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March 9, 2000

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SUBJECT: 8EHQ-1198-14311

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This letter contains an update on the progress of a five part epidemiology investigation into the unusual occurrence of brain cancer among employees who worked in the 500 Building Complex of the BP Amoco Naperville Complex (formerly known as the Amoco Research Center). This investigation is independently conducted by researchers from the University of Alabama at Birmingham (UAB) and Johns Hopkins School of Hygiene and Public Health (JHU).

The five phases of the UAB and JHU investigation include a case-series investigation, a site-wide mortality study, a site-wide cancer incidence study, a tumor incidence study of the 500 Building Complex, and a case-control study of primary intracranial tumors in the 500 Building Complex. In previous correspondence, BP Amoco provided the EPA with reports on the first three phases of the health investigation: the case-series study, the site-wide mortality study, and the site-wide cancer incidence study.

Please find enclosed reports for the final two phases of the investigation titled "Cancer and Benign Tumor Incidence Among Employees in the 500 Building Complex at the Amoco Research Center" and "A Case-Control Study of Intracranial Tumors Among Amoco Research Center Employees Who Worked in the 500 Building Complex". If you have any questions about these reports, please contact me at (630) 420-4933.

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This marks the conclusion of the UAB and JHU investigation into the unusual occurrence of brain cancer at the BP Amoco Naperville Complex. The results of the

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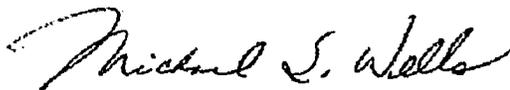
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studies indicate that occupational exposure at the facility may have contributed to the excess of gliomas among employees who worked in the 500 Complex, however, the results fall short of identifying specific etiologic agents. The studies did not indicate that benign intracranial tumors among employees at the facility were work-related.

UAB is in the process of publishing the results of the investigation in peer reviewed scientific journals and BP Amoco will continue to share our learnings with industry and the scientific community. Also, the programs that we previously put in place for our employees continue. We will continue to follow the employee population of the Naperville Complex and will fully investigate any new cases of brain cancer and we will continue to support research into the causation and treatment of primary intracranial brain tumors.

As we discussed previously, I will be glad to come to your offices at any time to discuss the investigation and the actions we have taken to make sure our employees have a safe environment in which to work.

Sincerely,

A handwritten signature in cursive script that reads "Michael S. Wells". The signature is written in black ink and is positioned above the typed name and title.

Michael S. Wells, Ph.D.  
Manager, HSE Chicago Region

Attachments

AP 00

A CASE-CONTROL STUDY OF INTRACRANIAL TUMORS  
AMONG AMOCO RESEARCH CENTER EMPLOYEES  
WHO WORKED IN THE 500 BUILDING COMPLEX

Submitted to  
BP Amoco Corporation

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## SUMMARY

This case-control study evaluated the relation between potential exposure to chemical and physical agents and the occurrence of intracranial tumors among employees at the Amoco Research Center (ARC) in Naperville, Illinois. All subjects had worked in the 500 building complex (C500) of the ARC. Cases were employees who had a glioma (N=6) or a benign intracranial tumor (N=6), confirmed by pathology review. Controls (total N=119; 60 for glioma cases, 59 for benign intracranial tumor cases) were matched to cases on gender and birth year ( $\pm$  2 years). Exposure information came from: 1) self-reports, obtained from interviews with subjects or surrogates and 2) accounting data identifying research and development projects on which subjects had worked, linked to historical records documenting agents used or made by each project.

Analyses computed odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for: 1) self-reported exposure to 15 ARC agents; 2) project-based estimates of potential contact with 29 agents (referred to as "project-based potential agent use"); and 3) self-reported exposure to 15 non-ARC factors. ORs estimated the intracranial tumor rate among subjects "exposed," compared to subjects "unexposed," to a particular agent, and CIs measured the statistical precision of the ORs.

The six glioma cases had worked longer at the ARC (median, 17 years) than their 60 controls (median, 11 years). The OR for glioma was elevated and statistically significant or of borderline significance for self-reported exposure to ionizing radiation (OR=15.7, CI=1.4-179.4), *n*-hexane (OR= $\infty$ , CI=1.4- $\infty$ ), organometallics (OR=9.4, CI=1.5-59.7) and amines other than nitrosoamines ("other amines"; OR=6.0, CI=1.0-35.7).

Project information was available for all six glioma cases and for 50 of their controls. We classified six controls with nontechnical backgrounds as unexposed to agents and excluded from analyses of project-based agent data three controls with technical background but without project accounting records. The OR was statistically significantly elevated for project-based potential use of ionizing radiation (OR=9.6, CI=1.7-55.2) and for relatively long-term potential use of *n*-hexane (OR=16.2, CI=1.1-227.6). No other agent was statistically significantly associated with glioma in analyses of project-based potential agent use. The OR was 0.9 (CI=0.1-5.8) for organometallics and 1.3 (CI=0.2-7.4) for other amines.

Five cases and 19 controls had potentially used or were exposed to more than one of the four agents associated with a statistically significant OR, i.e., ionizing radiation, *n*-hexane, organometallics and other amines. The one case without exposure to or use of multiple agents was classified as having project-based potential use of ionizing radiation. Because of the cases' complex exposure pattern, analytic efforts to characterize the independent effect of a particular agent were largely uninformative. However, the association between ionizing radiation and glioma was present in each analysis that adjusted for just one other agent (i.e., project-based use of *n*-hexane, self-reported exposure to organometallics or self-reported exposure to other amines).

The benign intracranial tumor cases included two meningiomas, two vestibular schwannomas and two pituitary adenomas. These six cases had worked at the ARC longer (median, 14 years) than their 59 controls (median, 6.4 years). For benign intracranial tumors, the OR for self-reported exposure to ionizing radiation was statistically significantly elevated (OR=5.4, CI=1.7-43.1), and the OR for self-reported exposure to other amines was elevated but

not statistically significant (OR=5.2, CI=0.9-29.5). Four cases and 36 controls had project data. No OR was statistically significantly elevated in analyses of project-based potential agent use.

The results of the case-control study indicate that occupational exposure at the ARC may have contributed to the excess of gliomas among C500 employees, but the results fall short of identifying specific etiologic agents. Ionizing radiation, or an unidentified agent correlated with ionizing radiation, or several agents acting in conjunction may have been responsible. Because of the small size of the study and the possibility of exposure misclassification, a firm conclusion about the neurocarcinogenicity of particular agents is not warranted. Nevertheless, certain characteristics of the glioma cases, especially their aggregation among technical employees who worked in the same company and building, make chance an unlikely explanation of the excess. The study does not indicate that benign intracranial tumors among C500 employees were work-related. The observed association between ionizing radiation and benign intracranial tumors was limited to self-reported data and may have been due to bias.

## CONTENTS

## INTRODUCTION

## METHODS

- Study base
- Cases
- Controls
- Interviews
- Work histories
- Project histories
- Potential agent use
- Analysis

## RESULTS

**Gliomas**

- Subject characteristics
- Self-reported exposure to agents of interest
- Self-reported exposure to non-ARC-related factors
- Project-based potential agent use
- Concordance

**Benign Intracranial Tumors**

- Subject characteristics
- Self-reported exposure to agents of interest
- Self-reported exposure to non-ARC-related factors
- Project-based potential agent use
- Concordance

## DISCUSSION

## REFERENCES

## TABLES

APPENDIX A—QUESTIONNAIRE FOR CURRENT AND FORMER  
EMPLOYEES AT THE 500 BUILDING COMPLEX OF THE AMOCO  
RESEARCH CENTER IN NAPERVILLE, ILLINOIS

APPENDIX B—ADDITIONAL SUBJECT EXPOSURE DATA

## INTRODUCTION

This nested case-control study was part of a series of investigations of disease incidence and mortality among the employees of the Amoco Research Center (ARC), now known as the BP Amoco Naperville Complex (8-11,17). Concerns about the occurrence of intracranial tumors among ARC employees, particularly among employees in the 500 building complex (C500), prompted the research.

The primary objective of the present study was to determine if work with specific chemical or physical agents or classes of agents at the ARC is associated with the occurrence of intracranial tumors. The study also examined the relation between certain nonoccupational factors and intracranial tumors.

## METHODS

### Study base

All subjects were ARC employees who had worked in C500 (11). C500 is a three-building complex. Building 501 consists of about 75000 square feet, building 502 of about 40000 square feet, and building 503 of about 80000 square feet. During the study period (1970-1998) buildings 501 and 503 consisted primarily of laboratory and combined laboratory-office space. Building 502 was predominantly office space. Research and development activities carried out in C500 included theoretical work and laboratory investigations of plastic monomers and polymers, metallic and organometallic catalysts, organic solvents and fine acids. We restricted the study base to C500 employees because most ARC employees with an intracranial tumor had worked in this complex, and employee and corporate concerns focused on that work location.

Delzell et al. (11) have described in detail the methods used to identify C500 employees. In brief, we developed a provisional roster of 2595 C500 employees that included: 1) all employees who had an ARC telephone book entry showing that they were assigned to an office, laboratory or other space (e.g., stockroom, lobby) in C500; 2) employees whose personnel records indicated that they had worked for the Amoco Chemical Company (ACC, the primary occupant of C500) and whom a group of 25 long-term ARC supervisors classified as having definitely or possibly worked in C500. To all subjects on the provisional roster we mailed a survey asking about C500 work history. We used responses from 2172 (84%) survey participants to confirm that 1735 persons had worked full- or part-time in C500 and that 437 had not worked full- or part-time in C500. We assumed initially that the 423 nonparticipants had worked in C500.

#### Cases

We identified 14 potential cases of primary intracranial tumor with a diagnosis date after their C500 hire date. We restricted cases to those confirmed by a review of medical records and pathology material, carried out by three "primary" and one "secondary" neuropathologists. When the three primary reviewers disagreed on a case's diagnosis, the secondary reviewer evaluated the case, and we accepted the diagnosis of the majority of the four neuropathologists.

The three primary neuropathologists agreed on the diagnosis of 10 of the cases. One of the primary neuropathologists classified a case as a schwannoma, whereas the others agreed that it was a meningioma. One of the primary neuropathologists declined to provide a diagnosis for another case because of a technical problem with the slides submitted for evaluation, whereas the others agreed that the case was a pituitary adenoma. For a third case, one neuropathologist

diagnosed glial atypia, suggestive but not diagnostic of astrocytoma, but the majority classification was glioma.

Three of the four neuropathologists classified one of the cases as a pineal cyst, and we excluded this case. Another case, initially diagnosed as an ependymoma, was excluded after all neuropathologists agreed that it was a melanoma of undetermined primary anatomic location.

The final group of 12 cases included six primary brain cancers ("gliomas": two astrocytomas, two glioblastomas and two oligodendrogliomas), two vestibular schwannomas, two meningiomas and two pituitary adenomas. Interviews (see below) confirmed that all 12 cases had worked in C500.

#### Controls

From the provisional group of C500 employees, we used incidence density sampling procedures to choose ten controls per case (18). If information obtained during subsequent interviews (see below) indicated that a subject had not, in fact, worked in C500, we selected a replacement control.

To implement incidence density sampling to obtain controls, we first identified a risk set for each case. A risk set consisted of all subjects who had the same gender, birth year ( $\pm 2$  years) and race as the case, who began working in C500 before the case's diagnosis date and who were alive and did not have an intracranial tumor at the time of the case's diagnosis. One case, an Asian woman, had an initial risk set of only two subjects; we expanded her risk set to include white women. Next, we selected randomly, without replacement, 10 subjects from each risk set. Survey responses on work location, obtained after initial subject selection, indicated that 49 controls had not worked in C500 or began work in C500 after their matched case's diagnosis

date. We replaced each of these controls by selecting randomly another subject from among those remaining in the original risk set after initial selection.

For the 12 cases, we chose a total of 120 controls. After completing interviews, we identified and excluded one control who was in C500 intermittently for training and meetings but who never worked there full- or part-time before the diagnosis date of the case to whom he was matched. Thus, analyses included 119 controls.

### Interviews

We conducted in-person or telephone interviews with subjects using a semistructured questionnaire. The questionnaire (Appendix A) elicited information about each job held at the ARC, at other BP Amoco facilities and at non-Amoco facilities; about the time periods of employment and potential exposures encountered in each job; and about certain nonoccupational factors.

Information on each ARC job included the job title, the project, the supervisor, an indicator of whether the job involved hands-on work in a laboratory or pilot plant, hours of work involving exposure to agents, agents used, work location (building and floor) and time period in each location. During interviews, we asked subjects to identify chemical and physical agents to which they were exposed in each job they had held. We obtained additional information from a checklist asking about occupational exposure to 15 specific agents or classes of agents, selected for their potential neurocarcinogenicity (see below).

We also asked about exposure to diagnostic and therapeutic irradiation; use of anticonvulsant and ototoxic drugs; history of serious head injury, seizures, meningitis and hearing loss; employment in noisy work settings; use of cellular phones and radiation badges; home activities including amateur radio operation, pesticide application and furniture refinishing.

and employment as a pesticide applicator or furniture refinisher. Tables 4 and 16 list these factors.

UAB staff conducted interviews with 6 (50%) cases and 111 (93%) controls. Of the case interviews, four were in person, and two were by telephone. Of the control interviews, 47 were in person, and 64 were by telephone. For deceased subjects (four cases, two controls), subjects too ill to participate (one case), subjects who declined to participate (no case, three controls) and subjects whom we could not locate (two controls), we conducted interviews with coworker surrogates (31 interviews for 16 subjects; one in person and 30 by telephone) and, where possible, with next-of-kin surrogates (four interviews for four subjects; one in person and three by telephone). It was not possible for interviewers to remain blind to subjects' status as a case or a control.

For cases, we truncated interview data as of the diagnosis date; for controls, we truncated data at the diagnosis date of the case to which they were matched. Data summarized periods of work in C500, at non-C500 locations at the ARC, at other Amoco facilities and in non-Amoco settings with respect to time periods, involvement in hands-on work with agents, exposure to specific agents and exposure to nonoccupational factors. A single staff member performed all data entry, and we conducted a 100% visual review of the resulting data file to ensure accuracy. In addition, internal edits examined the validity of values entered into various fields and evaluated the consistency among dates. External edits included comparisons with an Amoco work history file developed from corporate personnel data and with a building history file developed from corporate telephone directories.

### Work histories

We obtained Amoco work histories from computerized personnel files and from interviews with subjects or their surrogates. Through a comparison of these sources, we developed detailed information on the time period, location and activities of each of a subject's ARC jobs. For each job, we used interview data to assign an indicator of the extent to which the subject worked hands-on with chemical or physical agents. This indicator had three categories: 1) direct hands-on work, 2) limited hands-on work in a supervisory role and 3) no hands-on work.

### Project histories

For each subject, we used Amoco accounting records to develop a history of all projects on which a subject worked during each year of employment and the hours assigned to each project during a particular year. The accounting records identified each project by a "cost center" number, used for charging a particular account for project work; a project number and name; and a subproject number name. We linked each of a subject's project/year combinations to his or her work history data and assigned the indicator of hands-on work. In doing this, we assumed that, if a subject reported any hands-on work in a given year, all project-hours in that year entailed hands-on work. The final project history file consisted of a series of records for a subject, each containing the subject's name, the calendar year, the hands-on indicator, the project identifiers and the number of hours charged to the project.

### Potential agent use

Study analyses evaluated 29 chemical and physical agents or classes of agents (referred to henceforth as agents of interest). UAB and JHU investigators, in consultation with a neurotoxicologist and with Amoco staff, used suspicion of neurocarcinogenicity in animal

studies or other epidemiologic studies as the basis for selecting 15 agents of interest. We later added subcategories to some of the agents (e.g., halogenated hydrocarbons were divided into chlorinated, brominated or other hydrocarbons; chlorinated hydrocarbons were divided into tetrachlorethylene, chloroethanes or other chlorinated hydrocarbons). They also added two categories, glycidol and reactive monomers.

JHU investigators developed a project/year/agent matrix summarizing information on project/year-specific use of the 29 agents of interest. The matrix consisted of unique combinations of: 1) all projects on which at least one subject had worked, 2) each year in which any subject worked on a particular project and 3) an indicator for whether or not a particular project/year combination involved the use of each of the 29 agents of interest.

UAB investigators developed a list consisting of all project/year combinations in which at least one case or control had worked. This list, which contained 2092 entries, did not identify individual subjects or indicate whether the subjects in a particular project/year combination were cases, controls or both.

To obtain project/year-specific agent use data, JHU investigators located historical documents pertaining to each project on which at least one subject had worked and abstracted data on project-related use of chemicals (i.e., all chemicals, regardless of their classification as an agent of interest) and devices that might have entailed exposure to ionizing or nonionizing radiation (14). Project documents included periodic progress reports and final summary reports of work accomplished on individual projects.

Five Amoco research chemists devised rules for classifying agents. This group then reviewed the 6391 substances/devices mentioned in the historical documents and classified each substance/device as: 1) one or more of the 29 agents of interest, 2) another identified agent or 3)

an unknown agent. For project/year combinations with documentation available, JHU investigators classified use of each agent as a dichotomous variable (1=used; 0=not used). For years with no documentation, use was extrapolated from project documents for other years.

Next, we linked the project/year/agent matrix with individual subjects' project history data and added to the latter file indicators for agent use in each of a subject's project/year combinations. For each subject, we then developed a summary weighted measure of hours of use for each agent by: 1) multiplying the hours in a project/year combination by the agent use indicator (0 for no use, 1 for any use) and by a "weight" indicating the year-specific level of hands-on work (1.0 for direct hands-on work; 0.5 for supervisory work; 0 for work in a nonlaboratory, nonpilot plant setting) and 2) summing the weighted hours for each agent over all project/year combinations. A subject's summary weighted hours of potential exposure to each agent of interest were calculated as:

$$\sum_{x=1970}^{1997} [(hrs_x) (wt_x) (agt_x)]$$

where x = year worked at ARC 1970...1997; hrs = duration of potential exposure in a year; wt = hands-on weight (1.0, 0.5, 0.0); and agt = indicator of potential exposure to agent of interest (1, if present; else 0).

### Analysis

Analyses compared cases and controls with respect to: 1) self-reported exposure to 15 agents of interest, 2) project-based potential use of 29 agents of interest and 3) self-reported exposure to 15 non-ARC factors. We used conditional logistic regression to obtain maximum likelihood estimates of odds ratios (ORs) and their corresponding 95% confidence intervals (CIs). Such ORs are estimates of incidence density rate ratios for subjects exposed, compared to subjects unexposed, to a particular factor (27). The matched analysis controlled for age, race and

gender, three variables known to be associated with the incidence rates of various intracranial tumors.

Analyses of self-reported exposures considered subjects as exposed if they answered "yes" or "possibly" exposed to agents listed in the questionnaire. In most analyses, we represented "unknown" exposure status with an indicator variable in the conditional logistic regression model.

We explored possible duration-response effects by forming three length-of-potential-use categories (none,  $\leq$  median duration of "exposed" cases,  $>$ median duration of "exposed" cases) and estimating ORs for  $\leq$  median duration compared to none and for  $>$ median duration compared to none. These analyses considered project-based agent use data, only, because information on duration was incomplete for self-reported exposures. We based length of potential use categories for each agent on the distribution of duration among cases, rather than among all subjects (15), to minimize the number of agent use categories with no exposed case. We examined induction time effects by including indicator variables for the number of years ( $<10$ ,  $\geq 10$ ) between first potential use of an agent and cases' diagnosis dates or the corresponding date for controls. We conducted analyses separately for glioma cases and controls and for benign intracranial tumor cases and controls.

## RESULTS

### Gliomas

#### Subject characteristics

All of the six primary brain cancers occurred in men. Although the precise classification of these cancers (i.e., astrocytoma, glioblastoma multiforme or oligodendroglioma) differed slightly among neuropathologists, all were malignant tumors of glial cell origin. Each glioma

case had 10 controls. The median age, as of the case's diagnosis date, was 53 years for both cases and controls. Cases were more likely to be deceased (N=5) than were controls (N=2).

Cases and controls had an identical median year of hire at the ARC (1971), but cases tended to have worked longer at the facility than controls (16.8 vs. 10.9 years) (table 1). The OR was 3.8 (CI=0.4-35.1) for 10+ years, compared to <10 years, of work at the ARC. All glioma cases as compared to 55 (92%) of controls had worked for the ACC.

All of the glioma cases and 50 (83%) of their controls had accounting records on the various projects on which they had worked. The median hours assigned to projects was 31235 for cases and 15678 for controls. Of the 10 controls without project accounting records, six did not have a technical background but worked instead in secretarial, clerical, sales or maintenance jobs. Four of the controls without project records had a technical background, and we assumed that their accounting data were missing, for an unknown reason. We did not include these four subjects in analyses of project-based potential agent use.

Four cases and 35 controls reported that they had worked hands-on with chemicals in a laboratory or pilot plant setting. Those who did such work spent the majority of their time working directly with agents.

#### Self-reported exposure to agents of interest

Aromatic hydrocarbons and volatile hydrocarbons, including *n*-hexane, were the most commonly reported of the 15 agents of interest asked about during interviews (table 2). ORs, computed for definite or possible compared to no exposure, were statistically significantly elevated for ionizing radiation (OR=15.7, 95% CI=1.4-179.4), *n*-hexane (OR= $\infty$ , CI=1.4- $\infty$ ), organometallics (OR=9.4, CI=1.5-59.7). The OR also was elevated and of borderline statistical significance for other amines (OR=6.0, CI=1.0-35.7) (table 3). ORs were elevated but not

statistically significant for volatile hydrocarbons other than *n*-hexane (OR=5.8, CI=0.6-52.8) and for elemental metallics (OR=3.6, CI=0.5-25.8). For exposure to any catalyst (organometallic or elemental metallic) the OR was 16.5 (CI=1.7-157.7). Other ORs were close to or below the null value of 1.0. Appendix B provides detailed descriptive information about self-reported exposure to specific catalysts and other amines.

