroxy-derivative, white rats eliminate a hydroxylated compound and an acylate derivative. Workers exposed to chemicals containing benzidine excrete hydroxy-derivatives, while acyl derivatives and free benzidine have not yet been demonstrated in man.

Various aromatic azo compounds produce cancer of the liver in rats but not in rabbits. Observations suggest that this species specificity is not entirely of a constitutional nature, but depends in part on exogenous dietary influences which, through impairment of the normal liver function, cause an abnormal metabolism of the carcinogenic azo-compounds. While a constitutional factor which causes a rapid excretion of butter yellow may account for the resistance of rabbits and guinea pigs to the carcinogenic action of butter yellow, the exogenous dietary factor that is essential for the carcinogenic action of the chemical in the rat is the riboflavin deficient diet, without which liver cancer does not develop. Recent experiments showed that rats kept on an adequate diet and given 2,3 azotoluene excrete 2,1 aminophenol in the urine while rats given a riboflavin deficient diet in addition to the chemical eliminate aniline in the urine and develop bladder tumors.

Another example of the species specific quality of carcinogens is offered by tar. While it has been possible to elicit skin cancers readily by the application of various types of tar in man, mice, and rabbits and with some difficulty in rats and dogs, all attempts to obtain similar results in monkeys have failed.

It is not unlikely that species specific factors may be responsible for the equivocal results obtained in experiments aimed at a reproduction of arsenic cancers in animals. Since the average latent period of arsenic cancer of the skin is relatively short when compared with the latent period for oil cancers, it is improbable that the species specific differences in life span play an important role in preventing the carcinogenic action of arsenic to become manifest in animals. It may be possible that the generalized hair growth in experimental animals creates a higher excretory potential of arsenic and thereby lowers its carcinogenic action. However, the strikingly spotty appearance of arsenic cancer in man points to the action of other mechanisms, probably of abnormal nature, that must be present before arsenic can

produce cancerous responses even in man. It is remarkable in this connection that a high percentage of all medicinal arsenic cancers have been observed in individuals with psoriasis.

Another example of the great importance of species specificity is presented by the continued controversy as to the carcinogenicity of estrogenic substances in man. While there can be little doubt that estrogens are essentially involved in the development of mammary cancer of certain inbred strains of mice of both sexes, it is still questionable whether estrogens participate in the production of such tumors in man. There is little likelihood that a definite decision of this controversy will be obtained from observations made on women. However, recent observations made in males with intensive and prolonged medicinal or occupational contact with synthetic estrogens may soon provide the final answer to this question. Unilateral or bilateral mammary cancer has been found in several males who received large amounts of stilbestrol for the control of cancer of the prostate. Since normally less than 2 percent of all breast carcinomas occur in males, the continued therapeutic use of estrogens in the treatment of prostatic cancer may supply conclusive evidence as to the carcinogenicity of estrogens in man. The occurrence of hyperplasia of the breast in pharmaceutical workers in England and the United States engaged in the manufacture of synthetic estrogens may provide confirmatory evidence in this respect, if and when mammary cancers develop in male workers of this occupational group.

Brief mention may be made in this connection of two additional chemicals with potential or controversial carcinogenicity to man and definite or equivocal carcinogenicity to animals. Scattered occupational observations indict benzol as a leukemogenic agent in man. However, the experimental observations made so far entirely on mice are contradictory. Beryllium has been shown to elicit osteogenic sarcomas in rabbits only by means of intravenous injections. It is an open question whether this observation indicates that this substance may exert a similar effect in workers exposed to it by a different route.

Species specific differences exist also in the field of physical carcinogens and produce uncertainties and problems there identical with those encountered in connection with primary chemical carcinogens. Epidemiologic evidence strongly indicates that an excessive exposure to solar rays may result in cancer of the exposed skin among individuals especially predisposed by their light complexion. Observations made on mice and rats subjected to intensive treatment with ultraviolet rays seem to confirm this causal relation between exposure to solar actinic energy and cancer development. However, all attempts to produce experimentally ultraviolet cancer of the skin in guinea pigs and rabbits have failed. Thus, observations on two species seem to negate any relationship of solar irradiation and cancer. Such a

conclusion, however, is a fallacious one as far as man, mice and rats are concerned. The inability of ultraviolet rays to elicit skin cancers in guinea pigs and rabbits rather may be due to species specific differences in the photochemical reactions and reaction products produced in these species. These species specific differences in the response to ultraviolet rays, by the way, do not support the widely held concept that actinic energy elicits cancerous responses by causing primary direct cellular mutations. The available evidence favors the idea that physical carcinogenic agents also produce cancer through the mechanism of chemical deviations, of so far undetermined character.

Evaluating the evidence on the species specificity of physical and chemical carcinogens and its relation to occupational carcinogenesis the following conclusions may be reached:

1. Failure to reproduce cancers of certain sites in experimental animals, using agents which seemingly produce such cancers in man, does not disprove the carcinogenicity of the particular agents for man.

2. The employment of experimental animals in the screening of exogenous agents for potential carcinogenicity in man, while being at present the only available and practical method, is not an entirely reliable one.

3. In the experimental study of carcinogens which affect humans the selection of a suitable species represents the fundamental prerequisite for obtaining results that can be applied to man.

The planning, preparation and technical execution of animal experiments on occupational carcinogens present certain special aspects and considerations which may be worth mentioning since they may influence decisively the outcome of the experiment. Given a suitable test species, applied experimental occupational cancer research must aim to duplicate or at least closely approach in its experimental conditions the circumstances of exposure that are believed to lead to the development of cancer in man. Experimental evidence obtained in this way is most useful in its direct practical application to the existing occupational problem.

For instance, when designing the experimental conditions by which an occupational hazard entailing the inhalation of a carcinogen is to be studied, it is essential to ascertain first the physical status of the carcinogen under the existing working conditions; i. e., whether it is a gas, vapor, mist, spray, fume, dust, or a combination of several, and what its particle size is if it occurs in a dispersed form. It is especially important to ascertain the smallest particle size present and its proportion in the dispersed matter. Industrial hygienists are now paying marked attention to the determination of the particle size, since this factor is of utmost importance in determining the depth to which the inhaled particles penetrate the respiratory

tract, and thus in controlling the site and degree of exposure to the inhaled agent. Not infrequently the same agent undergoes several changes in its physical state when passing through various plant processes. For instance, chromite ores reach the factory coarsely ground. The particles in this stato may pass a sieve of 5 to 10 mesh. After the ore has been ground in steel ball mills to a fine powder the particle size is reduced so the chromite ore passes through a sieve of 100 mesh and half of it through a 250 mesh. When this powdered material is processed in the plant and dust is produced, it is obvious that the smaller dust particles will remain suspended in the air longer than the coarser ones and that the main exposure of the workers results from the inhalation of the portion of chromite or chromate compounds having the smaller particle size.

When applying such information to the experiment, it is necessary not only to select a dust of proper particle size but also an animal with respiratory passages that permit the penetration of the dust chosen into the bronchial tree. In view of the narrow respiratory passages of small animals such as mice, it is not likely that these species offer favorable anatomical conditions for administering effective exposures to carcinogenic dusts when the action of these dusts is dependent on direct contact of the bronchial tissue to the carcinogenic agent.

When determining the dose of carcinogen to be administered, it is not unusual that data used have been collected and recorded by industrial engineers and represent concentrations of the offending agent obtained in a number of random spot checks or are average values derived from tests of longer duration. Under practical working conditions, however, concentrations of injurious and carcinogenic agents may vary considerably during various phases of the operation and especially at times of accidents, during maintenance work or during repairs. It is for these reasons that special occupational groups employed within a carcinogenic operation often exhibit a particularly high incidence of occupational cancer as they are exposed intermittently to highly increased concentrations of the carcinogenic agent. In the experimental approaches to occupational cancer such observations deserve adequate considerations, as the use of insufficient doses calculated from averaged concentration figures may produce misleading negative results. Data on the concentration of radioactivity in the Schneeberg mines, for instance, indicate that there are not only appreciable variations in the degree of average radioactivity in the different mine shafts, but that the contents of radioactive gases within the same mine vary considerably in different parts and at different times, thereby causing an exposure to the miners that, as far as carcinogenic concentrations are concerned, should be measured more in peak values than in averaged values. Therefore, the proper appli-

cation of observations on exposure in the field seems to be an important part in experimental studies on occupational carcinogenesis.

Since there is an almost complete lack of reliable information as to the minimal effective doses for man of the various occupational carcinogens, and in view of the fact that the great majority of experimental reproductions of occupational cancers have been done with doses appreciably exceeding those encountered under working conditions in industry, it does not seem wise to attach too much significance to negative experimental results when low doses were used.

#### 4. Age Factors in Occupational Cancer

A survey of environmental cancer should include all cases in the area, regardless of age, sex, race, or site. The final analysis, however, should consider these factors separately and should make the proper adjustments for standardization, so as to obtain comparable figures.

Since occupational exposure to carcinogenic agents does not start, as a rule, before the age of 16 to 18 years, and inasmuch as the average latent period for occupational cancers is from 5 to 25 years it is advisable to restrict the evaluation of data in a study of occupational cancer to persons of the age group above 25 years. Although female workers often leave industrial occupations at an early age, the extensive employment of female workers in certain industries and professions with potential cancer hazards warrants their inclusion in such surveys. These industries include rubber goods manufacture, luminous dial painting, spinning and weaving, X-ray and laboratory work.

Many environmental carcinogenic factors, on the other hand, act on the human organism at a much earlier age than the occupational carcinogens. For instance, epidemiological studies on the incidence of penile cancer in circumcised and noncircumcised population groups indicate that the first 10 years of life are of definite importance in determining the occurrence and age of appearance of penile cancer. It is conceivable that even prenatal maternal influences, exerted on the fetus by exogenous factors penetrating the placental barrier may be active in eliciting cancer in the young. Thus, there are no definite age range limitations in general cancer surveys.

Detailed presentations of the problem of environmental and occupational cancers and related disorders are available in the following publications by W. C. Hueper:

Occupational Tumors and Allied Diseases, C. C. Thomas, Springfield, Illinois, 1942, p. 896.

Environmental and Occupational Cancer. Pub. Health Rep. Supp. 209, 1948.

These may be useful for the interpretation of the results obtained in environmental and occupational cancer surveys.