#### Self-reported exposure to non-ARC-related factors

A relatively large number of subjects was classified as having unknown exposure to non-ARC-related factors (table 4). This was the result of our having to obtain information from surrogates who were unfamiliar with many aspects of subjects' personal lives. None of the factors was clearly associated with glioma (table 5). One case, as compared to no control, reported a history of seizure and the use of anticonvulsant medication in the month preceding his cancer diagnosis; however, the seizure was probably secondary to the brain cancer. Only one case, as compared to 19 controls reported having worn a radiation badge.

#### Project-based potential agent use

No subject worked on a project that used tetrachloroethylene, freons or ethylene/ethylene oxide (table 6). The OR was below 1.0 for nine of the other 26 agents, including organometallics (OR=0.9, CI=0.1-5.8). The OR was above 1.0 for 17 agents but was statistically significantly elevated only for ionizing radiation (OR=9.6, CI=1.7-55.2). The OR was 2.3 (CI=0.4-13.7) for *n*-hexane and 1.3 (CI=0.2-7.4) for other amines. The OR for butadiene was elevated but not statistically significant (OR=5.3, CI=0.9-32.4). Appendix B provides descriptive information about project-based potential exposure to specific catalysts and other amines

Analyses by duration of agent use indicated that the OR for ionizing radiation was elevated both for short-term (OR=11.5, CI=1.3-98.4) and for long-term potential use (OR=8.1,

CI=1.0-66.7) (table 7). For *n*-hexane, the OR was 1.2 (CI=0.2-9.0) for short-term and was 16.2 (CI=1.1-227.6) for long-term potential use. The OR for catalysts rose with increasing duration of use, but the results by duration were not statistically significant. The number of subjects with potential use of organometallic catalysts was small, and the results by duration were uninformative for this agent. For other amines the OR was 1.2 (CI=0.2-8.5) for short-term and 1.5 (CI=0.2-11.2) for long-term potential use. The OR for butadiene did not rise with increasing length of potential use. Analyses by time since first potential use did not reveal any additional associations (table 8).

All cases and 29 controls were exposed to at least one of the agents having a statistically significantly elevated OR in analyses of self-reported exposure or project-based potential agent use (table 9). Two cases and no control were exposed to all four agents, one case and 11 controls to three agents, two cases and eight controls to two agents and one case and 10 controls to one agent. Because of these complex exposure patterns and because of small numbers of subjects, analytic efforts to characterize the independent effect of a particular agent were largely uninformative. In most analyses of one of the four agents that adjusted for just one other agent, the association with glioma persisted (table 10). The OR for project-based potential use of ionizing radiation was elevated after adjusting for any or for long-term project-based use of *n*-hexane, for self-reported exposure to organometallics or for self-reported exposure to other amines. The OR for potential use of *n*-hexane above the median duration was largely unchanged when adjusting for self-reported organometallic exposure or other amine exposure but was reduced by adjusting for potential use of ionizing radiation. The OR for self-reported exposure to organometallics remained elevated after adjusting for self-reported exposure to other amines or project-based use of ionizing radiation or *n*-hexane. The OR for self-reported exposure to

other amines was reduced to 2.2 (CI=0.3-16.0) after adjusting for self-reported exposure to organometallics.

Other analyses examined the joint effect of two agents and the effect of exposure to only one of the two agents, compared to exposure to neither agent. Many of these analyses failed because of small numbers, and all results were extremely imprecise. For example, analyses of joint potential use of ionizing radiation and *n*-hexane yielded ORs of 16.4 (CI=1.1-252.8) for project-based potential use of ionizing radiation and *n*-hexane, 6.6 (CI=0.4-118.1) for use of ionizing radiation but not *n*-hexane and 1.2 (CI=0.1-21.0) for use of *n*-hexane but not ionizing radiation (table 11).

#### Concordance

We compared each subject's classification as exposed or not exposed to each agent, as determined from interview data, with his potential use classification as determined from project data (table 12). The two classifications were concordant when both agreed that the subject was "exposed" or when both agreed that the subject was "unexposed." Concordance between the two classifications was at least 80% for six of 15 agents of interest among cases and for seven of 15 agents among controls. Concordance between cases' self-reported exposure and project-based potential use was 67% for ionizing radiation, *n*-hexane, organometallic catalysts and other amines. Concordance among controls' self-reported exposure and project-based potential use was, respectively, 85%, 77%, 72% and 65% for these four agents.

#### **Benign Intracranial Tumors**

##### Subject characteristics

The two subjects with meningioma were men; one woman and one man had vestibular schwannoma, and one woman and one man had pituitary adenoma (table 13). Five of the cases

each had 10 controls, and one case had nine controls. As a group, the benign tumor cases had a later median hire date than their controls (1977 vs. 1971) but had a greater median duration of work at the ARC (14.0 vs. 6.4 years). The OR was 8.1 (CI=0.7-98.0) for  $\geq 10$  years, compared to  $< 10$  years, of work at the ARC. All of the benign intracranial tumor cases, compared to 55 (93%) of the controls, had worked in ACC.

Four (67%) of cases and 51 (86%) of the controls had accounting records indicating the projects on which they had worked. The median hours assigned to projects was about twice as long for cases (22232 hours) as for controls (11170). The two cases without project accounting records and five of the eight controls without project accounting records did not have a technical background but worked in secretarial, clerical, sales or maintenance jobs. Three controls had a technical background but no project records. We did not include these three subjects in analyses of project-based potential agent use. All four cases with project histories, as compared to 31 (61%) of controls with project histories, reported time spent in direct hands-on work with chemicals in a laboratory or pilot plant setting.

#### Self-reported exposure to agents of interest

Aromatic hydrocarbons, volatile hydrocarbons and organometallic catalysts were the most commonly reported of the 15 agents of interest (table 14). No subject reported exposure to the energy beam, a process emitting nonionizing radiation. The OR, computed for definite or possible compared to no self-reported exposure, was 5.4 (CI=1.7-43.1) for ionizing radiation and was 5.2 (CI=0.9-29.5) for other amines (table 15). The OR was elevated but not statistically significant for seven other agents and was at or below 1.0 for six agents, including organometallics (OR=1.0; CI=0.1-6.9). The OR was 0.9 (CI=0.1-5.6) for the combined catalysts

category. Appendix B provides a description of self-reported exposure to individual catalysts and other amines

#### Self-reported exposure to non-ARC-related factors

One case, as compared to no control, reported a history of seizure that slightly predated the diagnosis of an intracranial tumor (table 16). The same case and two controls reported a history of anticonvulsant use, and the OR was 6.0 (CI=1.4-98.7) for this factor (table 17). None of the other medical or lifestyle variables was strongly or statistically significantly associated with benign intracranial tumors.

#### Project-based potential agent use

No subject worked on a project that used ethylene/ethylene oxide or nitrosamines (table 18). The OR was below 1.0 for 13 of the other 27 agent categories evaluated and was above 1.0 for 14 agents. None of these results was statistically significant. The OR was 2.1 (CI=0.3-13.3) for ionizing radiation, 2.2 (CI=0.4-13.5) for *n*-hexane, 1.5 (CI=0.3-8.6) for organometallic catalysts and 1.5 (CI=0.2-9.7) for other amines. Analyses by length of potential use indicated an OR of 5.6 (CI=0.7-43.3) for relatively short-term use of benzene and an OR of 12.6 (CI=0.9-174.4) for relatively short-term use of *n*-hexane (table 19). Other results of these analyses were unremarkable. Analyses by time since first potential use did not yield any statistically significant results, although for several agents the OR tended to be higher for the longer time since potential use category (table 20) than for the corresponding ever-used category (table 18). Appendix B provides detailed descriptive information about project-based potential exposure to specific organometallic and inorganic metallic catalysts and other amines

Table 21 presents data pertaining to joint exposure to or use of four agents. Four cases and 31 controls were exposed to at least one of the four agents. Two cases and four controls

were exposed to all four agents, no case and eight controls were exposed to three agents, two cases and 12 controls were exposed to two agents and no case and seven controls were exposed to a single agent.

### Concordance

Table 22 displays concordance data for benign intracranial tumor cases and their controls. For cases, concordance was 80% or better for 11 of the 15 agents and was 67% for each of the other four agents. Concordance was lower for controls (at least 80% for five agents; 51-78% for the other 10 agents). For ionizing radiation, self-reported exposure and project-based potential use were concordant for 100% of cases and 78% of controls.

## DISCUSSION

### **Gliomas**

Results of this study indicate that an occupational agent may have contributed to the occurrence of glioma among employees of C500, but the agent(s) responsible for the cancers remain uncertain. The small number of cases included in the study, the large number of agents of possible interest and the high correlation among some of the exposures hindered identification of a causal agent. Ionizing radiation and *n*-hexane had consistently elevated ORs for glioma, but certain observations indicate that these associations may not be causal.

### Ionizing radiation

The most internally and externally consistent result of this study was the positive association between ionizing radiation and glioma. The association was strong and statistically significant. It was present both for self-reported exposure and for project-based potential use. It persisted after adjustment for other agents. There is some support for the neurocarcinogenicity of ionizing radiation from previous research in humans, as discussed later.

Other aspects of the association argue against causality. The level of ionizing radiation to which C500 employees were potentially exposed is presumed to be quite low. Most potential exposure to ionizing radiation involved the use of enclosed gauges or radioisotopes. An examination of radiation badge data by JHU investigators indicated that among ARC employees who wore badges, all radiation exposures were a small fraction of the allowable limit.

Several considerations suggest that the project-based estimates of potential use of ionizing radiation were subject to misclassification. For example, it is possible that irradiation processes mentioned in project documents may not have been performed by ARC project personnel, but the review of documents did not resolve this issue. Moreover, a general limitation of this study, pertaining to all agents evaluated, is the fact that project-based data were useful for ascertaining whether the project involved agent use; however, they were not useful for determining whether specific individuals working on the project were exposed.

The imprecision of the ORs for ionizing radiation indicates that misclassification in the exposure status of only a few subjects could have had a major impact, producing invalid results. For example, the exposure of two glioma cases and nine controls to an agent would yield an OR of 2.6. The removal of one exposed case (i.e., leaving one case and nine controls) would result in an OR of about 1.0. The lack of concordance between ionizing radiation exposure as determined by self-reports and as assigned by project history supports the idea that misclassification occurred. The project data, unlike the self-reported data, were objective, but this does not ensure against differential misclassification errors in a small study.

The apparent association between ionizing radiation and glioma did not vary in magnitude with time since subjects' presumed first exposure to this agent. For solid tumors the association with ionizing radiation typically is stronger when allowance is made for an induction

time of at least ten years than when there is no such allowance (20,25). The lack of any induction time pattern for ionizing radiation in the present study may be due to the absence of a true causal relationship with glioma; or, it may reflect inaccurate measurement of the onset of exposure or a different induction time pattern for radiation-induced cancer than for cancer caused by chemicals. Another argument against a causal relation is the fact that no association was observed with radiation badge use, a marker for potential occupational exposure to external ionizing radiation, or with diagnostic or therapeutic exposure to X-rays.

Support from other research for an association between exposure to ionizing radiation as an adult and brain cancer is inconsistent. One case-control study reported that men exposed after age 25 to full-mouth dental X-rays had an increased risk of glioma (24); however other studies have not replicated this result (14,28). One study found that subjects receiving radiation therapy for pituitary adenoma had an OR of 7.9 (CI=1.0-28.6) for glioma as compared to the general population (2).

Several investigations have assessed brain cancer mortality among nuclear industry workers. Some of these studies reported a positive association (6-7,13,21,25), although mortality rate ratios have tended to be small and none was statistically significant. Other studies did not find an elevated brain cancer rate among nuclear industry workers (4-5,32-33). Also, studies of radiologists and radiologic technologists have not indicated excess brain cancer mortality (1,12).

#### N-hexane

In this study *n*-hexane was associated with glioma, both in self-reported and in project-based long-term use data. The association was strong and statistically significant. Also, it increased with increasing duration of potential use and, to some extent, with time since first potential use. The association was, however, limited to subjects also potentially exposed to

ionizing radiation. Moreover, despite some evidence that occupational exposure to *n*-hexane causes polyneuropathy in humans (16,31), this chemical has not previously been associated with cancer.

Possible alternative explanations for the observed association with *n*-hexane include differential exposure misclassification and confounding. Although we do not rule out the possibility that exposure to *n*-hexane and ionizing radiation, either concurrently or sequentially, might have an etiologic role, it remains plausible that exposure to some third agent correlated with these two might be implicated.

#### Organometallics and other amines

Associations with organometallics and other amines were strong and statistically significant in the self-reported data but were stronger among subjects reporting possible exposure than among subjects reporting definite exposure. Subjects' responses on questionnaires often confused organometallic catalysts and inorganic metallic catalysts. Neither association was present in project-based data. We are unaware of any support from previous research for either association.

Discrepancies between project-based exposure to organometallics and self-reported exposure were large and differed for cases and controls. Of the two cases with project-based potential use of this agent, both (100%) self-reported exposure, as compared to only seven of 13 (54%) controls with potential use. In addition, two cases classified as having no project-based potential use of organometallics self-reported exposure to this agent. The situation was similar for other amines: three of four (75%) potential-use cases self-reported reported exposure, as compared to 14 of 34 (41%) controls. In both instances the disproportionately smaller number of exposed controls is directly related to the elevated OR observed in the self-reported data.

Although abstraction of laboratory notebooks, in addition to other project documents, might have identified additional subjects as potential users, recall bias also may have played a role in cases' greater likelihood of reporting exposure to these agents. The fact that the potential adverse health effects of organometallics were of concern to ARC employees before the start of the present study reinforces the possibility of recall bias.

### **Benign Intracranial Tumors**

The results of this study are consistent with the absence of an association between ARC-related exposures and benign intracranial tumors among C500 employees. Although we observed an elevated OR for ionizing radiation, the association was limited in large part to the self-reported exposure data. As with glioma, there is some support from other studies for a relationship between ionizing radiation and benign intracranial tumors, but the evidence is inconclusive, especially for exposure in adulthood. Case-control studies of Los Angeles residents have reported associations between annual dental X-rays after age 25 and both meningioma (22,24) and vestibular schwannoma (23). Two other studies reported no or little association between brain tumor and diagnostic X-rays of the head and neck, including dental X-rays (3,30). Children treated with radiation for tinea capitis have increased rates of all intracranial tumors, but especially of nerve sheath tumors and meningiomas (19,26,29).

The absence of an association with the project-based data in our study, the possibility of erroneous self-reported exposure information due to recall bias and the inconsistency of external support for an association detract from an etiologic explanation of this association.

### Other agents

No other agent was strongly or consistently associated with benign intracranial tumors. Although the OR was elevated for self-reported exposure to other amines, these data were

subject to the same lack of specificity of recall as was seen among glioma subjects. There was no association between other amines and benign intracranial tumors in the project-based data, and we observed important differences between cases and controls with regard to their concordance for self-reported exposure and project-based use (cases: 4/4, or 100%, with project-based use had self-reported exposure; controls: 14/33, or 42%, with project-based use had self-reported exposure). There is no external research reporting an association between other amines and benign intracranial tumors.

### **Study Limitations**

This study had several limitations. The number of cases, both of glioma and of benign intracranial tumors, was small. Consequently, measures of association were imprecise, confidence intervals were wide and our ability to assess exposure to multiple agents was restricted.

As noted earlier, the project-based data were objectively derived. However, because of the small study size, one cannot assume that misclassification of subjects by potential agent use would be nondifferential (equal for cases and controls and for exposed and unexposed). Indeed, the reclassification of a single subject could, in some instances, halve or double the OR for an agent.

Study subjects worked with a wide variety of chemicals, and some of the chemicals associated with elevated brain cancer risk were moderately correlated, especially in the project-based data. Thus, assessing the independent effect of individual agents was difficult.

Because most of the glioma cases were impaired or deceased at the time of the interviews, we had to rely on surrogate information. We were rarely able to find coworkers who were familiar with the entire spectrum of a subject's work over time and across projects. Family

4

surrogates generally were unfamiliar with workplace factors. Consequently, we probably failed to obtain as accurate a record of cases' self-reported exposures as we did for most controls.

There was a substantial amount of discordance between self-reported exposures to agents of interest and project-based potential agent use. Despite reviews of data for categories with very high discordance (i.e., organometallics and other amines), we were unable to provide a complete explanation for the disagreement. Recall bias may have played a role. On the other hand, project-based potential use may not be a good surrogate measure of subjects' actual exposure to agents. It was not possible to ascertain from project documents whether certain procedures were done by people working directly on the projects or, alternatively, were performed by laboratory technicians in another location. Furthermore, not all individuals working on a project would have been exposed to all of the agents involved in that project. Also, documents were missing for some project-year combinations. Extrapolations of agent information from prior or subsequent years may have resulted in agents being assigned incorrectly to certain project-year combinations, while other agents used only in the missing years would have been omitted altogether. Finally, data were not abstracted for a large number of projects on which subjects worked for very small numbers of hours. Thus, agents used only on those projects were missed. We are unable to assess directly the impact of these factors on specific results.

## **Conclusions**

The results of the case-control study indicate that occupational exposure at the ARC may have contributed to the excess of gliomas among C500 employees, but the results fall short of identifying specific etiologic agents. Ionizing radiation, or an unidentified agent correlated with ionizing radiation, or several agents acting in conjunction may have been responsible. Because

of the small size of the study and the possibility of exposure misclassification, a firm conclusion about the neurocarcinogenicity of particular agents is not warranted. The study does not indicate that benign intracranial tumors among C500 employees were work-related. The observed association between ionizing radiation and benign intracranial tumors was limited to self-reported data and may have been due to bias.

## REFERENCES

1. Boice JD, Land CE, Preston DL. Ionizing radiation. In *Cancer Epidemiology and Prevention*, 2<sup>nd</sup> Edition, Shottenfeld D, Fraumeni JF, eds. New York: Oxford University Press, 1996.
2. Brada M, Ford D, Ashley S, et al. Risk of second brain tumour after conservative surgery and radiotherapy for pituitary adenoma. *Br Med J* 304:1343-1346, 1992.
3. Burch JD, Craib KJP, Choi BCK, et al. An exploratory case-control study of brain tumors in adults. *J Natl Cancer Inst* 78:601-609, 1987.
4. Cardis E, Gilbert ES, Carpenter L et al. Effects of low doses and low dose rates of external ionizing radiation: cancer mortality among nuclear industry workers in three countries. *Radiat Res* 142:117-132, 1995.
5. Carpenter L, Higgins C, Douglas A, Fraser P, Beral V, Smith P. Combined analysis of mortality in three United Kingdom nuclear industry workforces, 1946-1988. *Radiat Res* 138:224-238, 1994.
6. Checkoway H, Pearce N, Crawford-Brown DJ, Cragle DL. Radiation doses and cause-specific mortality among workers at a nuclear materials fabrication plant. *Am J Epidemiol* 127:255-266, 1988.
7. Cragle DL, Hollis DR, Qualters JR et al. A mortality study of men exposed to mercury. *J Occup Med* 26:817-821, 1984.
8. Delzell E, Beall C, Rodu B, Lees P, Breysse P, Cole P. Case-series investigation of intracranial neoplasms at a petrochemical research facility. *Am J Ind Med* 36:450-458, 1999.
9. Delzell E, Beall C, Rodu B, Sathiakumar N. Mortality among employees at the Amoco Research Center. Report dated September 10, 1999.

10. Delzell E, Beall C, Rodu B, Sathiakumar N. Cancer incidence among employees at the Amoco Research Center. Report dated September 24, 1999.
11. Delzell E, Beall C, Rodu B, Sathiakumar N. Cancer and benign tumor incidence among employees in the 500 building complex at the Amoco Research Center. Report dated September 24, 1999.
12. Doody MM, Mandel JS, Lubin JH, Boice JD. Mortality among United States radiologic technologists, 1926-90. *Cancer Causes Control* 9:67-75, 1998.
13. Hadjimichael OC, Ostfeld AM, D'Atri DA, Brubaker RE. Mortality and cancer incidence experience of employees in a nuclear fuels fabrication plant. *J Occup Med*: 25:48-61, 1983.
14. Hochberg F, Toniolo P, Cole P. Nonoccupational risk indicators of glioblastoma in adults. *J Neuro-Oncology* 8:55-60, 1990.
15. Hsieh C, Maisonneuve P, Boyle P, Macfarlane GJ, Robertson C. Analysis of quantitative data by quantiles in epidemiologic studies: classification according to cases, noncases, or all subjects? *Epidemiology* 2:137-140, 1991.
16. Huang, C, Shih T, Cheng S, Chen S, Tchen P. *N*-hexane polyneuropathy in a ball-manufacturing factory. *J Occup Med* 33:139-142, 1991.
17. Lees PSJ, Breysse PN. Exposure assessment for case-control study of risk for intracranial tumors. Report dated October, 1999.
18. Lubin JH, Gail MH. Biased selection of controls for case-control analyses of cohort studies. *Biometrics* 40:63-75, 1984.
19. Modan B, Baidatz D, Mart H, Steinitz R, Levin SG. Radiation-induced head and neck tumours. *Lancet* 1:277-279, 1974.

20. National Academy of Sciences. Health effects of exposure to low levels of ionizing radiation: BEIR V. Washington, DC: National Academy Press, 1990.
21. Polednak AP, Stehney AF, Lucas HF. Mortality among male workers at a thorium processing plant. *Health Phys* 44(Suppl):239-251, 1983.
22. Preston-Martin S, Paganini-Hill A, Henderson BE, Pike MC, Wood C. Case-control study of intracranial meningiomas in women in Los Angeles County, California. *J Natl Cancer Inst* 65:67-73, 1980.
23. Preston-Martin S, Thomas DC, Wright WE, Henderson BE. Noise trauma in the aetiology of acoustic neuromas in men in Los Angeles County, 1978-1985. *Br J Cancer* 59:783-786, 1989.
24. Preston-Martin S, Mack W, Henderson BE. Risk factors for gliomas and meningiomas in males in Los Angeles County. *Cancer Res* 49:6137-6143, 1989.
25. Ritz B. Radiation exposure and cancer mortality in uranium processing workers. *Epidemiol* 10:531-538, 1999.
26. Ron E, Modan B, Boice JD, et al. Tumors of the brain and nervous system after radiotherapy in childhood. *N Engl J Med* 319:1033-1039, 1988.
27. Rothman KJ, Greenland S. *Modern epidemiology* (2nd ed). Philadelphia, PA: Lippincott-Raven, 1998.
28. Ryan P, Lee MW, North JB, McMichael AJ. Risk factors for tumors of the brain and meninges: results from the Adelaide Adult Brain Tumor Study. *Int J Cancer* 51:20-27, 1992.
29. Sadetzki S, Modan B, Chetrit A, Freedman L. An iatrogenic epidemic of benign meningioma. *Am J Epidemiol* 151:266-272, 2000.