## APPENDIX A

### Occupational and Nonoccupational Groups Suggested for Survey

1. Exposure to benzol and its derivatives, naphthal, aromatic amines, toluol, xylo (with possible relation to leukemia, lymphosarcoma, and myeloma).

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
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| <p>           Airplane-dope workers.<br/>           Airplane hangar employees.<br/>           Alcohol (denatured) workers.<br/>           Aniline workers.<br/>           Art-glass workers.<br/>           Asbestos-products impregnators.<br/>           Battery (dry) makers.<br/>           Beauty parlor operators.<br/>           Belt spongers.<br/>           Benzol purifiers.<br/>           Benzol workers.<br/>           Brake lining makers.<br/>           Bronzers.<br/>           Burnishers.<br/>           Can (rubber gasket) manufacturers.<br/>           Can (rubber gasket) sealers.<br/>           Carbolic acid makers.<br/>           Chemists.<br/>           Chlorodiphenyl makers.<br/>           Clutch-disk impregnators.<br/>           Coal tar still cleaners.<br/>           Coal tar workers.<br/>           Cobblers.<br/>           Color makers.<br/>           Coke oven tar workers.<br/>           Compositors.<br/>           Degreasers.<br/>           Disinfectant makers.<br/>           Dry cleaners.<br/>           Dye makers.<br/>           Dyers.<br/>           Electroplaters.<br/>           Electroplate cast scrubbers.<br/>           Enamelers.<br/>           Enamel makers.<br/>           Engravers.<br/>           Explosive makers.<br/>           Feather workers.<br/>           Fertilizer makers.<br/>           Flavoring extract makers.<br/>           Galvanizers.<br/>           Gas house workers.<br/>           Gasoline blenders.<br/>           Gilders.<br/>           Glue makers.<br/>           Ink makers.<br/>           Lacquerers.<br/>           Lacquer makers.<br/>           Leather makers (artificial and patent).<br/>           Linoleum workers.<br/>           Lithographers.<br/>           Metal washers.<br/>           Millinery workers.<br/>           Mirror silverers.         </p> | <p>           Mordanters.<br/>           Nitrobenzol makers.<br/>           Nitrocellulose workers.<br/>           Oil extractors.<br/>           Paint remover manufacturers.<br/>           Painters.<br/>           Paraffin makers.<br/>           Pencil makers.<br/>           Perfume makers.<br/>           Petroleum distillery and refinery workers.<br/>           Pharmaceutical workers.<br/>           Phenol makers.<br/>           Photoengravers.<br/>           Photographic chemical makers.<br/>           Picric acid makers.<br/>           Plastic textile makers.<br/>           Polish makers.<br/>           Polishers.<br/>           Pottery decorators.<br/>           Printers.<br/>           Putty makers.<br/>           Pyroxylin plastic workers.<br/>           Rotogravure workers.<br/>           Rubber buffers.<br/>           Rubber cementers.<br/>           Rubber cement mixers.<br/>           Rubber compounders.<br/>           Rubber dippers.<br/>           Rubber driers.<br/>           Rubberized asbestos board makers.<br/>           Rubber mixers.<br/>           Rubber pressroom workers.<br/>           Rubber reclaimers.<br/>           Rubber tire builders.<br/>           Rubber treaders.<br/>           Rubber workers.<br/>           Shade cloth workers.<br/>           Shellackers.<br/>           Shellac makers.<br/>           Shoe finishers.<br/>           Shoe factory workers.<br/>           Shoe-heel (wood) coverers.<br/>           Smokeless powder makers.<br/>           Soap makers.<br/>           Tar distillery workers.<br/>           Tar, pitch, oil, etc., tank cleaners.<br/>           Textile fullers.<br/>           Tobacco seedling treaters.<br/>           Trinitrotoluol makers.<br/>           Type cleaners.<br/>           Varnishers.<br/>           Varnish makers.<br/>           Varnish remover manufacturers.         </p> |
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War gas makers.  
Waterproof fabric makers.  
Wax makers.

Welders.  
Wire insulators.  
Window shade makers.

2. Exposure to aromatic amines, aniline dyes and related aromatic chemicals (with possible relation to cancers of the bladder, ureter and kidney).

(a) Occupational exposure:

Agricultural laborers.  
Blue print makers.  
Candle makers.  
Candy (colored) makers.  
Cosmetic manufacturers (colored lipstick, powder, cream, eye-brow pencil, skin tan lotions).  
Citrus fruit dyers.  
Dye handlers, packers, mixers.  
Dye makers (aniline, naphthylamine, benzidine, xylidine, toluidine, etc.).  
Fur dyers and workers.  
Gardeners (aromatic pesticides).  
Ink makers.  
Leather dyers and workers.  
Lithographers.  
Margarine (colored) makers.  
Marmalade and jelly (colored) makers.  
Ore flotation workers (beta-naphthylamine, cresylic acid, etc.).  
Painters.  
Paint makers.  
Paper dyers and manufacturers.  
Pharmaceutical workers.  
Photographers.

(a) Occupational exposure—Continued

Photographic chemical workers.  
Printers.  
Rubber workers (antioxidants: beta-naphthylamine, phenyl-beta-naphthylamine, butyl-beta-naphthylamine, etc.).  
Shoe manufacturers.  
Soft drink (colored) manufacturers.  
Textile dyers.  
Textile printers.  
Wax pencil makers.

(b) Nonoccupational exposure:

Consumers of colored foodstuffs.  
Users of colored cosmetics.  
Users of dyed textiles and leather goods that bleed excess dye when coming in contact with sweat and sebum.  
Users (frequent) of medical preparations containing aromatic amino groups: antihistamines—allergies, hay fever, etc.; analgesics—headache, neuralgia, dysmenorrhea, arthritis, migraine; medicines (liquids, tablets, capsules, ointments) colored with aniline dyes.

3. Exposure to tar, pitch, oil, soot, asphalt, creosote, carbon blacks, paraffin, anthracene (with possible relation to cancers of the skin, lung, bladder, and leukemia).

Artificial-stone makers.  
Asbestos goods workers.  
Asphalt workers.  
Anthracene manufacturers.  
Battery (dry) workers.  
Brick layers.  
Brickyard workers.  
Briquet makers.  
Brush makers.  
Cable makers and layers.  
Carbon black makers and users.  
Chimney sweepers.  
Coal carbonization workers.  
Coal-tar still cleaners.  
Coal-tar workers.  
Coke-oven workers.  
Cordage-factory workers.  
Corkstone makers and carpenters.  
Cotton spinners.  
Creosoting plant workers.  
Diesel engine attendants.  
Electrical equipment manufacturers.  
Electrode makers.  
Engineers.  
Foundry workers.  
Fishermen.  
Flue cleaners.

Fuel oil suppliers, truck drivers.  
Furnace workers.  
Gas house workers.  
Gas (illuminating) workers.  
Generator stokers.  
Grease monkeys.  
Grease pit workers.  
Ink makers.  
Insulators.  
Lamp black makers and users.  
Machinists.  
Mechanics.  
Metal workers.  
Oilers.  
Oil refinery workers.  
Oil well workers.  
Optical lens grinders.  
Ore flotation plant workers.  
Paint sprayers.  
Paraffin distillery workers.  
Paraffin plant workers.  
Pavers.  
Pharmaceutical workers.  
Pitch workers.  
Plastic cement workers.  
Printers.  
Road repairers.

Roofers.  
Roofing-paper workers.  
Rope makers.  
Rubber workers.  
Sanitary pipe makers.  
Shipyard workers.  
Soap makers.  
Shale oil workers.  
Stokers.

Tank cleaners.  
Tar painters.  
Tar paint manufacturers.  
Tar workers.  
Textile workers.  
Waterproofers.  
Water proof paper makers.  
Wood picklers.  
Wood preservers.

4. Exposure to chromium and chromium compounds (chromium metal dust, chromates, chromium pigments, chromic acid, chromium carbonyl) (with possible relation to cancer of the lung and nasal sinuses).

(a) Occupational exposure:

Abrasive makers.  
Abrasive workers and polishers.  
Asphalt refinery workers.  
Battery (dry) makers.  
Bleachers.  
Blueprint makers.  
Candle (colored) makers.  
Coal tar workers.  
Chromate, chromium pigments, chromic acid and leather tanning compound manufacturers.  
Chromium ore miners and miners of other metal ores with chromium admixtures (cobalt).  
Crayon and pencil (colored) makers.  
Dock workers unloading chromite ore.  
Electroplaters.  
Electrolytical chromium metal manufacturers.  
Enamellers.  
Enamel makers.  
Explosive manufacturers.  
Furniture polishers.  
Glass and pottery frosters.  
Ink makers.  
Linoleum workers.  
Lithographers.

(a) Occupational exposure—Continued

Metal-factory workers.  
Mordanters.  
Paint manufacturers.  
Painters.  
Paper dyers.  
Paper makers.  
Paper money makers.  
Paper waterproofers.  
Photoengravers.  
Photographic workers.  
Photogravure workers.  
Pottery glaze makers.  
Pottery makers.  
Printers.  
Refractory brick makers and masons.  
Rubber vulcanizers.  
Soap makers.  
Stainless steel workers.  
Tannery workers.  
Textile dyers.  
Textile printers.  
Textile waterproofers.  
Wax-ornament workers.  
Welders.  
Wood stainers.

(b) Nonoccupational exposure:

Persons living or working in fume and dust zone of chromate plants.

5. Exposure to nickel and nickel compounds (nickel metal dust, nickel carbonyl vapors, nickel oxide, nickel sulfide, nickel alloys) (with possible relation to cancer of the lung and nasal sinuses).

Abrasive manufacturers.  
Ceramic glazers.  
Chemical workers in operations using nickel catalysts.  
Coin makers.  
Electroplaters.  
Enamellers.  
Enamel makers.  
German silver manufacturers.  
German silver smiths.  
Hydrogen manufacturers.  
Monel metal makers.  
Nickel alloy makers (copper, silver, aluminum).

Nickel-chrome alloy manufacturers.  
Nickel-chrome wire manufacturers.  
Nickel extractors.  
Nickel ore miners.  
Nickel ore smelter and refinery workers.  
Nickel polishers.  
Nickel-steel workers.  
Oil refinery workers.  
Storage battery manufacturers.  
Talc manufacturers.