30. Schlehofer B, Blettner M, Becker N, Martinsohn C, Wahrendorf J. Medical risk factors and the development of brain tumors. *Cancer* 69:2541-2547, 1992.
31. Wang J, Chang Y, Kao K, Huang C, Lin C, Yeh W. An outbreak of n-hexane induced polyneuropathy among press proofing workers in Taipei. *Am J Ind Med* 10:111-118, 1986.
32. Wiggs LD, Cox-DeVore CA, Wilinson GS, Reyes M. Mortality among workers exposed to external ionizing radiation at a nuclear facility in Ohio. *J Occup Med* 33:632-637, 1991.
33. Wiggs LD, Johnson ER, Cox-DeVore CA, Voelz GL. Mortality through 1990 among white male workers at the Los Alamos National Laboratory: considering exposures to plutonium and external ionizing radiation. *Health Phys* 67:577-588, 1994.

TABLES

Table 1. Characteristics of glioma cases and matched controls (numbers are medians unless otherwise noted)

Characteristic	Cases N=6	Controls N=60
ARC years	16.8	10.9
ARC hire date	1971	1971
Company		
Ever ACC	6	55
Never ACC	0	5
ACC years	16.8	9.9
ACC hire date	1972	1971
Project histories*		
Yes	6	50
No	0	10
Project hours, median†	31235	15678
Project years, median†	16.8	9.6
Job type†		
Ever hands-on	4	35
Ever supervisory/never hands-on	1	3
Always non-lab	1	12
Time in job type		
Ever hands-on		
% time in hands-on	97.8	82.1
% time supervisory	0.0	5.6
% time non-lab	2.2	12.3
Ever supervisory, never hands-on		
% time supervisory	32.1	100.0
% time non-lab	67.9	0.0
Always non-lab		
% time non-lab	100.0	100.0

\* Frequencies.

† Restricted to 6 cases and 50 controls with project histories.

Table 2. Number of glioma cases and matched controls with self-reported exposure to agents of interest

Agent	Cases				Controls			
	Yes	Poss	No	Unk	Yes	Poss	No	Unk
Ionizing radiation	1	1	4	0	2	0	58	0
Energy beam*	0	0	6	0	2	0	58	0
Aromatic hydrocarbons	4	0	2	0	40	1	19	0
Methylene chloride	1	0	4	1	10	1	48	1
Other chlorinated hydrocarbons	0	0	5	1	16	4	37	3
Other halogenated hydrocarbons	0	0	4	2	9	0	49	2
N-hexane	5	1	0	0	26	0	33	1
Other volatile hydrocarbons	4	1	1	0	27	0	32	1
Catalysts	3	2	1	0	15	0	44	1
Organometallics	2	2	2	0	11	0	48	1
Elemental metallics	2	0	3	1	10	0	49	1
Acrylonitrile	1	0	5	0	8	3	49	0
Vinyl chloride	0	0	6	0	4	1	55	0
Formaldehyde	0	1	5	0	11	1	48	0
Nitroso compounds	0	0	6	0	2	1	57	0
Other amines	2	2	2	0	13	2	44	1

\* A radio frequency plasma generator used in building 503 in 1979.

Table 3. Number of glioma cases and controls by self-reported definite or possible exposure to agents, corresponding odds ratios (ORs) and 95% confidence intervals (CIs) (unknown exposure modeled by an indicator variable)

Agent	No. of subjects		OR	95% CI
	Cases	Controls		
Ionizing radiation	2	2	15.7	1.4-179.4
Energy beam*	0	2	0.0	0.0-175.5
Aromatic hydrocarbons	4	41	0.9	0.1-6.2
Methylene chloride	1	11	1.0	0.1-10.0
Other chlorinated hydrocarbons	0	20	0.0	0.0-2.4
Other halogenated hydrocarbons	0	9	0.0	0.0-13.2
<i>N</i> -hexane	6	26	∞	1.4-∞
Other volatile hydrocarbons	5	27	5.8	0.6-52.8
Catalysts	5	15	16.5	1.7-157.7
Organometallics	4	11	9.4	1.5-59.7
Elemental metallics	2	10	3.6	0.5-25.8
Acrylonitrile	1	11	0.9	0.1-8.3
Vinyl chloride	0	5	0.0	0.0-13.9
Formaldehyde	1	12	0.8	0.1-7.2
Nitroso compounds	0	3	0.0	0.0-35.3
Other amines	4	15	6.0	1.0-35.7

\* A radio frequency plasma generator used in building 503 in 1979.

Table 4. Number of glioma cases and controls with self-reported exposure to medical and lifestyle factors

Factor	Cases				Controls			
	Yes	Poss	No	Unk	Yes	Poss	No	Unk
Diagnostic/therapeutic X-rays*	0	0	5	1	9	0	45	6
Serious head injury†	0	0	5	1	12	2	42	4
Seizure history	1§	0	4	1	0	0	55	5
Anticonvulsant drug use	1§	0	4	1	0	0	55	5
Meningitis	0	0	5	1	0	0	55	5
Hearing loss	1	0	3	2	23	3	31	3
Ototoxic drug use‡	2	0	2	2	29	8	16	7
Noisy work settings¶	2	2	2	0	31	0	29	0
Cellular phone use	1	0	4	1	12	0	44	4
Amateur radio use	0	0	5	1	2	0	54	4
Home pesticide use	5	0	1	0	47	1	7	5
Professional pesticide applicator	0	0	5	1	0	0	56	4
Home refinishing	3	0	1	2	26	0	29	5
Professional refinishing	0	0	5	1	0	0	56	4
Radiation badge use	1	0	5	0	16	3	41	0

\* Diagnostic X-rays of head or neck or therapeutic X-rays for tonsillitis, ringworm, etc.

† Head injury resulting in concussion or unconsciousness.

‡ Any of the following: quinine; quinidine; chloroquine; hydroxychloroquine; furosemide; bumetanide; ethracrynic acid; erythromycin; streptomycin; kanamycin; gentamycin; neomycin; vancomycin; rifampin; capreomycin; deferoxamine; aspirin -4+ per day for 15+ consecutive days; other NSAIDs -2+ per day for 15+ consecutive days

¶ Setting where noise level "interfered with normal conversation: or hearing protection was required."

§ Associated with but prior to tumor diagnosis.

Table 5. Number of glioma cases and controls by medical and lifestyle history, corresponding ORs and 95% CIs (unknown exposure modeled by an indicator variable)

Factor	No. of subjects		OR	95% CI
	Cases N=6	Controls N=60		
Diagnostic/therapeutic x-rays*	0	9	0.0	0.0-6.1
Serious head injury†	0	14	0.0	0.0-3.7
Seizure history	1§	0	∞	0.3-∞
Anticonvulsant drug use	1§	0	∞	0.3-∞
Meningitis	0	0	—	—
Hearing loss	1	26	0.3	0.0-3.5
Ototoxic drug use‡	2	37	0.5	0.1-3.5
Noisy work settings¶	4	31	2.0	0.3-14.2
Cellular phone use	1	12	0.9	0.1-12.9
Amateur radio use	0	2	0.0	0.0-53.2
Home pesticide use	5	48	0.7	0.1-7.6
Professional pesticide use	0	0	—	—
Home refinishing	3	26	3.8	0.4-39.6
Professional refinishing	0	0	—	—
Radiation badge	1	19	0.4	0.0-4.0

\* Diagnostic x-rays of head or neck or therapeutic x-rays for tonsillitis, ringworm, etc.

† Head injury resulting in concussion or unconsciousness.

‡ Any of the following: quinine; quinidine; chloroquine; hydroxychloroquine; furosemide; bumetanide; ethracrynic acid; erythromycin; streptomycin; kanamycin; gentamycin; neomycin; vancomycin; rifampin; capreomycin; deferoxamine; aspirin—4+ per day for 15+ consecutive days; other NSAIDs—2+ per day for 15+ consecutive days

¶ Setting where noise level “interfered with normal conversation: or hearing protection was required.”

§ Associated with but preceding diagnosis for case.

Table 6. Number of glioma cases and controls by project-based potential agent use, corresponding ORs and 95% CIs (excludes 4 controls with a technical background but without a project history)

Agent	No. of subjects		OR	95% CI
	Cases N=67	Controls N=56		
Ionizing radiation	4	8	9.6	1.7-55.2
Nonionizing radiation	3	12	0.7	0.1-6.8
Energy beam	0	2	0.0	0.0-175.5
Aromatic hydrocarbons	5	37	2.7	0.3-24.8
Xylene	5	30	4.4	0.5-40.2
Benzene	4	26	2.2	0.4-12.8
Toluene	4	27	2.1	0.4-11.7
Halogenated hydrocarbons	5	32	3.6	0.4-32.0
Chlorinated hydrocarbons	4	29	1.8	0.3-10.3
Methylene chloride	1	17	0.5	0.1-4.5
Tetrachloroethylene	0	0	—	—
Chloroethanes	1	13	0.6	0.1-6.2
Brominated hydrocarbons	3	18	2.0	0.4-10.1
Bromoethanes	2	10	2.3	0.4-14.1
Freons	0	0	—	—
Volatile aliphatic hydrocarbons (solvents)	5	37	2.7	0.3-24.8
N-hexane	4	26	2.3	0.4-13.7
Catalysts	5	36	2.9	0.3-26.2
Organometallics	2	20	0.9	0.1-5.8
Inorganic metalics	5	36	2.9	0.3-26.2
Acrylonitrile	0	11	0.0	0.0-4.1
Ethylene/ETO	0	0	—	—
Butadiene	2	4	5.3	0.9-32.4
Glycidol	0	2	0.0	0.0-45.1
Nitrosoamines	0	1	0.0	0.0-332.3
Other amines	4	34	1.3	0.2-7.4
Reactive monomers	5	36	2.9	0.3-26.2
Styrene	2	16	1.2	0.2-7.2
Vinyl chloride	0	1	0.0	0.0-389.1
Other known chemicals	5	37	2.7	0.0-24.8
Chemicals of unknown type	5	35	3.0	0.3-27.3

Table 7. Number of glioma cases and controls by weighted duration of project-based potential agent use, corresponding ORs and 95% CIs (excludes 4 controls with a technical background but without a project history)

Agent/Duration (M, median)	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
Ionizing radiation				
Unexposed	2	48	1.0	
≤ M	2	3	11.5	1.3-98.4
> M	2	5	8.1	1.0-66.7
Aromatic hydrocarbons				
Unexposed	1	19	1.0	
≤ M	3	32	1.7	0.2-18.0
> M	2	5	6.2	0.5-72.5
Xylene				
Unexposed	1	26	1.0	
≤ M	3	16	4.7	0.5-48.5
> M	2	14	3.9	0.3-47.9
Benzene				
Unexposed	2	30	1.0	
≤ M	2	15	1.9	0.3-14.3
> M	2	11	2.7	0.3-21.6
Toluene				
Unexposed	2	29	1.0	
≤ M	2	11	2.5	0.3-19.7
> M	2	16	1.8	0.2-13.0
Halogenated hydrocarbons				
Unexposed	1	24	1.0	
≤ M	3	16	4.2	0.4-41.3
> M	2	16	3.0	0.3-34.3
Chlorinated hydrocarbons				
Unexposed	2	27	1.0	
≤ M	2	22	1.2	0.2-9.1
> M	2	7	3.3	0.5-24.6
Brominated hydrocarbons				
Unexposed	3	38	1.0	
≤ M	2	10	2.3	0.4-14.2
> M	1	8	1.5	0.1-15.3
Bromoethanes				
Unexposed	4	46	1.0	
≤ M	1	7	1.6	0.2-17.6
> M	1	3	3.3	0.3-33.4

Table 7. Number of glioma cases and controls by weighted duration of project-based potential agent use, corresponding ORs and 95% CIs (excludes 4 controls with a technical background but without a project history)

Agent/Duration (M, median)	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<b>Volatile aliphatic hydrocarbons</b>				
Unexposed	1	19	1.0	
≤ M	3	32	1.6	0.2-17.4
> M	2	5	6.8	0.6-83.2
<b>N-hexane</b>				
Unexposed	2	30	1.0	
≤ M	2	24	1.2	0.2-9.0
> M	2	2	16.2	1.1-227.6
<b>Catalysts</b>				
Unexposed	1	20	1.0	
≤ M	3	29	2.0	0.2-21.5
> M	2	7	5.7	0.5-69.7
<b>Organometallics</b>				
Unexposed	4	36	1.0	
≤ M	1	20	0.4	0.0-4.3
> M	1	0	∞	0.2-∞
<b>Inorganic metalics</b>				
Unexposed	1	20	1.0	
≤ M	3	29	2.0	0.2-21.5
> M	2	7	5.7	0.5-69.7
<b>Butadiene</b>				
Unexposed	4	52	1.0	
≤ M	1	2	5.5	0.5-61.5
> M	1	2	5.0	0.4-57.8
<b>Other amines</b>				
Unexposed	2	22	1.0	
≤ M	2	19	1.2	0.2-8.5
> M	2	15	1.5	0.2-11.2
<b>Reactive monomers</b>				
Unexposed	1	20	1.0	
≤ M	3	28	2.2	0.2-23.2
> M	2	8	4.6	0.4-53.5
<b>Styrene</b>				
Unexposed	4	40	1.0	
≤ M	1	2	4.1	0.4-46.0
> M	1	14	0.7	0.1-6.7

Table 7. Number of glioma cases and controls by weighted duration of project-based potential agent use, corresponding ORs and 95% CIs (excludes 4 controls with a technical background but without a project history)

Agent/Duration (M, median)	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<b>Other types of known chemicals</b>				
Unexposed	1	19	1.0	
≤ M	3	23	2.6	0.2-27.5
> M	2	14	2.7	0.2-32.3
<b>Chemicals of unknown type</b>				
Unexposed	1	21	1.0	
≤ M	3	31	1.9	0.2-19.4
> M	2	4	9.9	0.7-136.1

Table 8. Number of glioma cases and controls by years since first project-based potential agent use, corresponding ORs and 95% CIs (excludes 4 controls with a technical background but without a project history)

Agent/Years since first use	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<b>Ionizing radiation</b>				
Unexposed	2	48	1.0	
< 10	3	1	$\infty$	3.2- $\infty$
$\geq 10$	1	7	1.7	0.1-19.6
<b>Nonionizing radiation</b>				
Unexposed	5	44	1.0	
< 10	0	0	—	—
$\geq 10$	1	12	0.7	0.1-6.8
<b>Energy beam</b>				
Unexposed	6	54	1.0	
< 10	0	0	—	—
$\geq 10$	0	2	0.0	0.0-175.5
<b>Aromatic hydrocarbons</b>				
Unexposed	1	19	1.0	
< 10	1	7	3.3	0.1-78.3
$\geq 10$	4	30	2.6	0.3-24.8
<b>Xylene</b>				
Unexposed	1	26	1.0	
< 10	1	6	5.8	0.2-166.5
$\geq 10$	4	24	4.2	0.4-40.1
<b>Benzene</b>				
Unexposed	2	30	1.0	
< 10	1	3	6.7	0.3-150.9
$\geq 10$	3	23	1.8	0.3-11.6
<b>Toluene</b>				
Unexposed	2	29	1.0	
< 10	1	5	3.2	0.2-49.3
$\geq 10$	3	22	1.9	0.3-11.6
<b>Halogenated hydrocarbons</b>				
Unexposed	1	24	1.0	
< 10	1	7	3.5	0.2-73.2
$\geq 10$	4	25	3.6	0.4-34.4
<b>Chlorinated hydrocarbons</b>				
Unexposed	2	27	1.0	
< 10	1	5	2.9	0.2-41.7
$\geq 10$	3	24	1.6	0.3-10.2

Table 8. Number of glioma cases and controls by years since first project-based potential agent use, corresponding ORs and 95% CIs (excludes 4 controls with a technical background but without a project history)

Agent/Years since first use	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
Methylene chloride				
Unexposed	5	39	1.0	
< 10	0	4	0.0	0.0-16.5
≥ 10	1	13	0.6	0.1-5.8
Chloroethanes				
Unexposed	5	43	1.0	
< 10	0	1	0.0	0.0-356.7
≥ 10	1	12	0.7	0.1-6.8
Brominated hydrocarbons				
Unexposed	3	38	1.0	
< 10	1	3	5.4	0.3-102.1
≥ 10	2	15	1.4	0.2-9.2
Bromoethanes				
Unexposed	4	46	1.0	
< 10	1	1	∞	0.1-∞
≥ 10	1	9	1.2	0.1-11.7
Volatile aliphatic hydrocarbons (solvents)				
Unexposed	1	19	1.0	
< 10	1	7	3.3	0.1-78.3
≥ 10	4	30	2.6	0.3-24.8
<i>N</i> -hexane				
Unexposed	2	30	1.0	
< 10	1	4	4.2	0.3-64.2
≥ 10	3	22	2.0	0.3-13.4
Catalysts				
Unexposed	1	20	1.0	
< 10	1	6	4.6	0.2-133.8
≥ 10	4	30	2.7	0.3-25.7
Organometallics				
Unexposed	4	36	1.0	
< 10	0	1	0.0	0.0-373.8
≥ 10	2	19	1.0	0.2-6.3
Inorganic metalics				
Unexposed	1	20	1.0	
< 10	1	6	4.6	0.2-133.8
≥ 10	4	30	2.7	0.3-25.7

Table 8. Number of glioma cases and controls by years since first project-based potential agent use, corresponding ORs and 95% CIs (excludes 4 controls with a technical background but without a project history)

Agent/Years since first use	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<b>Acrylonitrile</b>				
Unexposed	6	45	1.0	
< 10	0	0	—	—
≥ 10	0	11	0.0	0.0-4.1
<b>Glycidol</b>				
Unexposed	6	54	1.0	
< 10	0	1	0.0	0.0-351.0
≥ 10	0	1	0.0	0.0-312.8
<b>Nitroso amines</b>				
Unexposed	6	55	1.0	
< 10	0	0	—	—
≥ 10	0	1	0.0	0.0-350.9
<b>Other amines</b>				
Unexposed	2	22	1.0	
< 10	1	6	2.1	0.1-32.2
≥ 10	3	28	1.2	0.2-7.3
<b>Reactive monomers</b>				
Unexposed	1	20	1.0	
< 10	1	6	4.6	0.2-133.8
≥ 10	4	30	2.7	0.3-25.7
<b>Styrene</b>				
Unexposed	4	40	1.0	
< 10	1	2	6.3	0.4-106.1
≥ 10	1	14	0.7	0.1-6.3
<b>Vinyl chloride</b>				
Unexposed	6	55	1.0	
< 10	0	0	—	—
≥ 10	0	1	0.0	0.0-389.1
<b>Other types of known chemicals</b>				
Unexposed	1	19	1.0	
< 10	1	7	3.3	0.1-78.3
≥ 10	4	30	2.6	0.3-24.8
<b>Chemicals of unknown type</b>				
Unexposed	1	21	1.0	
< 10	1	7	3.4	0.2-71.2
≥ 10	4	28	2.0	0.3-27.9

Table 9. Distribution of glioma cases and controls by project-based potential use of ionizing radiation (IR-PB) and *n*-hexane (NH-PB) and by self-reported exposure to organometallics (OM-SR) and other amines (OA-SR) (excludes 4 controls with a technical background but without a project history)

IR-PB	NH-PB	OM-SR	OA-SR	Cases	Controls
<b>No use of or exposed to any of the four agents</b>					
-	-	-	-	0	27
<b>Used/exposed to all four agents</b>					
+	+	+	+	2	0
<b>Used/exposed to any three of the four agents</b>					
+	+	+	-	1	1
+	+	-	+	0	4
+	-	+	+	0	0
-	+	+	+	0	6
<b>Used/exposed to any two of the four agents</b>					
+	+	-	-	0	1
+	-	+	-	0	0
+	-	-	+	0	0
-	+	+	-	0	4
-	+	-	+	1	3
-	-	+	+	1	0
<b>Used/exposed to only one of the four agents</b>					
+	-	-	-	1	2
-	+	-	-	0	7
-	-	+	-	0	0
-	-	-	+	0	1

Table 10. Odds ratios (ORs) and 95% confidence intervals (CIs) from models including two agents of interest (excludes 4 controls with a technical background but without a project history)

Model	Agent(s) in model	OR	95% CI
1	Ionizing radiation-ever-project based	9.4	1.5-58.3
	<i>N</i> -hexane-ever-project based	1.7	0.2-12.8
2	Ionizing radiation-ever-project based	6.7	0.9-49.2
	<i>N</i> -hexane-> median-project based	4.0	0.3-55.3
3	Ionizing radiation-ever-project-based	15.2	1.5-153.1
	Organometallics-ever-self report	13.3	1.3-141.2
4	<i>N</i> -hexane-> median-project based	13.6	0.7-256.9
	Organometallics-ever-self report	6.8	1.0-44.2
5	Ionizing radiation-ever-project based	9.3	1.3-64.4
	Other amines-ever-self report	4.7	0.7-32.2
6	<i>N</i> -hexane-ever-project based	0.8	0.1-7.3
	Other amines-ever-self report	6.6	0.7-60.8
7	<i>N</i> -hexane-> median-project based	13.6	0.8-228.8
	Other amines-ever-self report	4.3	0.7-25.5
9	Organometallics-ever-self report	6.0	0.9-40.5
	Other amines-ever-self report	2.2	0.3-16.0

Table 11. Number of glioma cases and controls, ORs and 95% CIs, by project-based potential use of ionizing radiation and *n*-hexane (excludes 4 controls with a technical background but without a project history)

Exposure model	Cases	Controls	OR	95% CI
Ionizing radiation-ever-project based & <i>n</i> -hexane-ever-project based				
Used both	3	6	16.4	1.1-252.8
Used only ionizing radiation	1	2	6.6	0.4-118.1
Used only <i>n</i> -hexane	1	20	1.2	0.1-21.0
Used neither (referent category)	1	28	1.0	-

Table 12. Concordance between self-reported exposure and project-based potential use for 15 agents of interest among glioma cases and controls

Agent	Cases N=6				Controls N=60			
	Concordant		Discordant		Concordant		Discordant	
	No.	%	No.	%	No.	%	No.	%
Ionizing radiation	4	67	2	33	51	85	9	15
Energy beam	6	100	0	0	58	97	2	3
Aromatic hydrocarbons	5	83	1	17	52	87	8	13
Halogenated hydrocarbons	2	33	4	67	44	73	16	27
Chlorinated hydrocarbons	3	50	3	50	44	73	16	27
Methylene chloride	4	67	2	33	42	70	18	30
Volatile hydrocarbons	5	83	1	17	50	83	10	17
<i>N</i> -hexane	4	67	2	33	46	77	14	23
Catalysts	4	67	2	33	39	65	21	35
Organometallics	4	67	2	33	43	72	17	28
Inorganic metallics	3	50	3	50	34	57	26	43
Acrylonitrile	5	83	1	17	50	83	10	17
Nitrosoamines	6	100	0	0	56	93	4	7
Other amines	4	67	2	33	39	65	21	35
Vinyl chloride	6	100	0	0	54	90	6	10

Table 13. Selected characteristics of benign intracranial tumor cases and matched controls  
(numbers are medians unless otherwise noted)

Characteristics	Cases N=6	Controls N=59
ARC years	14.0	6.4
ARC hire date	1977	1971
Company*		
Ever ACC	6	55
Never ACC	0	4
ACC years	9.2	6.2
ACC hire date	1977	1971
Project histories*		
Yes	4	51
No	2	8
Project hours†	22232	11170
Project years†	14.0	7.0
Job type†		
Ever hands-on	4	31
Ever supervisory, never hands-on	0	6
Always non-lab	0	14
Time in job type		
Ever hands-on		
% time in hands-on	98.8	77.3
% time supervisory	0.0	8.3
% time non-lab	1.2	14.4
Ever supervisory, never hands-on		
% time supervisory	—	77.7
% time non-lab	—	22.3
Always non-lab		
% time non-lab	—	100.0

\*Frequencies

†Restricted to 4 cases & 36 controls with project histories.