6. Exposure to arsenic and arsenicals (arsenic metal, arsenious oxide, calcium arsenate, sodium arsenate, lead arsenate, cupric acetoarsenite, Paris green, London purple, Scheele's green, Schweinfurt green, Wolman salts, realgar, orpiment, Fowler's solution, Donovan's pills, arsphenamine, cacodylates, Lewisite, Asiatic pills, etc.) (with possible relation to cancer of skin, lung, bladder, liver).

(a) Occupational exposure:

Arsenic roasters.  
Artificial flower makers.  
Book binders.  
Bronze workers.  
Cannery workers peeling fruit treated with insecticides.  
Citrus fruit orchard workers.  
Cotton plantation workers.  
Cut-glass workers.  
Dyers.  
Dyestuff makers.  
Electroplaters.  
Enamellers.  
Farmers.  
Felt hat carroters.  
Ferro-silicon workers.  
Fur handlers and preparers.  
Galvanizers.  
Gardeners.  
Glass mixers.  
Glass workers.  
Glue manufacturers.  
Gold refiners.  
Ink manufacturers.  
Insecticide manufacturers.  
Insecticide sprayers and dusters.  
Japan makers.  
Jewelers.  
Lead factory workers.  
Lead shot makers.  
Linoleum color workers.  
Lithographers.  
Miners of arsenic, copper, zinc, silver, lead ores.  
Oil cloth manufacturers.  
Oil refinery workers.  
Paper (colored) makers.  
Paper glazers.  
Paper hangers.  
Paper printers.

(b) Nonoccupational exposure:

Users of arsenic containing drinking water, especially near arsenic ore smelters and mines, of foodstuffs and liquor contaminated with arsenicals.

Users of arsenic containing medicines (arsphenamines, cacodylates, Fowler's solution, Asiatic pills, Donovan's solution, arsenious oxide in tonics, antiseptics, antipsoriasis or caustic ointments, antispasmodics), cosmetics (hair lotions).

Persons exposed to inhalation of arsenical dust spread from arsenic ore smelters or by dusting arsenicals from airplanes.

7. Exposure to asbestos (silicates containing calcium, magnesium, iron, nickel and copper) (with possible relation to cancer of the lung).

Artificial-wood manufacturers.  
Asbestos construction-material workers (mill-board, wallboard, shingle, tile, mortar, clincker).

(a) Occupational exposure—Continued

Pelt and hair factory workers.  
Pencil makers (colored).  
Pharmaceutical workers.  
Photographers.  
Polson ball makers.  
Pottery decorators.  
Pottery plant glaze dippers and mixers.  
Pyrites burners.  
Rotogravure workers.  
Rubber compounders.  
Rubber mordant mixers.  
Rubber pressors.  
Rubber tire workers.  
Sealing wax makers.  
Seamstresses handling fabric dyed or treated with arsenicals.  
Sheep dip manufacturers.  
Smelters of arsenic, copper, zinc, silver, lead ores.  
Sulfur burners.  
Sulfuric acid workers.  
Tannery workers (carriers).  
Taxidermists.  
Textile printers.  
Tinner.  
Velvet makers.  
Vinery workers.  
Vineyard workers.  
War gas manufacturers.  
Wax ornament workers.  
Weavers using yarn dyed with use of arsenicals.  
Weed killer manufacturers.  
Wire drawers.  
Wood preserve makers.  
Wood preservers.  
Zinc mixers.  
Zinc smelter chargers.

Asbestos-insulation workers.  
Asbestos-mill workers (crushers, fiberizers, molders, carders).  
Asbestos miners.

|                                                                                          |                                      |
|------------------------------------------------------------------------------------------|--------------------------------------|
| Asbestos spinners.                                                                       | Electric-wire manufacturers.         |
| Asbestos-textile workers (cloth, blanket, curtain, sheets, ropes, cords, twine, thread). | Filter-material manufacturers.       |
| Asbestos weavers.                                                                        | Gasket makers.                       |
| Brake-lining manufacturers.                                                              | Insulation workers (pipes, boilers). |
| Brake-lining workers.                                                                    | Plumbers.                            |
| Carpenters.                                                                              | Pump-packing mechanics.              |
| Dye workers (acid and fireproof).                                                        | Roofers.                             |
|                                                                                          | Rubber production workers.           |

8. Exposure to solar radiation and ultraviolet radiation (with possible relation to cancer of the skin).

|                                  |                                            |
|----------------------------------|--------------------------------------------|
| Agricultural laborers.           | Oil operators.                             |
| Boatmen.                         | Pharmaceutical manufacturers of vitamin D. |
| Cattlemen.                       | Railroad engineers.                        |
| Construction workers.            | Railroad workers.                          |
| Cowboys.                         | Ranchers.                                  |
| Drivers.                         | Road workers.                              |
| Farmers.                         | Rural mail carriers.                       |
| Fishermen.                       | Sailors.                                   |
| Gardeners.                       | Sportsmen.                                 |
| Herders.                         | Stockmen.                                  |
| House painters.                  | Sunbathers.                                |
| Lumbermen.                       | Vine growers.                              |
| Miners working in surface mines. | Welders.                                   |
| Nurserymen.                      |                                            |
| Oilfield workers.                |                                            |

9. Exposure to roentgen-rays and radioactive chemicals (with possible relation to cancer of the skin, lung, bone, liver, and leukemia).