Table 14. Number of benign intracranial tumor cases and matched controls with self-reported exposure to agents of interest

Agent	Cases				Controls			
	Yes	Poss	No	Unk	Yes	Poss	No	Unk
Ionizing radiation	2	0	4	0	5	1	53	0
Energy beam*	0	0	6	0	0	0	59	0
Aromatic hydrocarbons	4	0	2	0	29	1	28	1
Methylene chloride	1	0	5	0	6	4	47	2
Other chlorinated hydrocarbons	2	0	3	1	14	2	40	3
Other halogenated hydrocarbons	0	0	5	1	9	1	46	3
<i>N</i> -hexane	2	0	3	1	14	2	41	2
Other volatile hydrocarbons	3	0	2	1	22	2	32	3
Catalysts	2	0	4	0	20	1	37	1
Organometallics	2	0	4	0	18	1	38	2
Elemental metallics	2	0	4	0	6	0	52	1
Acrylonitrile	1	0	5	0	3	3	51	2
Vinyl chloride	0	0	6	0	5	1	51	2
Formaldehyde	0	0	5	1	9	2	47	1
Nitroso compounds	0	0	6	0	1	2	53	3
Other amines	4	0	2	0	13	2	42	2

\* A radio frequency plasma generator used in building 503 in 1979.

Table 15. Number of benign intracranial tumor cases\* and controls by self-reported definite or possible exposure to agents, corresponding ORs and 95% CIs (unknown exposure modeled by an indicator variable)

Agent	No. of subjects		OR	95% CI
	Cases N=6	Controls N=59		
Ionizing radiation	2	6	5.4	1.7-43.1
Energy beam †	0	0	—	—
Aromatic hydrocarbons	4	30	2.1	0.3-13.8
Methylene chloride	1	10	0.9	0.1-8.6
Other chlorinated hydrocarbons	2	16	1.7	0.2-11.5
Other halogenated hydrocarbons	0	10	0.0	0.0-5.0
<i>N</i> -hexane	2	16	1.8	0.3-11.9
Other volatile hydrocarbons	3	24	2.0	0.3-14.0
Catalysts	2	21	0.9	0.1-5.6
Organometallics	2	19	1.0	0.1-6.9
Elemental metalics	2	6	4.0	0.6-24.5
Acrylonitrile	1	6	1.7	0.2-19.3
Vinyl chloride	0	6	0.0	0.0-8.5
Formaldehyde	0	11	0.0	0.0-5.0
Nitroso compounds	0	3	0.0	0.0-21.4
Other amines	4	15	5.2	0.9-29.5

\* Benign intracranial tumor cases include meningioma (n=2), vestibular schwannoma (n=2) and pituitary adenoma (n=2).

† A radio frequency plasma generator used in building 503 in 1979.

Table 16. Number of benign intracranial tumor cases and matched controls self-reported exposure to medical and lifestyle factors among

Factor	Cases				Controls			
	Yes	Poss	No	Unk	Yes	Poss	No	Unk
Diagnostic/therapeutic x-rays*	1	0	5	0	8	1	47	3
Serious head injury†	1	0	5	0	6	1	47	5
Seizure history	1§	0	5	0	0	0	56	3
Anticonvulsant drug use	1§	0	5	0	2	0	54	3
Meningitis	0	0	6	0	0	0	56	3
Hearing loss	3	0	3	0	25	1	31	2
Ototoxic drug use‡	1	1	4	0	34	7	11	7
Noisy work settings¶	4	0	2	0	33	0	26	0
Cellular phone use	0	1	5	0	9	0	47	3
Amateur radio use	0	0	6	0	1	0	55	3
Home pesticide use	4	0	2	0	45	0	11	3
Professional pesticide applicator	0	0	6	0	0	0	56	3
Home refinishing	3	0	3	0	25	0	31	3
Professional refinishing	0	0	6	0	0	0	56	3
Radiation badge	3	0	3	0	18	4	36	1

\* Diagnostic x-rays of head or neck or therapeutic x-rays for tonsillitis, ringworm, etc.

† Head injury resulting in concussion or unconsciousness.

‡ Any of the following: quinine; quinidine; chloroquine; hydroxychloroquine; furosemide; bumetanide; ethracrynic acid; erythromycin; streptomycin; kanamycin; gentamycin; neomycin; vancomycin; rifampin; capreomycin; deferoxamine; aspirin-4+ per day for 15+ consecutive days; other NSAIDs-2+ per day for 15+ consecutive days

¶ Setting where noise level "interfered with normal conversation: or hearing protection was required."

§ Associated with but preceding diagnosis.

Table 17. Number of benign intracranial tumor cases and controls by definite exposure to medical and lifestyle history, corresponding ORs and 95% CIs (unknown exposure modeled by an indicator variable)

Factor	No. of subjects		OR	95% CI
	Cases N=6	Controls N=59		
Diagnostic/therapeutic x-rays*	1	9	1.1	0.1-11.3
Serious head injury†	1	7	1.3	0.1-11.9
Seizure history	1§	0	∞	0.2-∞
Anticonvulsant drug use	1§	2	6.0	1.4-98.7
Meningitis	0	0	—	—
Hearing loss	3	26	1.3	0.2-8.5
Ototoxic drug use‡	2	41	0.1	0.0-1.0
Noisy work settings¶	4	33	1.6	0.3-10.2
Cellular phone use	1	9	1.0	0.1-12.1
Amateur radio use	0	1	0.0	0.0-351.0
Home pesticide use	4	45	0.4	0.1-3.1
Professional pesticide use	0	0	—	—
Home refinishing	3	25	1.2	0.2-6.3
Professional refinishing	0	0	—	—
Radiation badge	3	22	1.6	0.3-8.7

\* Diagnostic x-rays of head or neck or therapeutic x-rays for tonsillitis, ringworm, etc.

† Head injury resulting in concussion or unconsciousness.

‡ Any of the following: quinine; quinidine; chloroquine; hydroxychloroquine; furosemide; bumetanide; ethracrynic acid; erythromycin; streptomycin; kanamycin; gentamycin; neomycin; vancomycin; rifampin; capreomycin; deferoxamine; aspirin—4+ per day for 15+ consecutive days; other NSAIDs—2+ per day for 15+ consecutive days

¶ Setting where noise level “interfered with normal conversation: or hearing protection was required.”

§ Associated with but preceding diagnosis for case.

Table 18. Number of benign intracranial tumor cases and controls by project-based potential agent use, corresponding ORs and 95% CIs (excludes 3 controls with a technical background but without a project history)

Agent	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
Ionizing radiation	2	11	2.1	0.3-13.3
Nonionizing radiation	1	16	0.5	0.1-4.8
Energy beam	1	1	∞	0.1-∞
Aromatic hydrocarbons	4	35	1.3	0.2-8.6
Xylene	3	29	1.2	0.2-5.7
Benzene	4	28	2.5	0.4-17.0
Toluene	4	26	2.8	0.4-18.3
Halogenated hydrocarbons	3	35	0.5	0.1-3.6
Chlorinated hydrocarbons	3	33	0.7	0.1-4.3
Methylene chloride	1	18	0.4	0.0-4.4
Tetrachloroethylene	0	4	0.0	0.0-22.5
Chloroethanes	2	20	0.9	0.1-5.4
Brominated hydrocarbons	1	24	0.3	0.0-2.5
Bromoethanes	0	10	0.0	0.0-4.6
Freons	0	2	0.0	0.0-53.2
Volatile aliphatic hydrocarbons (solvents)		36	1.1	0.2-7.7
<i>N</i> -hexane	4	28	2.2	0.4-13.5
Catalysts	4	35	1.3	0.2-8.6
Organometallics	3	23	1.5	0.3-8.6
Inorganic metalics	4	35	1.3	0.2-8.6
Acrylonitrile	0	5	0.0	0.0-12.1
Ethylene/ETO	0	0	—	—
Butadiene	1	3	3.8	0.3-43.1
Glycidol	0	4	0.0	0.0-17.6
Nitroso-amines	0	0	—	—
Other amines	4	33	1.5	0.2-9.7
Reactive monomers	4	35	1.3	0.2-8.6
Styrene	1	17	0.5	0.1-4.3
Vinyl chloride	0	4	0.0	0.0-18.2
Other known chemicals	4	36	1.1	0.2-7.7
Chemicals of unknown type	4	34	1.3	0.2-8.4

Table 19. Number of benign intracranial tumor cases and controls by weighted duration of project-based potential agent use, corresponding ORs and 95% CIs (excludes 3 controls with a technical background but without a project history)

Agent/Duration (M, median)	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<b>Ionizing radiation</b>				
Unexposed	4	45	1.0	
≤ M	1	3	3.2	0.3-31.7
> M	1	8	1.4	0.1-17.0
<b>Aromatic hydrocarbons</b>				
Unexposed	2	21	1.0	
≤ M	2	25	0.9	0.1-7.0
> M	2	10	2.7	0.3-27.3
<b>Xylene</b>				
Unexposed	3	27	1.0	
≤ M	2	0	∞	0.0-∞
> M	1	29	0.3	0.0-3.0
<b>Benzene</b>				
Unexposed	2	28	1.0	
≤ M	2	4	5.6	0.7-43.3
> M	2	24	1.2	0.1-10.1
<b>Toluene</b>				
Unexposed	2	30	1.0	
≤ M	2	20	1.9	0.2-15.7
> M	2	6	7.2	0.6-79.6
<b>Halogenated hydrocarbons</b>				
Unexposed	3	21	1.0	
≤ M	2	14	0.8	0.1-6.4
> M	1	21	0.2	0.0-4.0
<b>Chlorinated hydrocarbons</b>				
Unexposed	3	23	1.0	
≤ M	2	15	0.9	0.1-6.8
> M	1	18	0.4	0.0-5.4
<b>Chloroethanes</b>				
Unexposed	4	36	1.0	
≤ M	1	20	0.5	0.1-5.3
> M	1	0	∞	0.2-∞
<b>Volatile aliphatic hydrocarbons</b>				
Unexposed	2	20	1.0	
≤ M	2	23	0.9	0.1-6.9
> M	2	13	1.9	0.2-19.4

Table 19. Number of benign intracranial tumor cases and controls by weighted duration of project-based potential agent use, corresponding ORs and 95% CIs (excludes 3 controls with a technical background but without a project history)

Agent/Duration (M, median)	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<i>N</i> -hexane				
Unexposed	2	28	1.0	
≤ M	2	3	12.6	0.9-174.4
> M	2	25	1.2	0.2-9.6
Catalysts				
Unexposed	2	21	1.0	
≤ M	2	18	1.2	0.1-10.3
> M	2	17	1.4	0.2-12.4
Organometallics				
Unexposed	3	33	1.0	
≤ M	2	13	1.7	0.2-12.5
> M	1	10	1.2	0.1-13.6
Inorganic metallics				
Unexposed	2	21	1.0	
≤ M	2	18	1.2	0.1-10.3
> M	2	17	1.4	0.2-12.4
Other amines				
Unexposed	2	23	1.0	
≤ M	2	30	0.8	0.1-6.1
> M	2	3	10.7	0.7-150.5
Reactive monomers				
Unexposed	2	21	1.0	
≤ M	2	21	1.0	0.1-8.4
> M	2	14	1.9	0.2-18.5
Other types of known chemicals				
Unexposed	2	20	1.0	
≤ M	2	26	0.8	0.1-6.1
> M	2	15	2.5	0.2-25.0
Chemicals of unknown type				
Unexposed	2	22	1.0	
≤ M	2	24	0.9	0.1-6.7
> M	2	10	2.8	0.3-27.4

Table 20. Number of benign intracranial tumor cases and controls by years since first project-based potential agent use, corresponding ORs and 95% CIs (excludes 3 controls with no technical background but without a project history)

Agent/Years since first use	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<b>Ionizing radiation</b>				
Unexposed	4	45	1.0	
< 10	1	2	5.5	0.3-101.2
≥ 10	1	9	1.2	0.1-13.6
<b>Nonionizing radiation</b>				
Unexposed	5	40	1.0	
< 10	0	4	0.0	0.0-21.0
≥ 10	1	12	0.8	0.1-8.7
<b>Energy beam</b>				
Unexposed	5	55	1.0	
< 10	0	0	—	—
≥ 10	1	1	∞	0.1-∞
<b>Aromatic hydrocarbons</b>				
Unexposed	2	21	1.0	
< 10	0	11	0.0	0.0-7.8
≥ 10	4	24	4.6	0.4-54.0
<b>Xylene</b>				
Unexposed	3	27	1.0	
< 10	1	8	1.1	0.1-13.0
≥ 10	2	21	0.9	0.1-6.8
<b>Benzene</b>				
Unexposed	2	28	1.0	
< 10	1	12	1.2	0.1-16.8
≥ 10	3	16	4.6	0.4-53.0
<b>Toluene</b>				
Unexposed	2	30	1.0	
< 10	1	12	1.3	0.1-17.0
≥ 10	3	14	6.1	0.5-73.3
<b>Halogenated hydrocarbons</b>				
Unexposed	3	21	1.0	
< 10	0	13	0.0	0.0-4.1
≥ 10	3	22	2.3	0.2-13.0
<b>Chlorinated hydrocarbons</b>				
Unexposed	3	23	1.0	
< 10	0	14	0.0	0.0-4.1
≥ 10	3	19	3.0	0.2-40.9
<b>Methylene chloride</b>				
Unexposed	5	38	1.0	
< 10	0	7	0.0	0.0-8.1
≥ 10	1	11	0.7	0.1-8.3

Table 20. Number of benign intracranial tumor cases and controls by years since first project-based potential agent use, corresponding ORs and 95% CIs (excludes 3 controls with no technical background but without a project history)

Agent/Years since first use	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
Tetrachloroethylene				
Unexposed	6	52	1.0	
< 10	0	2	0.0	0.0-156.4
≥ 10	0	2	0.0	0.0-175.5
Chloroethanes				
Unexposed	4	36	1.0	
< 10	0	8	0.0	0.0-6.0
≥ 10	2	12	3.2	0.2-43.8
Brominated hydrocarbons				
Unexposed	5	32	1.0	
< 10	1	10	0.7	0.1-6.9
≥ 10	0	14	0.0	0.0-2.9
Bromoethanes				
Unexposed	6	46	1.0	
< 10	0	3	0.0	0.0-91.1
≥ 10	0	7	0.0	0.0-7.8
Freons				
Unexposed	6	54	1.0	
< 10	0	1	0.0	0.0-389.1
≥ 10	0	1	0.0	0.0-389.1
Volatile aliphatic hydrocarbons (solvents)				
Unexposed	2	20	1.0	
< 10	0	12	0.0	0.0-6.4
≥ 10	4	24	4.2	0.4-47.0
<i>N</i> -hexane				
Unexposed	2	28	1.0	
< 10	0	8	0.0	0.0-9.0
≥ 10	4	20	∞	0.6-∞
Catalysts				
Unexposed	2	21	1.0	
< 10	0	11	0.0	0.0-7.8
≥ 10	4	24	4.6	0.4-54.0
Organometallics				
Unexposed	3	33	1.0	
< 10	0	6	0.0	0.0-11.4
≥ 10	3	17	4.5	0.4-50.6

Table 20. Number of benign intracranial tumor cases and controls by years since first project-based potential agent use, corresponding ORs and 95% CIs (excludes 3 controls with no technical background but without a project history)

Agent/Years since first use	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
<b>Inorganic metallics</b>				
Unexposed	2	21	1.0	
< 10	0	11	0.0	0.0-7.8
≥ 10	4	24	2.4	0.4-54.0
<b>Acrylonitrile</b>				
Unexposed	6	51	1.0	
< 10	0	1	0.0	0.0-389.1
≥ 10	0	4	0.0	0.0-18.2
<b>Butadiene</b>				
Unexposed	5	53	1.0	
< 10	1	2	4.8	0.4-53.3
≥ 10	0	1	0.0	0.0-545.5
<b>Glycidol</b>				
Unexposed	6	52	1.0	
< 10	0	3	0.0	0.0-22.5
≥ 10	0	1	0.0	0.0-351.0
<b>Other amines</b>				
Unexposed	2	23	1.0	
< 10	1	12	0.9	0.1-10.7
≥ 10	3	21	2.4	0.3-19.9
<b>Reactive monomers</b>				
Unexposed	2	21	1.0	
< 10	0	11	0.0	0.0-7.8
≥ 10	4	24	4.6	0.4-54.0
<b>Styrene</b>				
Unexposed	5	39	1.0	
< 10	1	4	2.1	0.2-23.1
≥ 10	0	13	0.0	0.0-3.7
<b>Vinyl chloride</b>				
Unexposed	6	52	1.0	
< 10	0	0	—	—
≥ 10	0	4	0.0	0.0-18.2
<b>Other types of known chemicals</b>				
Unexposed	2	20	1.0	
< 10	0	12	0.0	0.0-6.4
≥ 10	4	24	4.2	0.4-47.0

Table 20. Number of benign intracranial tumor cases and controls by years since first project-based potential agent use, corresponding ORs and 95% CIs (excludes 3 controls with no technical background but without a project history)

Agent/Years since first use	No. of subjects		OR	95% CI
	Cases N=6	Controls N=56		
Chemicals of unknown type				
Unexposed	2	22	1.0	
< 10	0	13	0.0	0.0-4.1
≥ 10	4	21	∞	0.5-∞

Table 21. Distribution of benign intracranial; tumor cases and controls by project-based potential use of ionizing radiation (IR-PB) and *n*-hexane (NH-PB) and by self-reported exposure to organometallics (OM-SR) and other amines (OA-SR)

IR-PB	NH-PB	OM-SR	OA-SR	Cases	Controls
<b>No use of or exposure to any of the four agents</b>					
-	-	-	-	2	25
<b>Used/exposed to all four agents</b>					
+	+	+	+	2	4
<b>Used/exposed to any three of the four agents</b>					
+	+	+	-	0	1
+	+	-	+	0	1
+	-	+	+	0	0
-	+	+	+	0	6
<b>Used/exposed to any two of the four agents</b>					
+	+	-	-	0	4
+	-	+	-	0	1
+	-	-	+	0	0
-	+	+	-	0	4
-	+	-	+	2	3
-	-	+	+	0	0
<b>Used/exposed to only one of the four agents</b>					
+	-	-	-	0	0
-	+	-	-	0	5
-	-	+	-	0	2
-	-	-	+	0	0

Table 22. Concordance between self-reported exposure and project-based potential use for 15\* agents of interest among benign intracranial tumor cases and controls

Agent	Cases N=6				Controls N=59			
	Concordant		Discordant		Concordant		Discordant	
	No.	%	No.	%	No.	%	No.	%
Ionizing radiation	6	100	0	0	46	78	13	22
Energy beam	5	83	1	17	58	98	1	2
Aromatic hydrocarbons	6	100	0	0	48	81	11	19
Halogenated hydrocarbons	5	83	1	17	42	71	17	29
Chlorinated hydrocarbons	5	83	1	17	42	71	17	29
Methylene chloride	4	67	2	33	43	73	16	27
Volatile hydrocarbons	6	100	0	0	42	71	17	29
<i>N</i> -hexane	4	67	2	33	35	59	24	41
Catalysts	4	67	2	33	41	69	18	31
Organometallics	5	83	1	17	41	69	18	31
Inorganic metalics	4	67	2	33	30	51	29	49
Acrylonitrile	5	83	1	17	52	88	7	17
Nitrosoamines	6	100	0	0	56	95	3	5
Other amines	6	100	0	0	39	66	20	34
Vinyl chloride	6	100	0	0	51	86	8	14

\* Because the questionnaire did not assess nonionizing radiation exposure, apart from the energy beam, at the ARC, this category is not included.