(a) Occupational exposure:

Atomic energy plant workers.  
 Biologists.  
 Chemists.  
 Gas mantle manufacturers.  
 Laboratory technicians and attendants.  
 Luminous dial painters, handlers and shippers, metal scrap handlers.  
 Nurses.  
 Pharmaceutical workers using radioactive isotopes and making radioactive tracer substances.  
 Physicists.  
 Radioactive electrostatic eliminator manufacturers and operators of such devices in textile and paper plants.  
 Radiologic technicians.  
 Radiologists.  
 Radium laboratory workers.  
 Radium refinery workers.  
 Research workers handling radioactive isotopes and tracer substances.  
 Roentgen and radium technicians.  
 Roentgen mechanics.  
 Roentgen-tube manufacturers.  
 Roentgenologists (medical, electric industry, aviation, metallurgic, chemical, textile, art and jewelry, shoe sales, beauty parlors, research).  
 Shoe salesmen in stores using fluoroscopes for fitting.  
 Uranium dye makers.  
 Uranium glass makers.  
 Uranium glaze makers (tile).  
 Uranium miners and miners of radioactive ores (pitch blende, carnotite, etc.).  
 Uranium paint makers.

(b) Nonoccupational exposure:

Customers of shoe stores using fluoroscopes.  
 Patients consuming radioactive water for medicinal purposes over long periods.  
 Patients receiving large doses of ionizing radiation for medicinal purposes.  
 People living in regions with radioactive ores and drinking or bathing in water of radioactive springs, or residing in the waste disposal area of radioactive operations.

# APPENDIX B Occupational Cancer Record

|                                                 |                                                                           |                                        |                                            |
|-------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------|--------------------------------------------|
| 1. Name                                         |                                                                           | 2. Place of Death: City<br>Hospital    |                                            |
| 3. Residence: State                             | City                                                                      | Street                                 |                                            |
| 4. Social Security No.                          | 5. Sex                                                                    | 6. Color or Race                       |                                            |
| 7. Date of Birth                                | 8. Age: Years                                                             | Mos.                                   | Days                                       |
| 9. Date of Death                                |                                                                           |                                        |                                            |
| 10. Occupation                                  | 11. Industry or Business                                                  |                                        |                                            |
| 12. Cause of Death                              | 13. Method of Diagnosis:<br>Clinical ( ) Biopsy ( ) Autopsy ( ) Other ( ) |                                        |                                            |
| 14. Name of Physician                           | 15. Street                                                                | 16. City                               |                                            |
| 17. Clinical Diagnosis                          | 18. Pathologic Diagnosis:<br>Microscopic ( ) Gross ( )                    | 19. Primary Site                       |                                            |
| 20. Date of First Symptoms                      | 21. Date of First Visit to Physi-<br>cian                                 | 22. Date of First Diagnosis            | 23. Stage of Disease at First<br>Diagnosis |
| 24. History of Other Illnesses of Site Affected |                                                                           | 25. History of Injury to Site Affected |                                            |

26. Occupational History: List occupations in chronological order beginning with last or present one

| Dates |    | Name of Plant | Location of Plant | Type of Business or Product Made | Title of Job | Type of Work Performed |
|-------|----|---------------|-------------------|----------------------------------|--------------|------------------------|
| From  | To |               |                   |                                  |              |                        |
|       |    |               |                   |                                  |              |                        |
|       |    |               |                   |                                  |              |                        |

27. Exposure: (Investigator will name carcinogenic substances to which employee has been exposed.)

| Name of Substance | Name of Plant | Date of Last Exposure | Duration of Exposure |        | Describe Type of Exposure and Estimate Percent of Working Time Exposed |
|-------------------|---------------|-----------------------|----------------------|--------|------------------------------------------------------------------------|
|                   |               |                       | Years                | Months |                                                                        |
|                   |               |                       |                      |        |                                                                        |

28. Name any other important materials to which employee has been exposed. (Hobbies; Habits; Medicines; Cosmetics; Diets; Environment.)

29. Additional Information Obtainable at: Physician; Laboratory; Hospital; Insurance Co.; Plant Medical Department; Clinic; Tumor Registry, etc.

| Name | Address |
|------|---------|
|      |         |

30. Any other information pertaining to tumor (Multiplicity, Sites, etc.)

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Date

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Investigator

NOTE: More blocks should be added under Nos. 26, 27 and 28 on actual record form.

## APPENDIX C

### Occupational Hazard Code

[Prepared in cooperation with Dr. H. F. Dora]

- A. Abnormalities of air pressure:
  - 001 Compressed air (increased atmospheric pressure).
  - 002 Altitude; rarefied air (decreased atmospheric pressure)
- B. Abnormalities of temperature and humidity:
  - 010 Heat.
  - 011 Cold.
  - 012 Sudden variations of temperature.
- C. Dampness:
  - 020 Dampness.
  - 021 Dryness.
- D. Defective illumination:
  - 030 Defective illumination.
- E. Dust:
  - Organic dust:
    - 040 Textile dust.
    - 041 Flour.
    - 042 Sugar.
    - 043 Wood dust.
    - 044 Leather dust.
    - 045 Feathers.
    - 046 Coal dust.
    - \*047 Tobacco dust.
    - 050 Organic dust other than specified.
  - Inorganic dust:
    - 060 Abrasive dust.
    - 061 Brick dust.
    - 062 Clay dust.
    - 063 Flint dust.
    - 064 Glass dust.
    - 065 Rock dust.
    - 066 Quartz dust.
    - 067 Talc.
    - \*068 Asbestos.
    - 069 Iron ore.
    - 070 Inorganic dust other than specified.
- F. Infections:
  - 090 Amoeba and other unicellular organisms.
  - 001 Bacteria and spirochetes.
  - 092 Fungus.
  - 003 Rickettsia and related microorganisms.
  - 004 Virus.
  - \*095 Worms and other multicellular parasites.
  - 000 Other parasites.
- G. Radiant energy:
  - \*100 X-rays.
  - \*101 Radium.
  - \*102 Radiothorium.
  - \*103 Mesothorium.
  - \*104 Radioactive isotopes.
  - \*100 Radioactive substances other than specified.
- Ultraviolet and infrared rays:
  - \*110 Ultraviolet rays.
  - \*111 Infrared rays.

\*Carcinogenicity recognized or suspected.

H. Repeated motion, pressure, shock, etc.:

120 Repeated motion, pressure, shock, etc.

J. Poisons:

- 130 Acetaldehyde.
- 131 Acetone.
- 132 Acids, inorganic.
- 133 Acids, organic.
- 134 Acridine.
- 135 Acrolein.
- 136 Alcohols.
- 137 Aldehydes.
- 138 Aluminum.
- 139 Ammonia.
- 140 Amyl acetate; butyl acetate.
- 141 Amyl alcohol.
- \*142 Aniline and other amine compounds of benzol and its homologues;  
acetanilide; naphthylamines; nitraniline; toluidine; xyldine;  
cumidine.
- \*143 Aniline dyes.
- \*144 Anthracene.
- 145 Antimony and its compounds.
- \*146 Arsenic and its compounds (except arseniuretted hydrogen).
- 147 Arseniuretted hydrogen (arsine).
- \*148 Asphalt, natural.
- \*149 Azo compounds.
- 150 Barium.
- \*151 Benzidine and derivatives.
- 152 Benzine; gasoline; naphtha.
- \*153 Benzol (benzene) and its homologues (toluol and xylol):  
o-aminoazotoluene.
- \*154 Beryllium.
- 155 Bromine.
- 156 Butanone.
- 157 Butyl alcohol.
- 158 Cadmium.
- 159 Calcium cyanamide (cyanamide).
- \*160 Carbazoles.
- 161 Carbolle acid: lysol-phenol.
- \*162 Carbon black.
- 163 Carbon dioxide.
- 164 Carbon disulphide.
- 165 Carbon monoxide.
- \*166 Carbon tetrachloride.
- 167 Cellosolve (mono-ethyl ether of ethylene glycol).
- 168 Chloride of lime.
- 169 Chlorinated diphenyls.
- \*170 Chlorinated hydrocarbons.
- \*171 Chlorinated naphthalenes.
- 172 Chlorine.
- \*173 Chloroprene (2-chloro-butadiene).
- \*174 Chromium carbonyl.
- \*175 Chromium compounds.
- 176 Coal.
- 177 Cobalt.
- 178 Copper.
- \*179 Creosote.
- \*180 Cresol (oresylic acid).
- 181 Cyanogen compounds, hydrocyanic acid.
- 182 Dichloroethylene.
- 183 Dichloroethyl ether.
- 184 Dimethyl sulphate.
- 185 Dinitrophenol (1-2-4).
- 186 Dioxan (diethylene dioxide).
- \*187 Estrogens, synthetic.
- \*188 Estrogens, natural.
- 189 Ethyl benzene.

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\*Carcinogenicity recognized or suspected.