APPENDIX A

QUESTIONNAIRE FOR CURRENT AND FORMER EMPLOYEES  
AT THE 500 BUILDING COMPLEX OF THE AMOCO  
RESEARCH CENTER IN NAPERVILLE, ILLINOIS

QUESTIONNAIRE FOR CURRENT AND FORMER  
EMPLOYEES AT THE 500 BUILDING COMPLEX  
OF THE AMOCO RESEARCH CENTER IN  
NAPERVILLE, ILLINOIS

By:

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Subject: \_\_\_\_\_ SSN: \_\_\_\_\_

Respondent (if other): \_\_\_\_\_ Relationship: \_\_\_\_\_

Record of Contact(s):

Telephone No.: \_\_\_\_\_ Date: \_\_\_\_\_ Init.: \_\_\_\_\_

Telephone No.: \_\_\_\_\_ Date: \_\_\_\_\_ Init.: \_\_\_\_\_

Telephone No.: \_\_\_\_\_ Date: \_\_\_\_\_ Init.: \_\_\_\_\_

Case-control Study Questionnaire

Subject (name) \_\_\_\_\_ SSN: \_\_\_\_\_

Respondent name (if other than subject) \_\_\_\_\_

Respondent's relation to subject \_\_\_\_\_  
(e.g., spouse, child, coworker, supervisor)

[ Interviewer (name) \_\_\_\_\_ Date of interview \_\_\_\_\_ ]

Interviewer should explain that the questions to be asked will be grouped into 5 areas: ARC Work History; Non-ARC Amoco Work History; Non-Amoco Work History, Educational Background and Medical History.

Job history at ARC-Naperville (refer to print-out from work history file and complete attached form.) FIRST, the interviewer should verify the start and end dates of employment at the ARC. THEN, the interviewer should ask about each job the employee held. A "new job" corresponds to a change in job title, type of research project, agents, or location of work within the ARC. If the job involved laboratory work, the interviewer should ask the number of hours per day/week/month spent in the lab and the number of hours per day/week/month spent working with chemical or physical agents in the lab. Within each job, the interviewer should ask what chemical or physical agents the employee used most often in his/her work. All agents named should be recorded--using the back of the form if necessary. After the respondent has supplied a list of agents in this free recall format, the interviewer should ask specifically if the employee ever worked with any of the agents, or classes of agents, listed on the next page of the questionnaire. If you are unsure about how to classify a specific agent named by the respondent, please record the agent named as precisely as possible at the bottom of the form. If the answer, for any agent, is "yes," the interviewer should obtain the time period of use, enter the agent on the preceding table in the appropriate time period, request an estimate of the frequency with which the agent was used; for example, daily (for some time each day), at least weekly, at least monthly, or intermittently (less often than monthly) and ask for an estimate of the average volume of the agent used on each occasion. (If no average is provided ask for maximum and minimum volumes).

Non-ARC Amoco Employment History (apply instructions above).

Non-Amoco Employment History (apply instructions above except employment dates given should be recorded exactly as given; they cannot be verified at this time).

Educational Background.

Medical and Personal History Questions - see last 2 pages.

I. ARC EMPLOYMENT HISTORY

List all periods of ARC employment dates (list all periods):

From:                      To:                      Average number of hours per week

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

FROM (date)	TO (date)	BLDG/FLOOR/ROOM	JOB TITLE

Unusual events might include fires, spills, etc.

Involved in "hands-on work"?

PROJECT	LAB/PILOT PLAN Y/N	IN LAB/PP ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M
	Y/N	IN LAB ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M
	Y/N	IN LAB ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M
	Y/N	IN LAB ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M
	Y/N	IN LAB ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M
	Y/N	IN LAB ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M
	Y/N	IN LAB ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M
	Y/N	IN LAB ____ HRS D/W/M	WORKING WITH AGENTS ____ HRS D/W/M

NTS  
NTS  
NTS  
NTS  
NTS  
NTS  
NTS  
NTS  
NTS

SUPERVISOR	AGENTS	ANY UNUSUAL EVENT

I. ARC EMPLOYMENT HISTORY (continued)

AGENT	FROM (date)	TO (date)	PROJECT/NATURE OF WORK/SUPV
Ionizing radiation			
Energy beam			
Aromatic hydrocarbons*			
Methylene chloride			
Other chlorinated hydrocarbons*			
Other halogenated hydrocarbons*			
N-hexane			
Other volatile hydrocarbons*			
Organo-metallics*			
Elemental metallics			
Acrylonitrile			
Vinyl chloride			
Formaldehyde			
Nitroso compounds*			
Other amines			

\* Refer to Agents list



II. NON-ARC AMOCO EMPLOYMENT HISTORY

Inclusive non-ARC Amoco employment dates (list all periods):

From:

To:

- 1. \_\_\_\_\_
- 2. \_\_\_\_\_
- 3. \_\_\_\_\_

FROM (date)	TO (date)	LOCATION	JOB TITLE

<b>DUTIES / TASKS</b>	<b>AGENTS</b>

## II. NON-ARC AMOCO EMPLOYMENT HISTORY (continued)

AGENT	FROM (date)	TO (date)	PROJECT/NATURE OF WORK/SUPV
Ionizing radiation			
Nonionizing rad			
Aromatic hydrocarbons*			
Methylene chloride			
Other chlorinated hydrocarbons*			
Other halogenated hydrocarbons*			
N-hexane			
Other volatile hydrocarbons*			
Organo-metallics*			
Elemental metallics			
Acrylonitrile			
Vinyl chloride			
Formaldehyde			
Nitroso compounds*			
Other amines			

\* Refer to Agents list





JOB TITLE	DUTIES	AGENTS

III. NON-AMOCO EMPLOYMENT HISTORY (continued)

AGENT	FROM (date)	TO (date)	COMPANY	LOCATION
Ionizing radiation				
Energy Nonionizing rad				
Aromatic hydrocarbons*				
Methylene chloride				
Other chlorinated hydrocarbons*				
Other halogenated hydrocarbons*				
N-hexane				
Other volatile hydrocarbons*				
Organo-metallics*				
Elemental metallics				
Acrylonitrile				
Vinyl chloride				
Formaldehyde				
Nitroso compounds*				
Other amines				

\* Refer to Agents list

IV. EDUCATIONAL BACKGROUND

How many years of education did you complete? \_\_\_\_\_

[NOTE: Interviewer should ask the following questions of anyone completing 12 or more years of education.]

List all periods of post-high school education, including the years and school attended, your major and any chemical or physical agents or processes with which you worked in a laboratory setting.

YEARS ATTENDED		NAME OF SCHOOL OR INSTITUTION	MAJOR SUBJECTS
From:	To:		

What was the title of your Master's thesis? \_\_\_\_\_

What was the title of your doctoral dissertation? \_\_\_\_\_



IF LAB, HRS per D/W/M

IN LAB <u>    </u> HRS D/W/M	WORKING WITH AGENTS <u>    </u> HRS D/W/M	CHEMICAL OR PHYSICAL AGENTS
IN LAB <u>    </u> HRS D/W/M	WORKING WITH AGENTS <u>    </u> HRS D/W/M	
IN LAB <u>    </u> HRS D/W/M	WORKING WITH AGENTS <u>    </u> HRS D/W/M	
IN LAB <u>    </u> HRS D/W/M	WORKING WITH AGENTS <u>    </u> HRS D/W/M	
IN LAB <u>    </u> HRS D/W/M	WORKING WITH AGENTS <u>    </u> HRS D/W/M	
IN LAB <u>    </u> HRS D/W/M	WORKING WITH AGENTS <u>    </u> HRS D/W/M	

## IV. EDUCATIONAL BACKGROUND (continued)

Did you work with any of the following agents:

AGENT	FROM (date)	TO (date)	PROJECT/NATURE OF WORK
Ionizing radiation			
Energy Nonionizing rad			
Aromatic hydrocarbons*			
Methylene chloride			
Other chlorinated hydrocarbons*			
Other halogenated hydrocarbons*			
N-hexane			
Other volatile hydrocarbons*			
Organo-metallics*			
Elemental metallics			
Acrylonitrile			
Vinyl chloride			
Formaldehyde			
Nitroso compounds*			
Other amines			

\* Refer to Agents list



V. MEDICAL HISTORY\*

1. Have you ever had diagnostic x-rays (other than routine dental x-rays) of your head and/or neck?  
When ? (list all occurrences)

YES / NO

Physician/Hospital & City/State

---



---

2. Have you ever had a head injury that:  
(a) caused a concussion?  
When ? (list all occurrences)

YES / NO

Physician/Hospital & City/State

---



---

(b) caused unconsciousness?  
When? (list all occurrences)

YES / NO

Physician/Hospital & City/State

---



---

3. Have you ever been told that you have a seizure disorder or been diagnosed with epilepsy?  
When? (list all occurrences)

YES / NO

Physician/Hospital & City/State

---



---

4. Have you ever taken any anticonvulsant medication ?  
(e.g., dilantin, depakote or tegretol)  
When? (list all periods)

YES / NO

Physician/Hospital & City/State

---



---

5. Have you ever had meningitis?  
When? (List all occurrences)

YES / NO

Physician/Hospital & City/State

---



---

6. Have you noticed (or had diagnosed) any hearing loss?  
When did it begin?

YES / NO

Physician/Hospital & City/State

---



---

7. Have you ever taken any of the following drugs?  
(e.g., refer to Drugs list)  
List all drugs and periods

YES / NO

drug period

---



---

8. Have you ever worked in a setting where the noise level interfered with routine conversation?

YES / NO

Employer

---



---

9. Were you ever required to wear hearing protection as a part of your job? YES / NO

List all time periods and jobs

\_\_\_\_\_  
\_\_\_\_\_

10. Have you ever used a cellular telephone? YES / NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

11. Have you ever operated an amateur (ham) radio? YES / NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

12. Have you ever used pesticides in your home?(herbicides, weedkillers, insecticides, etc.) YES/NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

What kind(s)?

\_\_\_\_\_  
YES/NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

\_\_\_\_\_  
YES/NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

13. Have you ever applied pesticides professionally? YES/NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

What kind(s)?

14. Have you ever stripped or refinished furniture in your home? YES/NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

What products did you use?

15. Have you ever stripped or refinished furniture professionally? YES/NO      Earliest year of use:      Years of use:      Frequency/Times used: \_\_\_\_\_ per D/W/M/Y

What products did you use?

16. Were you ever required to wear a radiation badge as part of your job? YES/NO

List all time periods and jobs

\_\_\_\_\_  
\_\_\_\_\_

APPENDIX B  
ADDITIONAL SUBJECT EXPOSURE DATA

## SUMMARY

In response to questions raised by our original analyses of the case-control study of intracranial tumors among workers at the Amoco Research Center 500 building complex (C500), the UAB project staff examined patterns of potential and self-reported exposures to specific catalysts and amines other than nitroso-amines among cases and controls. This report summarizes the results of those analyses.

## BACKGROUND

Workers at the ARC handled many hundred of individual agents (Lees & Breysse, 1999). During our initial analyses (Delzell et al, 1999), we observed an association between self-reported exposures to catalysts, especially organometallic (OM) catalysts, and gliomas and an association between other amine (OA) exposure and gliomas. To attempt to clarify the nature of the association, we asked Johns Hopkins University (JHU) researchers to provide the portion of their exposure data base pertaining to project-based use of specific agents, which they had classified in these categories.

## METHODS

We linked the new JHU data base by project number into our existing data base that listed the number of hours accrued by subjects in various projects. This data base also contained an indicator, derived from subject interviews, of whether subjects worked hands-on with chemicals, either directly or in a supervisory role. Subjects who (1) worked on a project entailing work with a specific agent and (2) reported hands-on work were counted as potentially exposed to agents used in the projects to which they were assigned.

Also, UAB one UAB research assistant searched through the interview schedules which recorded subjects' responses to questions involving agent exposures at the ARC. The research assistant recorded every individual exposure reported by a subject to questions involving the use

of organometallic agents, inorganic metallic (MET) agents and amines, other than nitroso-compounds. One project manager reviewed and corrected these abstracts and assigned agent numbers from the JHU data base corresponding to the chemicals named. We then entered the abstracts into a new UAB data base, and we linked the abstract data by agent number to the JHU data base which, in addition to classifying agents, identified synonyms for various chemical names.

We used SAS to develop tables of frequencies of case and control exposure to each individual agent in the categories, OM, MET and OA.

## RESULTS

### Project-based data.

The number of subjects exposed to any single agent was small. In the glioma series, no more than two of the six glioma cases or 14 of the matched controls were potentially exposed in the project-based data to a specific OM, MET or OA (tables 1-3). In these data, one glioma case as compared to no corresponding control was potentially exposed to inorganic chromium. When looking within matched sets, no case had more than three controls (from a maximum of 10 controls per set) exposed to an agent (tables 4-6).

Similarly, among the benign intracranial tumor set, no more than three cases or 18 controls were potentially exposed to a specific OM, MET or OA (tables 7-9). In comparison to the result seen within the glioma series for elemental chromium, in the benign series no case and four controls had potential exposure to this element. Four cases were classified as potentially exposed to at least one of OM, MET or OA. However, within matched sets no case had more than three controls exposed to the same agent (tables 10-12).

### Self-reported data

Only one case reported an exposure to any organometallic or other amine and no more than two controls reported such an exposure (tables 13, 15). Two cases reported being exposed to titanium dichloride and magnesium chloride as compared to four controls and no control, respectively (table 14). Within the matched sets of the four cases who reported any exposure to an OM, MET or OA, all had one or no exposed control to an agent (tables 16-18).

Among benign intracranial tumor sets, only one case reported being exposed to any given agent, whereas three to four controls occasionally reported an exposure (tables 19-21). Three cases reported an exposure to one or more individual chemicals and, within their matched sets, no or one control reported such an exposure (tables 22-24).

### DISCUSSION

- No more than two cases were exposed to any specific agent, either within the project-based data or the self-reported data. The number of controls reporting an individual exposure also was small, never exceeding 14 (25% of possible controls). Data for self-reported chemical exposures are even more sparse. Thus, the information that we can obtain from these data is limited.
- Despite the limitations, some look interesting. For example, one glioma case as compared to no corresponding control was potentially exposed, in project-based data, to inorganic chromium; whereas, in the benign series no case and four controls had potential chromium exposures. A similar but less striking pattern exists for cobaltous bromide, to which two glioma cases and one associated control were exposed, as compared to no benign intracranial tumor case and five controls.
- The chemical composition of some of the agents remains unknown, at least to the UAB project staff. For example, while AMSAC-1500 catalyst, is classified as an inorganic metallic

catalyst, we are unable to identify the metal associated with this chemical. We have similar problems with other inorganic catalysts, such as CINMAC II, ZSM-5, mineral colloid BP and with amines, such as HiForm-160. This limits our ability to suggest any meaningful grouping of the agents.

- Some confusion remains regarding the classification of compounds containing acetate.

Without exception, these compounds were named as organometallic catalysts in responses to our questionnaire. To be consistent, we reported them as inorganic catalysts in questionnaire-based results, according to the JHU classification scheme.

## REFERENCES

1. Delzell E, Beall C, Rodu B, Sathiakumar N, Lees PSJ, Breysse PN. A case-control study of intracranial tumors among Amoco Research Center employees who worked in the 500 building complex. Report dated October 15, 1999.
2. Lees PSJ, Breysse PN. Exposure assessment for the case-control study of risk for intracranial tumors. Report dated October, 1999.

Table 1. Number of glioma cases and controls by project-based potential use (weighted exposure >0) of organometallic catalysts.

	Agent no.	Cases	Controls
triisobutyl aluminum	112	1	9
triethyl aluminum	113	2	14
diethyl zinc	1582	1	3
<i>n</i> -butyl lithium	1734	0	8
dibutyl tin maleate	1804	0	3
butyl stannic anhydride	1836	0	3
( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> Mg(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> Al [Magala 7.5-E]	2239	1	0
tetrabutyltin	2406	0	2
diethylaluminum chloride	311	2	11
ethylaluminum sesquichloride	312	1	14
tri- <i>n</i> -butylvanadate	3769	0	5
ethylaluminum dichloride [EADC]	413	1	6
bis(tri- <i>n</i> -butyltin) sulfide	419	2	11
methylcyclopentadienylmanganese tricarbonyl [CI-2]	5646	0	1
dicobalt octacarbonyl	6248	0	1
dimanganese decacarbonyl	6252	0	1
pentacarbonyl (I) nitrite	6254	0	1
chlorocarbonylbis(triphenyl phosphino)iridium (I)	6312	0	1
triphenylantimony sulfide	738	1	3
triphenylantimony oxide [TPAO]	752	1	3
diisobutylaluminum chloride	903	0	2

Table 2. Number of glioma cases and controls by project-based potential use (weighted exposure >0) of inorganic metallic catalysts.

	Agent no.	Cases	Controls
magnesium montmorillonite gelling and suspending agent [Ben-a-gel]	1077	1	11
organoclay gelling agent [Bentone LT]	1078	1	11
dimethyl dioctadecyl ammonium hectorite [Bentone 38]	1115	1	11
dimethyl dioctadecyl ammonium montmorillonite [Bentone 18C]	1117	1	11
CrO <sub>3</sub> -SiO <sub>2</sub> [chromium catalyst]	115	0	4
mineral colloid BP	1223	1	11
hydrophobic formed silicon dioxide [Silanox 101]	1269	1	11
potassium titanate	1333	1	11
Amoco Brown beta-TiCl <sub>3</sub> catalyst	1366	1	11
silicon tetrachloride	1381	1	13
purple catalyst [Hg3048-126-1]	1388	1	11
alumina [Al <sub>2</sub> O <sub>3</sub> ]	1584	0	11
boron trifluoride	1596	0	5
nickel	1638	0	6
titanium dioxide	1788	1	12
antimony [Sb]	1811	0	7
tin [Sn]	1812	0	4
nickel oxide [NiO]	2065	0	1
zinc borate	2089	1	11
Al <sub>2</sub> O <sub>3</sub> -H <sub>2</sub> O	2108	1	11
tungsten hexachloride	2408	0	2
zinc	2413	0	5
molybdenum oxide on aluminum silicate catalyst	2451	0	2
cobalt [Co]	2473	1	7
chromium [Cr]	2475	2	0
molybdenum	2477	0	4
manganese [Mn]	2541	0	3
potassium	2607	0	5
AMSAC-1500 catalyst	2669	2	4
antimony tris-butoxide	2688	1	7
antimony triacetate	2703	0	3
copper aluminum borate	2748	0	1
palladium	2754	0	4
ZSM-5	2857	0	3
NaY [LZY-52]	2860	1	2
HY [LZY-20; LZY-82]	2861	1	1
zinc dialkyl dithiophosphate [ZDDP]	2932	1	8
copper	2946	0	3

Table 2. Number of glioma cases and controls by project-based potential use (weighted exposure >0) of inorganic metallic catalysts.

	Agent no.	Cases	Controls
lead	2954	0	3
lead oxide	3013	0	3
boron trifluoride etherate	3025	0	4
vanadium oxytrichloride	310	0	2
platinum	3227	0	3
bismuth	3244	0	2
yttrium	3248	0	2
AMSAC-2400 catalyst	3254	0	1
Davidson CBZ-1 equilibrium catalyst	3291	0	2
Whiting catalyst	3310	0	1
neodymium [Nd]	3316	0	2
cerium [Ce]	3317	0	1
lanthanum [La]	3318	0	4
CoMo ultracracking catalyst	3348	0	1
tungsten	3356	0	1
iron	336	0	5
cobaltous bromide [CoBr <sub>2</sub> -6H <sub>2</sub> O]	3378	2	1
Pd/C catalyst	3424	0	5
zinc dithiophosphates [ZDP]	3525	0	9
Engelhard P-5 catalyst [monolith VOC destruction catalyst]	3542	0	1
AMSAC-5397 catalyst [Amoco molecular sieve alkylation catalyst 5397]	3549	0	2
sample of grey deposit from Geel plant [metal terephthalic acid salts]	3569	1	4
copper chromite catalyst	4062	0	2
silver [Ag]	4096	0	1
titanium trichloride	411	2	11
magnesium hydroxide	417	1	6
vanadium	421	1	2
zirconium	422	1	3
titanium tetrachloride	435	1	6
tellurium dioxide	4523	0	1
silver nitrate	4533	0	5
nickel acetate	4624	0	1
Ni/kieselguhr catalyst [Girdler G-47A]	5845	0	4
CINMAC II [AM2-6.5 catalyst]	5876	1	6
red iron oxide	6005	0	2
chrome oxide green	6008	0	2
tetrakis(triphenylphosphio) platinum (0) [(Ph <sub>3</sub> P) <sub>4</sub> Pt]	6295	0	1
cuprous peroxide	6319	0	1
aluminum chloride	639	1	6

Table 2. Number of glioma cases and controls by project-based potential use (weighted exposure >0) of inorganic metallic catalysts.

	Agent no.	Cases	Controls
dicumyl peroxide on Burgess KE clay [Di-Cup 40 KE]	6417	1	11
aluminum isopropoxide	650	1	6
antimony trioxide	75	0	3
zinc stearate	807	0	8
magnesium ethoxide [Mg(Oet) <sub>2</sub> ]	848	2	8
copper sulfate	948	1	11

Table 3. Number of glioma cases and controls by project-based potential use (weighted exposure >0) of other amines.