# J. Poisons—Continued

- 190 Ethyl bromide and ethyl chloride.
- 191 Ethylene dibromide.
- 192 Ethylene dichloride (dichlorethane).
- 198 Ethylene oxide.
- 194 Ethyl silicates; tetraethyl-ortho-silicate; tetramethyl-ortho-silicate.
- 195 Formaldehyde.
- 196 Formic acid.
- 197 Furfural.
- 198 Geringulum compounds.
- 199 Glycols.
- \*200 Halogenated hydrocarbons, aliphatic (chlorine, bromine, fluorine).
- \*201 Halogenated hydrocarbons, aromatic.
- 202 Hexanone (methyl butyl ketone).
- 203 Hexone (methyl isobutyl ketone).
- 204 Hydrazines.
- 205 Hydrochloric acid.
- 206 Hydrofluoric acid, fluorine and its compounds.
- 207 Iron carbonyl.
- \*208 Isopropyl compounds.
- 209 Ketones.
- 210 Lead and its compounds.
- \*211 Lead arsenate.
- 212 Magnesium.
- 213 Manganese.
- 214 Mercury and its compounds.
- 215 Methanol (methyl alcohol).
- 216 Methyl bromide.
- 217 Methyl cellosolve (ethylene glycol monomethyl ether).
- 218 Methyl chloride.
- 219 Methylene chloride (dichloromethane).
- 220 Methyl formate.
- \*221 Mineral oil, crude; mineral oil, processed or grease prepared by fractionation or cracking).
- \*222 Naphthols.
- \*223 Nickel.
- \*224 Nickel carbonyl.
- 225 Nicotine.
- \*226 Nitrobenzol and other nitro compounds of benzol and its homologues; chlorodinitrobenzol; chloronitrobenzol; dinitrobenzol; nitronaphthalene; trinitrotoluol.
- 227 Nitroglycerin.
- 228 Nitrous fumes and nitric acid.
- \*229 Oil, shale.
- 230 Oxalic acid.
- 231 Ozono.
- \*232 Paraffin; paraffin oil, crude.
- 233 Pentanone (methyl propyl ketone).
- \*234 Petroleum.
- 235 Phenol.
- 236 Phenyl hydrazine.
- 237 Phosgene.
- 238 Phosphorus.
- 239 Phosphuretted hydrogen (phosphine).
- 240 Picric acid (trinitrophenol).
- \*241 Polycyclic hydrocarbon, e. g., benzpyrene; methyleholanthrene; dibenz-carbazole; various derivatives of benzanthracene.
- 242 Porphyrins.
- 243 Potassium hydroxide.
- 244 Pyridine.
- 245 Quinones.
- \*246 Selenium compounds.
- 247 Silver.
- 248 Sodium hydroxide.
- \*249 Sodium nitrate, crude.
- \*250 Soot.

\*Carcinogenicity recognized or suspected.

**J. Poisons—Continued**

- \*251 Soot (lamp black, carbon black, gas black, etc.).
- \*252 Spindle oil.
- \*253 Sterols.
- 254 Sulphur chloride.
- 255 Sulphur dioxide.
- 256 Sulphuretted hydrogen (hydrogen sulphide).
- 257 Sulphuric acid.
- \*258 Tar and pitch; artificial asphalt; bitumen-lignite.
- 259 Tellurium compounds.
- \*260 Tetrachlorethane (acetylene tetrachloride).
- \*261 Tetrachlorethylene (perchlorethylene).
- 262 Tetraethyl lead.
- 263 Thallium.
- 264 Tin.
- 265 Titanium oxide.
- \*266 Trichlorethylene.
- 267 Triorthocresyl phosphate.
- 268 Turpentine.
- \*269 Uranium.
- 270 Vanadium.
- 271 Vinyl chloride.
- 272 Zinc; brass, metal fume fever.
- 273 Styrene.

**K. Trauma (not covered in any of the above):**

**Chemical:**

- 300 Chemical, acute.
- 301 Chemical, chronic.

**Physical:**

- 302 Mechanical, acute.
- 303 Mechanical, chronic.
- \*304 Thermic, acute (burn).
- \*305 Thermic, chronic.

**Scars, fistulas:**

- \*306 Scars, fistulas, etc.

If there are present more than three hazards, each of which is from a different major hazard group, code in preference as follows: G, J, B, F, K, B, H, C, A, D.

\*Carcinogenicity recognized or suspected.

# APPENDIX D

## Plant Survey Record

Date.....

1. Company.....
2. Location.....
3. Plant manager.....
4. Plant physician.....
5. Insurance carrier.....
6. In operation since.....
7. Products manufactured.....
8. Known or suspected carcinogens.....
9. Medical service.....
10. Rate of labor turnover.....percent annually.....

### 11. Number of employees:

|              | Production | Office | Total |
|--------------|------------|--------|-------|
| Male.....    |            |        |       |
| White.....   |            |        |       |
| Colored..... |            |        |       |
| Female.....  |            |        |       |
| White.....   |            |        |       |
| Colored..... |            |        |       |
| Total.....   |            |        |       |

| 12.            | Operations involving known or suspected carcinogenic hazards— |                     |       |   |               |                  |          |              |                   |            |      | Duration of exposure for worker (years) |       |  |
|----------------|---------------------------------------------------------------|---------------------|-------|---|---------------|------------------|----------|--------------|-------------------|------------|------|-----------------------------------------|-------|--|
|                | Operation                                                     | Number of employees |       |   |               | Type of exposure |          |              | Route of exposure |            |      |                                         |       |  |
|                |                                                               | Total               | Male  |   | Female        |                  | Constant | Intermittent | Occasional        | Inhalation | Skin | Ingestion                               | Other |  |
|                |                                                               |                     | W     | C | W             | C                |          |              |                   |            |      |                                         |       |  |
|                |                                                               |                     |       |   |               |                  |          |              |                   |            |      |                                         |       |  |
| a.<br>b.<br>c. |                                                               |                     |       |   |               |                  |          |              |                   |            |      |                                         |       |  |
|                | Pre- or peri-cancerous effects noted                          |                     |       |   | Cancers noted |                  |          |              |                   |            |      |                                         |       |  |
|                | Site                                                          | Number              | Dates |   | Site          | Number           | Dates    |              |                   |            |      |                                         |       |  |
| a.<br>b.<br>c. |                                                               |                     |       |   |               |                  |          |              |                   |            |      |                                         |       |  |