	Agent no.	Cases	Controls
2-,2-,6-,6-tetramethylpiperidine nitroxide	1015	1	11
pyridine N-oxide [PNO]	1019	1	11
3-picoline N-oxide [3-picNO]	1021	1	11
4-picoline N-oxide [4-picNO]	1023	1	11
quinoline N-oxide [QNO]	1025	1	11
4-nitropyridine N-oxide [NPNO]	1032	1	11
bis-2-ethoxyethylamine [b-2-EEA]	1279	1	11
diethylene triamine [DETA]	1413	1	14
1-,3-,5-tris(3-,5-di-t-butyl-4-hydroxybenzyl)-s-triazine-2/4/6(1H/3H/5H)-trione [Irganox 3114]	1468	1	11
tetramethylethylene diamine [TMEDA]	1736	0	8
methylene diphenyldiisocyanate [DMI]	1780	0	6
4-,4'-diphenylether diisocyanate [ODI]	1782	0	6
diethylamine	1897	0	2
N-beta-(aminoethyl)-gamma-aminopropyltrimethoxysilane [A-1120]	2123	1	11
triethylamine	22	0	8
2-,2-bis(4-aminophenoxphenyl)propane [BAPP]	2278	0	3
4-4'-oxybisaniiline [OBA]	2290	0	4
diethyl N-N-bis(2-hydroxyethyl)aminoethyl phosphate [Fryol HMP]	2318	0	2
p-phenylenediamine [PDA]	2328	0	4
hexamethoxymethylmelamine [Cymel 300]	2329	0	2
hexamethylenetetramine [hexa]	2377	0	2
ethylene diamine tetraacetic acid [EDTA]	2565	0	5
2-,5-dimercapto 1-3-4-thiadiazole [DMTD]	2919	0	1
2-mercapto-5-t-dodecyl 5-t-dodecyldithio-1-,3-,4-thiadiazole [TSH]	2921	0	1
2-,5-bis (t-dodecyldithio)1-,3-,4-thiadiazole [TSR]	2924	0	1
Mannich A-749 [A-749; engine oil dispersant additive]	3092	0	3
HiForm-160 [A-160]	3168	0	6
tetraethylene pentamine [TEPA]	3417	1	8
hexamethylenediamine [HMDA]	3615	0	6
sec-arylamine antioxidant [Irganox L-57]	3626	1	9
coconut amines [Armeen CD]	3631	0	5
hydrogenated tallowamine [Armeen HT]	3637	0	5
tallowamine [Armeen T-97]	3639	0	5
N-tallow-1-,3-diaminopropane [Duomeen T]	3644	0	5
benzylphenylamine [BPA]	3858	0	1
benzalaniline [BZLA]	3860	0	1

Table 3. Number of glioma cases and controls by project-based potential use (weighted exposure >0) of other amines.

	Agent no.	Cases	Controls
diphenylamine [DPA]	4038	0	11
polybutene based Mannich gasoline additive [A-595]	4463	0	1
tris-2-hydroxyethyl isocyanate [THEIC]	4564	0	1
aminopropyl triethoxy silane	5380	0	4
<i>m</i> -phenylene diamine [m-PDA]	5723	0	1
bisaniline-P [BAP]	5724	0	1
3-,5-diamino- <i>t</i> -butyl benzene [3-,5-DATB]	5729	0	1
aminopropylmorpholine [APM]	6068	0	4
ethylene diamine	643	1	6
2-,4-,6-collidine [gamma collidine]	744	1	11
tris-(dimethylamino)phosphorylsulfide [TDPS]	767	1	3
tri- <i>n</i> -butylamine [TBA]	771	1	3
2-,6-dimethyl pyridine N-oxide [2-,6-lutidine N-oxide; N-luto]	782	1	11
2-,2-,6-,6-tetramethyl piperidine [TMPip]	872	1	11
ethyl <i>p</i> -anisate [EA]	880	1	4

Table 4. Organometallic catalyst exposure (weighted exposure>0) for glioma cases and their controls, project-based.

Case	Organometallic exposures	Agent number	Exposed controls in risk set
701	(n-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> Mg (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> Al	2239	0
	triphenyl antimony oxide [TPAO]	752	0
	bis (tri-n-butyl tin) sulfide	419	1
	diethyl zinc	1582	0
	diethyl aluminum chloride	311	1
	ethyl aluminum sesquichloride	312	1
	triethyl aluminum	113	1
	triphenyl antimony sulfide	738	0
1001	ethyl aluminum dichloride [EADC]	413	0
	bis (tri-n-butyl tin) sulfide	419	1
	diethyl aluminum chloride	311	1
	triethyl aluminum	113	3
	triisobutyl aluminum	112	3

Table 5. Inorganic metallic catalyst exposure (weighted exposure > 0) for glioma cases and their controls, project-based data.

Case	Inorganic metallic exposures	Agent number	Exposed controls in risk set
701	Al <sub>2</sub> O <sub>3</sub> -3H <sub>2</sub> O	2108	1
	Amoco Brown beta TiCl <sub>3</sub> catalyst	1366	1
	magnesium montmorillonite gelling & suspending agent [Ben-a-gel]	1077	1
	dimethyl dioctadecyl ammonium montmorillonite [Bentone 18C]	1117	1
	dimethyl dioctadecyl ammonium hectorite [Bentone 38]	1115	1
	organoclay gelling agent [Bentone LT]	1078	1
	dicumyl peroxide on Burgess KE clay [Di-Cup 40 KE]	6417	1
	magnesium ethoxide [Mg(OEt) <sub>2</sub> ]	848	1
	silicon tetrachloride	1381	1
	hydrophobic formed silicon dioxide [Silanox 101]	1269	1
	zinc borate	2089	1
	copper sulfate	948	1
	magnesium hydroxide	417	1
	mineral colloid BP	1223	1
	potassium titanate	1333	1
	purple catalyst [Hg 3048-126-1]	1388	1
	titanium dioxide	1788	1
	titanium trichloride	411	1
801	AMSAC 1500 catalyst	2669	0
	chromium [Cr]	2475	0
	cobaltous bromide	3378	0
901	AMSAC 1500 catalyst	2669	1
	chromium [Cr]	2475	0
	antimony tris-butoxide	2688	1
	cobaltous bromide	3378	0
	sample of grey deposit from Geel	3569	1
	zinc dialkyl dithiophosphate	2932	0

Table 5. Inorganic metallic catalyst exposure (weighted exposure > 0) for glioma cases and their controls, project-based data.

Case	Inorganic metallic exposures	Agent number	Exposed controls in risk set
1001	CINMAC II [AM2-6.5 catalyst]	5876	1
	cobalt	2473	2
	HY (LZY-20; LZY-82)	2861	0
	magnesium ethoxide [Mg(OEt) <sub>2</sub> ]	848	1
	NaY [LZY-52]	2860	0
	titanium tetrachloride [TiCl <sub>4</sub> ]	435	1
	aluminum chloride	639	1
	aluminum isopropoxide	650	1
	magnesium hydroxide	417	1
	titanium trichloride	411	1
	vanadium	421	0
	zirconium	422	0

Table 6. Other amine exposure (weighted exposure > 0) for glioma cases and their controls, project-based data.

Case	Other amine exposures	Agent number	Exposed controls in risk set	
701	2-,2-,6-,6-tetramethyl piperidine	872	1	
	2-,2-,6-,6-tetramethylpiperidine nitroxide	1015	1	
	2-,6-lutidine <i>n</i> -oxide	782	1	
	3-picoline <i>n</i> -oxide	1021	1	
	4-picoline <i>n</i> -oxide	1023	1	
	4-nitropyridine <i>n</i> -oxide	1032	1	
	collidine	744	1	
	Irganox 3114 [1-,3-,5-tris(3-,5-di- <i>t</i> -butyl-4-hydroxybenzyl)- <i>s</i> -triazine-2/4/5(1H/3H/5H)trione	1468	1	
	<i>n</i> -beta-(aminoethyl)-gamma-aminopropyltrimethoxy-silane	2123	1	
	bis-2-ethoxyethylamine	1279	1	
	diethylene triamine	1413	1	
	ethyl <i>p</i> -anisate	880	0	
	pyridine <i>n</i> -oxide	1019	1	
	quinoline <i>n</i> -oxide	1025	1	
	tri- <i>n</i> -butylamine	771	0	
	tris-(dimethylamino)phosphoryl- sulfide	767	0	
	901	Irganox L-57 (sec-arylamine antioxidant)	3626	2
		tetraethylene pentamine	3417	2
1001	ethylene diamine	643	1	

Table 7. Number of benign intracranial tumor cases and controls by project-based potential use (weighted exposure >0) of organometallic catalysts.

	Agent no.	Cases	Controls
triisobutyl aluminum	112	0	11
triethyl aluminum	113	1	18
dibutyltin diacetate	129	0	1
diethyl zinc	1582	1	9
<i>n</i> -butyl lithium	1734	0	5
dibutyl tin maleate	1804	0	2
butyl stannic anhydride	1836	1	7
( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> Mg(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> Al [Magala 7.5-E]	2239	1	5
tetrabutyltin	2406	0	1
diethylaluminum chloride	311	1	16
ethylaluminum sesquichloride	312	2	18
tri- <i>n</i> -butylvanadate	3769	1	4
ethylaluminum dichloride [EADC]	413	0	7
bis(tri- <i>n</i> -butyltin) sulfide	419	1	16
nickel carbonyl	4271	0	1
dicobalt octacarbonyl	6248	0	2
dimanganese decacarbonyl	6252	0	2
pentacarbonyl manganese (I) nitrite	6254	0	2
chlorocarbonylbistriphenyl phosphinoiridium (I)	6312	0	2
triphenylantimony sulfide	738	0	5
triphenylantimony oxide [TPAO]	752	0	5
diisobutylaluminum chloride	903	2	2

Table 8. Number of benign intracranial tumor cases and controls by project-based potential use (weighted exposure >0) of inorganic metallic catalysts.

	Agent no.	Cases	Controls
magnesium montmorillonite gelling and suspending agent [Ben-a-gel]	1077	1	16
organoclay gelling agent [Bentone LT]	1078	1	16
dimethyl dioctadecyl ammonium hectorite [Bentone 38]	1115	1	16
dimethyl dioctadecyl ammonium montmorillonite [Bentone 18C]	1117	1	16
CrO <sub>3</sub> -SiO <sub>2</sub> [chromium catalyst]	115	0	4
mineral colloid BP	1223	1	16
hydrophobic formed silicon dioxide [Silanox 101]	1269	1	16
potassium titanate	1333	1	16
stannous octoate	135	0	1
Amoco Brown beta-TiCl <sub>3</sub> catalyst	1366	1	16
stannous oleate	137	0	1
silicon tetrachloride	1381	1	16
purple catalyst [Hg3048-126-1]	1388	1	16
catalyst G-4	139	0	1
alumina [Al <sub>2</sub> O <sub>3</sub> ]	1584	0	7
boron trifluoride	1596	0	6
nickel	1638	1	6
titanium dioxide	1788	1	16
antimony [Sb]	1811	1	9
tin [Sn]	1812	1	3
nickel oxide [NiO]	2065	0	5
zinc borate	2089	1	16
Al <sub>2</sub> O <sub>3</sub> -H <sub>2</sub> O	2108	1	16
tungsten hexachloride	2408	1	16
zinc	2413	0	4
molybdenum oxide on aluminum silicate catalyst	2451	0	1
cobalt [Co]	2473	1	5
chromium [Cr]	2475	0	4
molybdenum	2477	1	3
antimony tristallate	26	0	1
potassium	2607	0	4
AMSAC-1500 catalyst	2669	0	6
antimony tris-butoxide	2688	1	6
antimony triacetate	2703	1	3
copper aluminum borate	2748	0	1
palladium	2754	0	3
ZSM-5	2857	1	2
NaY [LZY-52]	2860	0	1

Table 8. Number of benign intracranial tumor cases and controls by project-based potential use (weighted exposure >0) of inorganic metallic catalysts.

	Agent no.	Cases	Controls
HY [LZY-20; LZY-82]	2861	0	1
aluminum chloride/HCl mixture	2906	0	3
zinc dialkyl dithiophosphate [ZDDP]	2932	2	7
copper	2946	0	1
lead	2954	0	1
lead oxide	3013	0	2
boron trifluoride etherate	3025	0	4
vanadium oxytrichloride	310	0	3
platinum	3227	0	6
AMSAC-2400 catalyst	3254	0	2
Davidson CBZ-1 equilibrium catalyst	3291	0	1
Whiting catalyst	3310	0	1
neodymium [Nd]	3316	0	3
cerium [Ce]	3317	0	1
lanthanum [La]	3318	0	3
CoMo ultracracking catalyst	3348	0	1
tungsten	3356	0	1
iron	336	0	5
cobaltous bromide [CoBr <sub>2</sub> -6H <sub>2</sub> O]	3378	0	5
Pd/C catalyst	3424	0	4
zinc dithiophosphates [ZDP]	3525	2	6
Engelhard P-5 catalyst [monolith VOC destruction catalyst]	3542	0	4
AMSAC-5397 catalyst [Amoco molecular sieve alkylation catalyst 5397]	3549	0	1
sample of grey deposit from Geel plant [metal terephthalic acid salts]	3569	0	4
Claus alumina	3787	0	1
CoMo/alumina	3790	0	1
NiMo/alumina	3791	0	1
copper chromite catalyst	4062	0	3
silver [Ag]	4096	0	3
titanium trichloride	411	1	16
magnesium hydroxide	417	1	8
vanadium	421	1	2
zirconium	422	1	1
dinitro copper (II)	4239	0	1
iron oxynite	4249	0	1
copper nitrate	4253	0	3
titanium tetrachloride	435	0	7
silver nitrate	4533	1	4

Table 8. Number of benign intracranial tumor cases and controls by project-based potential use (weighted exposure >0) of inorganic metallic catalysts.

	Agent no.	Cases	Controls
nickel acetate	4624	0	2
Ni/kieselguhr catalyst [Girdler G-47A]	5845	0	4
CINMAC II [AM2-6.5 catalyst]	5876	0	7
tetrakis(triphenylphosphio) platinum (0) [(Ph <sub>3</sub> P) <sub>4</sub> Pt]	6295	0	2
cuprous peroxide	6319	0	2
aluminum chloride	639	0	7
dicumyl peroxide on Burgess KE clay [Di-Cup 40 KE]	6417	1	16
aluminum isopropoxide	650	0	7
antimony trioxide	75	0	2
zinc stearate	807	0	5
magnesium ethoxide [Mg(Oet) <sub>2</sub> ]	848	1	9
copper sulfate	948	1	16

Table 9. Number of benign intracranial tumor cases and controls by project-based potential use (weighted exposure >0) of other amines.

	Agent no.	Cases	Controls
2-,2-,6-,6-tetramethylpiperidine nitroxide	1015	1	16
pyridine N-oxide [PNO]	1019	1	16
3-picoline N-oxide [3-picNO]	1021	1	16
4-picoline N-oxide [4-picNO]	1023	1	16
quinoline N-oxide [QNO]	1025	1	16
4-nitropyridine N-oxide [NPNO]	1032	1	16
bis-2-ethoxyethylamine [b-2-EEA]	1279	1	16
diethylene triamine [DETA]	1413	2	16
1-,3-,5-tris(3-,5-di-t-butyl-4-hydroxybenzyl)-s-triazine-2/4/6(1H/3H/5H)-trione [Irganox 3114]	1468	1	17
tetramethylethylene diamine [TMEDA]	1736	0	5
methylene diphenyldiisocyanate [MDI]	1780	1	9
4-,4'-diphenylether diisocyanate [ODI]	1782	1	9
diethylamine	1897	0	1
N-beta-(aminoethyl)-gamma-aminopropyltrimethoxy-silane [A-1120]	2123	1	16
triethylamine	22	0	6
2-,2-bis(4-aminophenoxyphenyl)propane [BAPP]	2278	0	3
4-4'-oxybisaniiline [OBA]	2290	0	3
diethyl N-N-bis(2-hydroxyethyl)aminoethyl phosphate [Fryol HMP]	2318	0	2
p-phenylenediamine [PDA]	2328	0	2
hexamethoxymethylmelamine [Cymel 300]	2329	0	1
hexamethylenetetramine [hexa]	2377	0	1
ethylene diamine tetraacetic acid [EDTA]	2565	0	4
Mannich A-749 [A-749; engine oil dispersant additive]	3092	0	2
HiForm-160 [A-160]	3168	1	2
tetraethylene pentamine [TEPA]	3417	2	7
hexamethylenediamine [HMDA]	3615	1	6
sec-arylamine antioxidant [Irganox L-57]	3626	2	8
coconut amines [Armeen CD]	3631	1	4
hydrogenated tallowamine [Armeen HT]	3637	1	4
tallowamine [Armeen T-97]	3639	1	4
N-tallow-1-,3-diaminopropane [Duomeen T]	3644	1	4
dinitroanilinopropyl-silica	3830	0	1
diphenylamine [DPA]	4038	2	7
tris-2-hydroxyethyl isocyanate [THEIC]	4564	0	2
Mondur MR	5	0	1
aminopropyl triethoxy silane	5380	0	2
trimethylhexamethylene diamine [TMHMDA]	5625	1	4

Table 9. Number of benign intracranial tumor cases and controls by project-based potential use (weighted exposure >0) of other amines.

	Agent no.	Cases	Controls
aminopropylmorpholine [APM]	6068	1	1
triethylene tetramine	6364	0	1
ethylene diamine	643	0	8
2-,4-,6-collidine [gamma collidine]	744	1	16
tris-(dimethylamino)phosphorylsulfide [TDPS]	767	0	5
tri- <i>n</i> -butylamine [TBA]	771	0	5
2-,6-dimethyl pyridine N-oxide [2-,6-lutidine N-oxide; N-luto]	782	1	16
2-,2-,6-,6-tetramethyl piperidine [TMPip]	872	1	16
ethyl p-anisate [EA]	880	1	3

Table 10. Organometallic exposure (weighted exposure > 0) for benign intracranial tumor cases and their controls, project-based data.

Case	Organometallic exposures	Agent number	Exposed controls in risk set
401	( <i>n</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> Mg(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> Al	2239	0
	bis(tri- <i>n</i> -butyl tin)sulfide	419	2
	diethyl zinc	1582	0
	diethyl aluminum chloride	311	2
	ethyl aluminum sesquichloride	312	3
	triethyl aluminum	113	2
1201	butyl stannic anhydride	1836	4

Table 11. Inorganic metallic catalyst exposure (weighted exposure > 0) for benign intracranial tumor cases and their controls, project-based data.

Case	Inorganic metallic exposures	Agent number	Exposed controls in risk set
401	Al <sub>2</sub> O <sub>3</sub> -3H <sub>2</sub> O	2108	2
	Amoco brown beta TiCl <sub>3</sub> catalyst	1366	2
	magnesium montmorillonite gelling & suspending agent [Ben-a-gel]	1077	2
	dimethyl dioctadecyl ammonium montmorillonite [Bentone 18C]	1117	2
	dimethyl dioctadecyl ammonium hectorite [Bentone 38]	1115	2
	organoclay gelling agent [Bentone L1]	1078	2
	dicumyl peroxide on Burgess KE clay [Di-Cup 40 KE]	6417	2
	magnesium ethoxide [Mg(OEt) <sub>2</sub> ]	848	2
	silicon tetrachloride	1381	2
	hydrophobic formed silicon dioxide [Silanox 101]	1269	2
	zinc borate	2089	2
	copper sulfate	948	2
	magnesium hydroxide	417	1
	mineral colloid BP	1223	2
	potassium titanate	1333	2
	purple catalyst [Hg 3048-126-1]	1388	2
	titanium dioxide	1788	2
	titanium trichloride	411	2
	vanadium	421	0
	zirconium	422	0
1101	zinc dialkyl dithiophosphate	2932	2
	zinc dithiophosphates	3525	2
1201	cobalt	2473	3
	molybdenum	2477	2
	antimony (Sb)	1811	3
	tin (Sn)	1812	2
	ZSM-5	2857	2
	antimony triacetate	2703	1
	antimony tris-butoxide	2688	2
	nickel	1638	2
	silver nitrate	4533	3

Table 12. Other amine exposure (weighted exposure &gt; 0) for benign intracranial tumor cases and their controls, project-based data.

Case	Other amine exposures	Agent number	Exposed controls in risk set	
101	Armeen CD [coconut amines]	3631	0	
	Armeen HT [hydrogenated tallowamine]	3637	0	
	Armeen T97 [tallowamine]	3639	0	
	Irganox L-57 [sec-arylamine antioxidant]	3626	0	
	<i>n</i> -tallow-1-,3-diaminopropane	3644	0	
	aminopropylmorpholine	6068	0	
	diethylene triamine	1413	2	
	diphenylamine	4038	0	
	hexamethylenediamine	3615	1	
	tetraethylene pentamine	3417	0	
401	2-,2-,6-,6-tetramethyl piperidine	872	2	
	2-,2-,6-,6-tetramethylpiperidine nitroxide	1015	2	
	2-,6-lutidine <i>n</i> -oxide	782	2	
	3-picoline <i>n</i> -oxide	1021	2	
	4-picoline <i>n</i> -oxide	1023	2	
	4-nitropyridine <i>n</i> -oxide	1032	2	
	collidine	744	2	
	Irganox 3114 [1-,3-,5-tris(3-,5-di- <i>t</i> -butyl-4-hydroxybenzyl)- <i>s</i> -triazine-2/4/6/(1H/3H/5H)-trione	1468	2	
	<i>n</i> -beta-(aminoethyl)-gamma-aminopropyltrimethoxy-silane	2123	2	
	bis-2-ethoxyethylamine	1279	2	
	diethylene triamine	1413	2	
	ethyl <i>p</i> -anisate	880	1	
	pyridine <i>n</i> -oxide	1019	2	
	quinoline <i>n</i> -oxide	1025	2	
	1101	A-160 [HiForm-160; PS-0940]	3168	0
		Irganox L-57 [sec-arylamine antioxidant]	3626	2
diphenylamine		4038	2	
tetraethylene pentamine		3417	2	
1201	4-4'-diphenylether diisocyanate	1782	3	
	MDI [4-4'-diphenylmethane diisocyanate]	1780	3	
	TMHMDA (trimethylhexamethylene diamine)	5625	1	

Table 13. Number of glioma cases and controls by self-reported use of organometallic catalysts.

	Agent no.	Cases	Controls
triethyl aluminum	113	0	1
ferrocene	2454	0	1
dibenzene vanadium	2716	0	1
dibenzene chromium	2721	0	1
diethylaluminum chloride	311	0	2
Ziegler catalyst	3762	1	0
Ziegler Natta catalyst	409	0	1
methylcyclopentadienylmanganese tricarbonyl [MMT]	5646	0	1
aluminum alkyl	640	1	1
ethylaluminum dichloride [EADC]	413	1	0
other organometallics	—	0	1

The other "organometallics" named by one control in the glioma series were: bis(1-,3-,5-trimethylbenzene)vanadium; bis(1-,3-,5-trimethylbenzene)vanadium (I) chloroaluminum; dibenzene vanadium chloroaluminate; and vanadium hexacarbonyl.

Table 14. Number of glioma cases and controls by self-reported use of inorganic metallic catalysts.

	Agent no.	Cases	Controls
chromium catalyst	115	1	0
boron trifluoride	1596	0	1
silicon dioxide	1615	0	1
nickel	1638	0	2
stannous chloride	2349	1	0
zinc	2413	1	2
cobalt	2473	1	0
chromium	2475	0	1
molybdenum	2477	0	1
manganese	2541	1	0
chromium trioxide	2563	0	1
potassium	2607	0	1
vanadium tetrachloride	2712	0	1
vanadium trichloride	2714	0	1
silicon oxide	2873	0	1
copper	2946	1	0
aluminum	3008	0	1
boron trifluoride etherate	3025	0	1
magnesium	3039	1	2
silica gel	316	0	1
borosilicate	3228	0	1
iron	336	1	0
zinc dithiophosphates	3525	0	1
titanium trichloride	411	2	4
magnesium chloride	412	2	0
zirconium chloride	4243	1	0
vanadium catalyst	428	1	0
aluminum chloride	639	0	3
Mo catalyst	4799	0	1
aluminosilicate	4892	0	1
titanium tetrachloride	435	1	3
sodium potassium alloy	641	1	0

Table 15. Number of glioma cases and controls by self-reported use of other amines.

	Agent no.	Cases	Controls
trialkylamines	1011	0	1
diethylene triamine	1413	1	2
aromatic amines	1515	0	1
dimethylamine	1629	1	0
diethylamine	1897	0	1
triethylamine	22	1	1
diamines	2267	0	2
meta-phenylene diamine	2275	1	0
para-phenylene diamine	2328	1	0
diisopropylamine	2686	1	0
2-amino-pyridine	2756	1	1
tetramethylene diamine	2776	0	1
1-,6-hexane diamine	2828	0	1
tripropylamine	2853	1	0
oxybisaniiline	3185	0	1
tetraethylenepentamine [TEPA]	3417	0	1
diphenylamine	4038	0	1
dimethylethanol amine	4567	0	1
triethylenetetramine [TETA]	6364	0	1
ethylene diamine	643	1	2
other "other amines"	—	0	4

Table 16. Organometallic catalyst exposure for glioma cases and their controls, self-reported data.

Case	Organometallic exposures	Agent number	Exposed controls in risk set
1001	Ziegler catalyst	3762	0
	ethyl aluminum dichloride [EADC]	413	0
	aluminum alkyl	640	0

Table 17. Inorganic metallic catalyst exposure for glioma cases and their controls, self-reported data.

Case	Inorganic metallic exposures	Agent number	Exposed controls in risk set
201	zinc	2413	0
	cobalt	2473	0
	manganese	2541	0
	copper	2946	0
	magnesium	3039	0
	iron	336	0
301	titanium trichloride	411	1
	magnesium chloride	412	0
	titanium tetrachloride	435	1
701	titanium trichloride	411	0
1001	chromium catalyst	115	0
	stannous chloride	2349	0
	magnesium chloride	412	0
	zirconium chloride	4243	0
	vanadium catalyst	428	0
	sodium potassium alloy	641	0

Table 18. Other amine exposure for glioma cases and their controls, self-reported data.

Case	Other amine exposures	Agent number	Exposed controls in risk set
201	diethylene triamine	1413	0
	dimethylamine	1629	0
	triethylamine	22	0
	diisopropylamine	2686	0
	2-amino-pyridine	2756	0
	tripropylamine	2853	0
	ethylene diamine	643	0
1001	meta-phenylene diamine	2275	0
	para-phenylene diamine	2328	0

Table 19. Number of benign intracranial tumor cases and controls by self-reported use of organometallic catalysts.

	Agent no.	Cases	Controls
triisobutyl aluminum	112	0	1
triethyl aluminum	113	1	3
n-butylethyl magnesium	2190	0	1
diethylaluminum chloride	311	1	1
Ziegler Natta catalysts	409	0	1
aluminum alkyl	640	0	2
collidine	744	1	2
other organometallic*	—	0	1

\* Iron carbonyl (1)

Table 20. Number of benign intracranial tumor cases and controls by self-reported use of inorganic metallic catalysts.

	Agent no.	Cases	Controls
boron trifluoride	1596	1	3
nickel	1638	0	4
manganese acetate	1797	0	2
antimony [Sb]	1811	1	1
tin [Sn]	1812	1	1
zinc	2413	1	1
cobalt	2473	0	1
chromium	2475	1	1
cobalt acetate	2507	0	3
manganese	2541	1	1
chromium trioxide	2563	0	1
potassium	2607	0	1
antimony triacetate	2703	0	1
palladium	2754	0	1
lead	2954	0	2
aluminum	3008	1	1
magnesium	3039	0	2
bismuth	3244	0	1
iron	336	0	1
titanium	3428	1	0
zinc dithiophosphates	3525	0	1
titanium trichloride	411	1	4
magnesium chloride	412	0	2
vanadium	421	0	3
zirconium	422	0	2
thallium oxide	4288	0	1
aluminum chloride	639	1	3
titanium tetrachloride	435	1	2
chrome oxide green	6008	0	1
sodium potassium alloy	641	0	1

Table 21. Number of benign intracranial tumor cases and controls by self-reported use of other amines.

	Agent no.	Cases	Controls
hexamethylene diamine	1412	0	1
aromatic amines	1515	0	1
ethanol amine	1893	1	0
triethylamine	22	0	1
diamines	2267	1	2
oxydianiline	2274	0	1
meta-phenylene diamine	2275	0	1
Mannich A-749 [engine oil dispersant additive]	3092	0	1
tetraethylene pentamine	3417	0	1
para-phenylene diamine	3923	1	0
methylenebisaniiline	4573	0	1
bisaniline-P [BAP]	5724	0	1
ethylene diamine	643	1	0
collidine	744	1	0
other "other amines"	—	2	3

Other "other amines" included toluene ethanol diamine (1), ethanol triamine (1), diamines (1), aromatic diamines (2), polyacryamide (1). Because two of these were named by the same subject, a control, the number of agents exceeds the number of subjects in the table.

Table 22. Organometallic exposure for benign intracranial tumor cases and their controls, self-reported data.

Case	Organometallic exposures	Agent number	Exposed controls in risk set
401	triethyl aluminum	113	0
	diethylaluminum chloride	311	0
	collidine	5284	0

Table 23. Inorganic metallic catalyst exposure for benign intracranial tumor cases and their controls, self-reported data.

Case	Inorganic metallic exposures	Agent number	Exposed controls in risk set
401	titanium trichloride	411	0
	titanium tetrachloride	435	0
1101	boron trifluoride	1596	0
	aluminum chloride	639	0
1201	antimony [Sb]	1811	1
	tin [Sn]	1812	0
	zinc	2413	0
	chromium	2475	0
	manganese	2541	0
	aluminum	3008	1
	titanium	3428	0

Table 24. Other amine exposure for benign intracranial tumor cases and their controls, self-reported data.

Case	Other amine exposures	Agent number	Exposed controls in risk set
401	collidine	744	0
1101	ethanol amine	1893	0
	other [ethanol diamine; ethanol triamine]	—	0
1201	diamines	2267	1
	ethylene diamine	643	0
	other [aromatic diamines]	—	1

CANCER AND BENIGN TUMOR INCIDENCE  
AMONG EMPLOYEES IN THE 500 BUILDING COMPLEX  
AT THE AMOCO RESEARCH CENTER

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SUMMARY

During the period 1970-1998, six glioma cases occurred among employees at the Amoco Research Center (ARC), now known as the BP Amoco Naperville Complex. These cases prompted concern that a workplace exposure might be etiologically linked to glioma, and we began five studies to evaluate patterns of mortality and cancer incidence among employees at the ARC. This report describes the results of a study of the incidence of cancer, benign intracranial tumors and other tumors among employees of the 500 building complex (C500) at the ARC.

The study included 1847 subjects who worked in C500 and who participated in a tumor incidence survey (TIS). History of employment in C500 and in the three buildings comprising the complex came primarily from TIS responses. Identification of cancer and benign tumor cases during the period 1970-1998 was based on TIS self-reports, confirmed by medical records, and on data from death certificates and from a record linkage with the Illinois State Cancer Registry (ISCR). Using the standardized incidence ratio (SIR) with its 95% confidence interval (CI) as the measure of association, we compared the cancer incidence rates of C500 employees with the rates of the general population of states participating in the Surveillance Epidemiology and End Results program (SEER). The Central Brain Tumor Registry of the United States (CBTRUS) provided comparison rates for benign intracranial tumors.

A total of 1735 subjects had worked full-time (at least 30 hours per week for any period of time in C500) or part-time (fewer than 30 but at least eight hours per week for any period of time in C500) in C500. This group accrued a total of 29962 person-years and had a median of 18.2 years of follow-up. Their median duration of employment was 9.5 years at Amoco, 6.8 years at the ARC and 3.6 years in C500. White men comprised the majority (64%) of the group.

During the follow-up period (1970-1998), full- or part-time C500 employees experienced 92 observed compared to 108 expected cancers (SIR=85, 95% CI=69-104), indicating that the group had 15% fewer than expected cancer cases. This deficit was attributable in large part to fewer than expected respiratory cancer cases (9/20, SIR=46, CI=21-87) and bladder cancer cases (1/5.7, SIR=17, CI=0-97). The observed number of cases was similar to the expected number for cancers of the colon (8/7.5), rectum (6/3.9), breast (9/7.4) and prostate and testis (22/20) and for melanoma of the skin (4/5.1), non-Hodgkin's lymphoma (6/5.1) and leukemia (3/2.7).

C500 employees had a threefold increase in brain cancer cases (6/2.0, SIR=302, CI=111-657). This excess was restricted to white men (6/1.6, SIR=376, CI=138-819) and was greatest in, but not restricted to, white men with 10 or more years since hire and with five or more years of employment in C500 (4/0.7, SIR=602, CI=165-1552). A large, statistically imprecise brain cancer excess occurred in each of the three buildings comprising C500, in part because several of the cases worked in more than one of the buildings. For building 503, the brain cancer SIR was 592 (5/0.9, CI=192-1381) for all subjects and was 735 (5/0.7, CI=239-1716) for white men.

Studies evaluating mortality and cancer incidence patterns among all ARC employees found increases in colorectal cancer. Therefore, we assessed this form of cancer in detail among full-time/part-time C500 workers. The latter group had slightly more observed than expected colorectal cancers (14/11, SIR=122, CI=67-205). The increase was limited to C500 white men (14/9.2, SIR=152, CI=83-254) and, further, to white men who had worked in building 501 (11/4.5, SIR=247, CI=123-441). Among white men in building 501, colorectal cancer SIRs did not display a pattern of increasing consistently with time since hire and years worked.

C500 employees had more than expected cases of benign intracranial tumors (6/1.6, SIR=386, CI=142-839). This result reflected an increased incidence of meningioma, pituitary

adenoma and vestibular schwannoma among men and of pituitary adenoma and vestibular schwannoma among women. Each of the latter increases was based on only one or two observed cases and on expected numbers less than one. Each building of the complex had more than expected cases of all benign intracranial tumors combined; no single tumor type aggregated in any one building.

A total of 112 employees worked intermittently (fewer than eight hours per week), but not full-time/part-time, in C500. The intermittent C500 group had similar numbers of observed and expected cancers (7/5.9, SIR=119, CI=48-245) and had two observed compared to 0.09 expected benign intracranial tumors.

This study confirmed that C500 employees have an increased incidence of brain cancer. The excess is unlikely to be due to bias. The causes of brain cancer are not established, and observed and expected numbers of brain cancers were low. Therefore, we cannot exclude confounding by an unidentified cause of brain cancer or chance as possible reasons for the excess among C500 employees, although we regard these explanations as rather unlikely.

Other results included a large deficit of lung and bladder cancers among C500 employees and an excess of colorectal cancer among white men employed in building 501. Confounding by lifestyle factors probably explains the deficit of lung and bladder cancers and may explain the positive association seen for colorectal cancer. However, because the colorectal cancer increase was concentrated in one ARC building and because most of the cases had a history of employment at the BP Amoco Whiting refinery, we do not rule out the possibility that occupational factors contributed to the excess of colorectal cancer in building 501 employees.

CONTENTS

INTRODUCTION 1

METHODS 1

    Follow-up period and subject identification 1

    Identifying information and work histories 4

    Case identification 5

    Analysis 5

RESULTS 8

    Characteristics of TIS participants and nonparticipants 8

    Cases 8

    Characteristics of the FT/PT C500 subjects 9

    Cancer and benign intracranial tumor incidence, FT/PT C500 subjects 10

    Cancer and benign intracranial tumor incidence by building,  
    FT/PT C500 subjects 12

    Cancer and benign intracranial tumor incidence, intermittent C500 subjects 13

    Mortality and cancer incidence among TIS participants and nonparticipants 14

    "Other" tumors reported by FT/PT and intermittent C500 subjects 14

DISCUSSION 14

REFERENCES 25

TABLES 32

APPENDIX—SURVEY OF CURRENT AND FORMER EMPLOYEES AT THE  
AMOCO RESEARCH CENTER IN NAPERVILLE, ILLINOIS 52

## INTRODUCTION

This report describes a study of tumor incidence among persons who worked in the 500 building complex (C500) at the Amoco Research Center (ARC), now known as the BP Amoco Naperville Complex, located in Illinois (IL). The study was initiated in response to an unusual occurrence of glioma among employees in one building of the ARC (15). Its main purpose was to determine if the occurrence of cancer or benign intracranial tumors was related to employment factors such as duration of employment and years since hire in C500 and in various buildings of the complex.

## METHODS

### Follow-up period and subject identification

The study covered the time period of January 1, 1970, through September 11, 1998. The subjects were men and women classified as ever having been assigned to work in C500 full-time (at least 30 hours per week), part-time (fewer than 30 but at least eight hours per week) or only intermittently (fewer than eight hours per week).

All subjects were members of the study group identified for companion investigations of mortality and cancer incidence among ARC employees and referred to henceforth as the "ARC study group" (16,17). We initially identified ARC study group members as possibly having worked in C500 (the "provisional C500 study group") by using information from ARC telephone books and an *ad hoc* survey of a sample of supervisory and other long-term C500 personnel. We identified the final group of C500 employees on the basis of information obtained from a questionnaire survey of the provisional C500 subjects.

Telephone books, prepared approximately annually, contained the name and the building and office assignments of noncasual employees (i.e., all except summer and other short-term

temporary employees). These books were available for all years except 1970, 1972, 1979 and 1995. The majority of C500 employees identified in the telephone books had worked for the Amoco Chemical Company (ACC). The telephone books identified 2112 persons as having been assigned to C500.

To identify other C500 employees, we conducted a survey of 25 long-term supervisory and other senior personnel familiar with C500 employees. The survey asked participants to review the names of 1748 persons classified as ACC employees on the basis of their computerized Amoco personnel data or on the basis of a secondary record, such as a telephone book record or an organization chart. We focused on ACC employees because they had always been the main occupants of C500. Based on responses to these surveys, we classified 109 employees as definitely or probably in C500, 504 as definitely or probably not in C500 and 1135 as unknown and, hence, as possibly in C500.

We sent a pilot tumor incidence survey (TIS) to a sample of 148 ARC employees. The TIS requested information on full-time and part-time work locations in C500 (time period, building and floor/work area) and asked about medical history of cancers and other tumors (type of tumor, date and place of diagnosis). The survey also asked persons reporting cancers or other tumors to give us permission to review confirmatory medical records.

The pilot TIS sample included 124 people classified as definite, probable or possible C500 employees based on telephone books or supervisor responses and 24 people whom supervisors had classified as definitely or probably never in C500. A total of 136 (92%) pilot survey subjects participated, including 115 (93%) classified as provisional C500 employees and 21 (88%) classified as never in C500. Of the 115 provisional C500 employees, 102 (89%) confirmed full-time work, one (1%) reported part-time work, four (3%) reported intermittent

work and eight (7%) reported no work in C500. Of the 21 participants provisionally classified as not in C500, none reported having been full-time, two (10%) reported part-time work and five (24%) reported intermittent work in C500.

We sent a slightly revised TIS (Appendix) to 2471 additional people classified as definite, probable or possible C500 employees based on telephone books or supervisors' responses. Thus, of 6955 subjects in the mortality study (16), 2595 were in the total survey group (pilot and main surveys combined) of provisional C500 employees.

We searched extensively to locate the current address of each member of the provisional C500 study group or, if the subject was deceased, the address of the next-of-kin. Address information sources included Amoco records on current employees and retirees, Internet data, credit bureau records and data obtained from LEXIS-NEXIS, an address location data base. The TIS mailings proceeded in batches of about 500 questionnaires, with cover letters and postage-paid return envelopes, mailed approximately weekly. We mailed a follow-up TIS, either to the original address or to a newly identified address, to each subject not responding to the initial TIS. The survey group included 112 decedents. We sought a surrogate respondent for these subjects. If a subject or surrogate did not respond after the two mailings, we attempted to contact the person directly and to administer the survey questionnaire in a telephone interview.

Of the 2595 subjects surveyed, 2214 (85%) responded, 1691 (76%) by mail and 523 (24%) by telephone, and 2172 (84% of 2595) participated, including a surrogate for 87 (78%) of the 112 decedents (table 1). There were 381 nonrespondents.

We checked survey responses for completeness and consistency with corporate employment history and telephone book data. We recontacted participants to clarify inconsistent responses. Our review of all available data indicated that telephone books provided better

information on specific building assignments and dates for many subjects than memory alone. Thus, we supplemented survey data on C500 building assignments and dates with telephone book records for subjects who indicated difficulty remembering their work history.

Of the 2172 TIS participants, 325 reported that they never worked in C500. Thus, the final C500 study group included 1847 subjects. Of these, 1735 reported full-time or part-time assignment to an office or laboratory in C500 (the "FT/PT C500 study group"), and 112 reported intermittent (fewer than eight hours per week) assignments in the complex, most often to perform analytical tests or to attend training sessions or meetings (the "intermittent C500 study group").

Of the 1735 TIS respondents who reported being full-time or part-time in C500, 1405 (81%) had a telephone book record confirming their assignment to an office in C500. Only four (4%) of the 112 TIS respondents who reported intermittent C500 employment had a confirmatory telephone book record. Five TIS respondents reporting no work in C500 had a telephone book record indicating that they had been assigned to an office in the complex. One of those subjects later reported, during the course of our case-control investigation, that he had worked in C500.

#### Identifying information and work histories

Information for the final C500 study group came from several sources. We used Amoco corporate data and other records from the ARC to develop a master computerized subject information file for the companion mortality study (16). This file contained identifying and personal information on each subject (name, race, gender, social security number, date of birth, vital status), Amoco summary work history data (hire date, end date, employment status), information about each job held at the ARC (ARC start date, ARC end date, company, job) and,

for decedents, information on death date and cause of death. To this file, we added TIS information on subjects' start and end dates in C500, start and end dates for each building in the complex and years worked in the complex and each C500 building.

Case identification

We used responses to the TIS, information from a record linkage with the Illinois State Cancer Registry (ISCR) covering the period 1986 through 1997 (21) and death certificates (19) to identify cancers, intracranial tumors and other tumors diagnosed as of each subject's TIS response date. We attempted to obtain medical records for self-reported cancers and tumors, reviewed these records to confirm diagnoses and to establish diagnosis dates, coded the diagnoses according to the revision of the International Classification of Diseases in effect at the time of diagnosis and added diagnosis codes and dates to our master data file. We carried out the medical record review without referring to subjects' work histories. Medical record retrieval efforts concentrated on self-reported cancers, other than nonmelanotic skin cancer, and on benign intracranial tumors and were less complete for other self-reported tumors.

The TIS included a total of 41 self-reported cases who were diagnosed during 1986-1997 among 500 complex employees and who were IL residents at the time of diagnosis. Of these, two cases, both of whom were medically confirmed by IL hospitals, did not have an ISCR record. No case was identified exclusively from the ISCR.

Analysis

The analysis compared the incidence rates of specific cancers and benign intracranial tumors among C500 study group members with US general population incidence rates. We did not carry out epidemiologic analyses for benign tumors, other than benign intracranial tumors, because comparison data were not available. In calculating the cancer and benign intracranial

tumor rates of C500 employees, we counted only those reported cases confirmed by a medical record, an ISCR record or a death certificate.

For cancer incidence rate analyses, the general population comparison rates came from the Surveillance Epidemiology and End Results (SEER) program and were available for the time period of 1973-1995 (48). We used 1973-1974 SEER rates to estimate a comparison rate for the 1970-1974 time period. For analyses of benign intracranial tumors, we used comparison rates from the Central Brain Tumor Registry of the United States (CBTRUS), available for the period of 1990-1993 (10).

All analyses used the standardized incidence ratio (SIR) as the measure of association. We computed SIRs for the overall C500 study group and for subgroups specified on the basis of gender, race and C500 employment factors, including duration and time since hire in C500, history of employment in each building of C500 (buildings 501, 502 and 503) and duration and time since hire in each building.

We computed the SIR for a particular cancer or type of intracranial tumor as the ratio ( $\times 100$ ) of the observed number of cases to the number expected based on the age-, gender- and, for cancers, calendar time-specific incidence rates of the comparison population. Observed numbers included all confirmed cases diagnosed after a subject's C500 hire date. If a subject had multiple primary cancers, we included each cancer as an observed case in analyses of all cancers combined. Each cancer also counted as a case in the analysis of a particular type of cancer. No subject had both a form of cancer and a benign intracranial tumor.

Accumulation of a subject's person-years of observation began on the latest of the first date of employment in C500, in a particular building or in a particular years since hire and years worked category. For analyses of all cancers combined, person-year accumulation ended on the

earlier of the subject's death date or TIS response date. For analyses of a particular form of cancer or benign intracranial tumor, person-year accumulation ended on the earlier of the cancer or tumor diagnosis date, death date or TIS response date for a subject with that form of cancer or tumor and on the earlier of the death date or the TIS response date for other subjects.

We multiplied the person-years of follow-up by the corresponding SEER or CBTRUS rates to obtain expected numbers. We estimated 95% confidence interval (CIs) of the SIRs under the assumption that the observed number of cases follows a Poisson distribution. Except when examining cancer incidence patterns by years since hire (used as a surrogate for induction time) and years worked in C500 or in specific buildings, we computed the SIR and CI for a particular cancer only when there were at least three observed or expected cases. Software used for the data analysis consisted primarily of the Occupational Mortality Analysis Program (OCMAP) (35).

Detailed analyses of the occurrence of specific forms of cancer focused on the FT/PT C500 study group of 1735 subjects. We carried out a separate analysis of all cancers combined and of benign intracranial tumors among the 112 subjects in the intermittent C500 study group.

Participation in the TIS was not 100%. Thus, our results may have been biased by unequal participation by subjects with and without cancer. To assess this possibility, we compared TIS participants to nonrespondents/nonparticipants with respect to: 1) overall mortality and cancer mortality and 2) cancer incidence as determined primarily by record linkage with the ISCR. Data for the first set of analyses came from a companion study of mortality patterns among all ARC employees (16). The mortality study included all TIS subjects and used standardized mortality ratios (SMRs) to compare the mortality rates of TIS subjects to the rates of the IL general population, adjusting for race, gender, age and calendar time. Data for the

second set of analyses came from a companion study of cancer incidence during the period 1986 through 1997 among ARC employees who lived in IL (17). The latter study included 1762 TIS participants and 302 TIS nonrespondents/nonparticipants and used SIRs to compare the 1986-1997 cancer incidence rates of TIS subjects to the rates of the IL general population, again adjusting for race, gender, age and calendar time.

## RESULTS

### Characteristics of TIS participants and nonparticipants

Compared to the 423 TIS "nonparticipants" (nonrespondents and nonparticipants, combined), the 2172 TIS participants were more likely to have been provisionally classified as definitely in C500 (participants, 68%; nonparticipants, 48%), to have been active at Amoco (33% v. 12%) or retired (15% v. 7%) and to have been alive at the time of the TIS (96% v. 89%) (table 2). Also, TIS participants, except for the subgroup never in C500, were longer-term ARC and Amoco employees than were nonparticipants. The racial composition, age and year of hire of the participant and nonparticipant groups were similar.

### Cases

TIS participants in the FT/PT C500 group reported a total of 103 cancers, six benign intracranial tumors and 131 other tumors diagnosed after starting work in C500 (table 3). Confirmatory records were unavailable for three self-reported cancers in the FT/PT C500 group (one each of melanoma of the skin, prostate cancer and non-Hodgkin's lymphoma). Medical records indicated that eight self-reported cancers were not, in fact, cancer. Of the remaining 95 self-reported cancers, medical records, ISCR records or death certificates confirmed 92 (97%) as cancer. In addition, three neuropathologists reviewed histologic material from the brain cancer cases identified in the FT/PT C500 group. Their initial assessment confirmed the diagnoses of

all brain cancer cases. Subsequently, new material from one case became available, and a further review by the three neuropathologists indicated that the employee had melanoma of an unknown primary site, rather than brain cancer. In most analyses, we counted this case as a brain cancer in order to avoid bias (see discussion section).

Medical records and a review of histologic material by three neuropathologists confirmed all of the benign intracranial tumors. Medical records were available for 83 (63%) of other self-reported tumors and indicated that 58 (70% of 83) were, in fact, neoplasms.

TIS participants in the intermittent C500 group reported a total of nine cancers, two benign intracranial tumors and 11 other tumors diagnosed after starting work in C500. Medical records indicated that one self-reported cancer was not, in fact, cancer. Of the remaining eight self-reported cancers, medical records, ISCR records or death certificates confirmed seven as cancer. The one person without record confirmation reported having melanoma of the skin. Records confirmed both of the benign intracranial tumors and six of the 11 other tumors.

TIS participants never in C500 had 19 confirmed cancers, two confirmed benign intracranial tumors and three other confirmed tumors. Survey nonparticipants had a total of 16 cancers, identified by an ISCR record (N=12) or by a death certificate only (N=4).

#### Characteristics of the FT/PT C500 subjects

The FT/PT C500 study group consisted predominantly of white men (64%), with smaller proportions of white women (26%), nonwhite men (8%) and nonwhite women (3%) (table 4). About 35% of the group was active at the ARC or elsewhere at Amoco at the close of the study. Only 4% of the group was deceased. The median age of the FT/PT C500 study group at the close of the study was 47 years and varied from 39 years for nonwhite women to 49 years for white men (table 5). Other median values were 1979 for C500 hire year, 3.6 for years worked in

C500, 6.8 for years worked at the ARC and 9.5 for years worked at Amoco. The overall C500 FT/PT study group had a total of 29962 and a median of 18 person-years of follow-up.

When we classified subjects into mutually exclusive groups according to the individual buildings (501, 502, 503) of C500 in which they worked, 71% reported spending their entire time in the complex working in a single building (table 6). The distribution of subjects in the three individual buildings roughly reflected the size and office space available in each. Only 21 subjects could not recall the C500 building where they worked. We included these people in analyses of the entire C500 study group but not in analyses of specific buildings.

Further analyses classified subjects according to buildings where they had ever worked (table 7). In this classification, a person appears as ever in 501, regardless of whether he or she also was assigned to another building in another time period. The 874 subjects in 501 had 14446 person-years of follow-up, a median year of starting work in 501 of 1980 and a median duration of employment in 501 of 2.5 years. The 616 subjects in 502 had only 9867 person-years of follow-up, a median 502 hire date of 1981 and a median of 2.7 years worked in 502. The 816 subjects in 503 contributed 12669 person-years of observation and had a median 503 hire date of 1984 and a median of 2.5 years worked in the building.

#### Cancer and benign intracranial tumor incidence. FT/PT C500 subjects

The overall FT/PT C500 study group had an SIR for all cancers combined of 85 (92 observed/108 expected cases, 95% CI=69-104), indicating that the cancer rate of the study group was 15% lower than the SEER general population rate, adjusting for calendar time, age and race (table 8). The study group's low all-cancer SIR was due mainly to substantial deficits of respiratory cancer (9/20, SIR=46, CI=21-87), including lung cancer (7/17, SIR=41, CI=16-84), and of bladder cancer (1/5.7, SIR=17, CI=0-97). FT/PT C500 employees' brain cancer incidence

rate was three times higher than that of the SEER population (6/2.0, SIR=302, CI=111-657).

The observed number of cases in FT/PT C500 employees was similar to the expected number for cancers of the colon (8/7.5), rectum (6/3.9), breast (9/7.4), prostate and testis (22/20), for melanoma of the skin (4/5.1), for non-Hodgkin's lymphoma (6/5.1) and for leukemia (3/2.7).

The SIR for the combined category of colorectal cancer was 122 (14/11, CI=67-205).

Results for white men were similar to those observed for all FT/PT C500 subjects (table 8). White men had an all-cancer SIR of 91, indicating a cancer rate 9% lower than that of the SEER white male population. The excess of brain cancer in the overall FT/PT C500 study group was restricted to white men (6/1.6, SIR=376, CI=138-819). White men had a colorectal cancer rate 50% higher than expected (14/9.2, SIR=152, CI=83-254), a result that was not statistically significant.

White women working in C500 had an overall cancer incidence rate lower than that of their SEER population counterparts (14/20, SIR=71, CI=39-119). They had almost equal observed and expected numbers of breast cancers (8/7.0). There were too few cancer cases among nonwhite men and women for an informative analysis.

Further analyses of the C500 study group did not reveal any consistent pattern of increasing SIRs with increasing years since hire and years worked in the complex for all cancers, brain cancer or colorectal cancer (table 9). Although the brain cancer excess was not restricted to a particular years since hire/years worked subgroup, most cases occurred among subjects with 10+ years since hire and with 5+ years worked in C500 (4/0.8, SIR=521, CI=142-1330). Analysis of white men yielded similar patterns, with 4/0.7 brain cancers (SIR=602, CI=165-1552) in the group with 10+ years since hire and with 5+ years worked in C500.

Cancer and benign intracranial tumor incidence by building, FT/PT C500 subjects

Like the overall study group, subjects ever employed in buildings 502 and 503 had fewer than expected total cancers (tables 10 and 11). The SIR for all cancers combined was only slightly lower than expected among subjects ever in building 501, and their all-cancer SIR was higher than the corresponding SIR of ever-502 or ever-503 subjects, mainly because ever-501 employees had more than expected cases of colorectal cancer and prostate cancer, whereas the other two building groups had deficits of these cancers.

The deficit of lung cancer in the overall C500 study group occurred in each of the building subgroups (tables 10 and 11). There were more than expected brain cancers in each building subgroup, but the SIR for brain cancer was statistically significantly elevated only for 503 employees (all 503 employees: 5/0.9, SIR=592, CI=192-1381) (table 10) (white male 503 employees: 5/0.7, SIR=735, CI=239-1716) (table 11). Colorectal cancer was increased only among employees in 501 (11/5.4, SIR=204, CI=102-365) (table 10), and only among white men in 501 (11/4.5, SIR=247, CI=123-441) (table 11). Assessment of other cancers by building was of limited informativeness because the numbers of building-specific observed and expected cases were small; however, there were no other striking excesses or deficits.

Analyses stratifying the FT/PT C500 study group by building, years since hire and years worked yielded extremely imprecise results, as category-specific observed and expected numbers were very small (table 12). No systematic pattern in SIRs for overall cancer or colorectal cancer by years worked or years since hire in a particular building was apparent. The brain cancer excess observed in 503 employees occurred both among subjects with 10+ years since hire and 5+ years worked in that building (2/0.3, SIR=796, CI=97-2888) and among those with <10 years since hire and <5 years worked (2/0.3, SIR=695, CI=83-2490). The excess in 501 was

concentrated in subjects with <10 years since hire and <5 years of employment in that building (2/0.3, SIR=653, CI=78-2329). In 502 workers, the excess occurred among subjects with 10+ years since hire and 5+ years worked (2/0.2, SIR=1009, CI=121-3610). When restricting analyses to white men, the expected numbers generally were lower and the SIRs higher than in the all race/gender groups combined, but the patterns were quite similar. White men with 10+ years since hire and 5+ years worked in 503 had 2/0.2 brain cancers (SIR=920, CI=110-3282).

FT/PT C500 subjects had an excess of observed over expected benign intracranial tumors, based on 6 observed/1.6 expected total cases (SIR=385, CI=142-839) (table 13). Among men, observed/expected numbers were 2/0.4 for meningioma, 1/0.3 for vestibular schwannoma and 1/0.3 for pituitary adenoma. Among women, observed/expected numbers were 1/0.1 for vestibular schwannoma and 1/0.1 for pituitary adenoma. None of the results for particular forms of benign intracranial tumor was statistically significant.

An increase in all benign intracranial tumors combined occurred among subjects ever employed in each of the three buildings (table 14), but none of the results was statistically significant. In 501, there were 1/0.2 expected pituitary adenomas and 1/0.2 vestibular schwannomas. In 502, there were 1/0.3 meningiomas and 1/0.2 pituitary adenomas. Employees in 503 had 1/0.3 meningiomas and 1/0.2 vestibular schwannomas.

#### Cancer and benign intracranial tumor incidence, intermittent C500 subjects

A total of 112 subjects reported having worked intermittently in C500. Of these, 75 were white men, 10 were nonwhite men, 23 were white women and four were nonwhite women, a distribution similar to that observed in the FT/PT C500 study group. The 112 subjects had a total of 1710 person years of follow-up. Overall they had 7/5.9 cancers (SIR=119, CI=48-244). All but one cancer occurred among white men (6/4.7, SIR=127, CI=47-277). The total observed

number included cancers of the larynx (1 case), colon (1), breast (1), prostate (1) and testis (1) and melanoma of the skin (2).

The intermittent C500 study group had 2/0.09 benign intracranial tumors. There were 1/0.03 meningiomas (in a nonwhite man) and 1/0.02 vestibular schwannomas (in a white woman). No pituitary adenoma occurred in the intermittent C500 study group.

#### Mortality and cancer incidence among TIS participants and nonparticipants

The total group of TIS participants had 87 observed/189 expected total deaths (SMR=46, CI=37-57) and 27/49 cancer deaths (SMR=55, CI=36-80) during the period of 1970 through 1996. In contrast, TIS nonparticipants had 25/31 total deaths (SMR=81, CI=52-119) and 6/7.1 cancer deaths (SMR=85, CI=31-184) during the same time period. Analyses of cancer incidence that were based on cases identified primarily from ISCR records for 1986 through 1997 showed that TIS participants had 51/56 total cancers (SIR=92, CI=68-121), whereas TIS nonparticipants had 10/7.0 total cancers (SIR=142, CI=68-262).

#### "Other" tumors reported by FT/PT C500 and intermittent C500 subjects

As noted earlier, FT/PT C500 employees had 58 confirmed "other" tumors (table 15). These included three cancers *in situ*, 27 nonmelanotic skin cancers and 28 benign tumors, the most frequent of which were colorectal polyps (N=6). The intermittent C500 group had six confirmed "other" tumors, including four nonmelanotic skin cancers, one colorectal polyp and one other benign tumor. The most commonly self-reported but unconfirmed "other" tumor was nonmelanotic skin cancer (N=16) in the FT/PT C500 group.

#### DISCUSSION

The most striking results of this study were the excesses of brain and other intracranial tumors in C500 employees. Other findings of interest were the occurrence of a large deficit of

lung cancer cases and an increase in colorectal cancer cases. We noted both of the latter results in companion studies of mortality and cancer incidence in the overall ARC study group (16,17). The present study adds to previous results in further delineating the colorectal cancer increase as being restricted to white men who had worked in building 501.

#### Lung cancer and related results

The findings for lung cancer among FT/PT C500 employees were consistent with the results of the mortality and the cancer incidence studies of ARC employees. The very low SIRs for lung cancer in every category of employment examined, as well as the low SIRs for bladder cancer, probably are due to differences between C500 employees and the general comparison population with regard to smoking and other factors associated with socioeconomic status (SES).

#### Brain cancer

This study confirmed a previously identified excess of gliomas among C500 employees (15,17). The brain cancer excess was restricted to white men, was concentrated in the subgroup with at least 10 years of time since beginning work and with at least five years of employment in C500 and was present in each building of C500 but was concentrated in building 503. These patterns suggest that some of the cases were work-related, but we have not determined specific causal occupational agents.

Definite chemical neurocarcinogens in humans have not been identified (6,28,44). Although ionizing radiation has been associated with the development of brain tumors in some investigations, the relationship does not appear to be strong or consistent across studies of exposure occurring in adults (7). A number of chemicals with neurocarcinogenic action in animals has been identified (33), and a few of these are suspected, but not established, causes of brain cancer in humans (6). The results of epidemiologic studies of workers in the petrochemical

industry and of chemists are inconsistent with regard to brain cancer; however, most of the studies have reported a weak or no association (4,5,8,9,11-14,20,26,27,34,38-42,50,51,54,56,57,61).

A case-control study among C500 employees evaluated intracranial tumor cases and comparison subjects with regard to their potential exposure to 29 specific chemical and physical agents used at the ARC (18). This study found that brain cancer was associated with potential exposure to ionizing radiation and *n*-hexane. These associations were present both in analyses of self-reported exposure data and in analyses of exposure information derived from objective historical documents. However, the results may not represent causal relationships. Subjects' exposure to ionizing radiation at work was of doubtful biologic significance, and there is not sufficient epidemiologic or toxicologic evidence to conclude that *n*-hexane is a neurocarcinogen. Thus, confounding by an unidentified agent, exposure to which was correlated with use of ionizing radiation and/or *n*-hexane, cannot be ruled out. Chance, also, remains a possible explanation.

Some research has noted a positive relationship between SES and brain cancer, possibly due to better detection of cases among persons with relatively high educational attainment, income and access to medical care (25,44). However, studies of workers in the petrochemical industry have not reported consistently higher brain cancer rates for presumably higher SES subjects. For example, one study of chemical workers found higher brain cancer rates among salaried as compared to hourly employees (38). However, other investigations, including studies of chemists and petrochemical workers, have found no excess for subjects of higher SES (8,14,51,56,57,61).

Detection bias might have occurred in the present study if the subjects had better access to medical diagnostic procedures than the populations from which the comparison rates were derived (25). Some ARC employees have been screened for intracranial tumors using magnetic resonance imaging (MRI) examinations of the head. However, the brain cancer cases included in this report were initially evaluated medically because of clinical symptoms, not because of MRI results. Although ARC employees are of relatively high SES, it is somewhat implausible that their access to diagnostic services differed enough from that of the general SEER population to account for the observed brain cancer excess. Also, the fact that the ARC work force has had access to screening for intracranial tumors would not explain the concentration of diagnosed cases in workers at a single building complex.

Differential participation in the TIS by persons with cancer may have contributed to an overestimation of SIRs for brain and other cancers in this study. However, it is unlikely that such an error could completely explain the excesses that we observed for two reasons. First, analyses of mortality data indicated that the all-causes and all-cancer SMRs of TIS participants were actually lower than those of nonparticipants. Second, analyses for part of the study period of data obtained in an objective manner from the ISCR also found a lower cancer SIR for TIS participants than for nonparticipants. These results suggest that nonparticipation could have been due to illness or to our inability to enroll the next-of-kin of deceased employees. Thus, underestimation of SIRs seems, in general, to have been more likely than overestimation, although the direction of bias may have differed for various forms of cancer. We were unable to evaluate objectively cancer SIRs for TIS participants and nonparticipants before 1986, the first year for which the ISCR recorded cancer diagnoses, or after 1997, the last year for which ISCR data were available.

We know of one deceased C500 employee who had brain cancer and whose family did not participate in the TIS. This subject worked only in building 501. Also, as noted previously, among the participants counted in the study as having brain cancer was one subject whose original diagnosis of primary brain cancer was confirmed by a review of medical records and pathology material and was recorded in ISCR data. Recent further information on this case indicated a diagnosis of melanoma of an unknown primary site. To maintain comparability of observed and expected numbers, we counted this subject as a case, because he was so reported in a population-based cancer registry, and our expected numbers derived from such a registry. He worked in buildings 501 and 502, but not in 503.

Differential misclassification of ARC employees by building was possible in the present study because we relied on self-reported facility location data. However, results from our companion intracranial tumor case-series investigation (15) argue to some extent against this form of bias. That study found a 3.5-fold increase among men in C500 and a 5.4-fold increase among men in 503, results similar to the 3.8-fold increase among all white male C500 employees and the sevenfold increase among white men in building 503 observed in the present investigation. This degree of similarity in results is somewhat surprising given that: 1) building assignment data came from somewhat different sources in the two investigations; and 2) one case was not counted in the present study because of nonparticipation and another case, omitted from observed numbers in our case-series investigation (15) because he was diagnosed after that study's closing date, was included as a case in computing SIRs for the present study, which had a longer follow-up period. However, it is not surprising that both investigations found an excess, as they began as an *a posteriori* investigation of a known unusual occurrence of brain cancer.

Results from our all-ARC cancer incidence study (17), which identified cases primarily from ISCR data, argue further against differential misclassification by building as an explanation of the brain cancer patterns. That investigation used objective building assignment information derived entirely from historical telephone books and found a ninefold increase in brain cancer among white male C500 employees. The latter study did not evaluate brain cancer incidence in specific C500 buildings; thus, comparative data are not available for building 503.

#### Benign intracranial tumors

The finding in this study of an overall benign intracranial tumor excess, like the confirmation of the brain cancer excess, was expected. In addition to an elevated rate for all intracranial tumors combined, rates were elevated for each category of benign intracranial tumor in which at least one tumor was observed, including meningioma, pituitary adenoma and vestibular schwannoma.

Even less is known about the etiology of benign intracranial tumors than is known about the causes of brain cancer. Occupational studies have tended to focus on glioma, or have not differentiated among tumors of the central nervous system, although tumors involving various types of tissue (e.g., pituitary or nerve sheath) would not be anticipated to have similar etiologies. Noise trauma has been associated with vestibular schwannoma in one study (46), and ionizing radiation is suspected as a cause of this form of intracranial tumor (30,49,52,55). Little is known about exogenous causes of pituitary tumors (24). The few studies that have considered meningioma have not found strong associations with environmental agents, occupational exposures or even job groups, although one study reported an elevated risk for persons exposed to petroleum products (45). Epidemiologists have noted that SES is fairly strongly associated

both with meningioma and with nerve sheath tumors, including vestibular schwannoma, and have interpreted this relationship as possibly being due to detection bias (44).

The case-control study of intracranial tumors among ARC employees, mentioned earlier, found a positive relation between potential exposure to ionizing radiation and benign as well as malignant brain tumors (18). However, unlike the results for glioma, the association seen for benign intracranial tumors was limited in large part to self-reported exposure data and may have been due to recall bias. In the present study, there was no concentration by building of the benign tumor excess: 501, 502 and 503 each showed an excess for one or more tumor type.

Detection bias, which seemed implausible as an explanation for the glioma excess, seems more plausible as an explanation for the apparent increase in benign intracranial tumors, as these did not aggregate in a particular building or job group. At least one case of vestibular schwannoma was screening detected.

#### Colorectal cancer

The mortality study of ARC employees (16) and the all-ARC cancer incidence study (17), as well as the present investigation, found an increase in colorectal cancer. In each study, the observed association was weak, but the present study found a statistically significant 2.5-fold increase among FT/PT white male employees who had worked in building 501.

Bias is not a plausible explanation of these results. Selective participation in the TIS by persons with colorectal cancer could have occurred and, if so, could have produced an elevated SIR. However, results from our all-ARC cancer incidence study argue against such a bias. As noted earlier, the latter study used objective procedures to identify cases and included an assessment of cancer incidence by ARC work location that used historical telephone book information, rather than self-reports, to classify subjects according to building complex. The all-

ARC cancer incidence study found a colorectal cancer SIR of 164 for white men in C500, a result that is very similar to the SIR of 152 found in the present study for white men in C500. Biased recall of work in particular C500 buildings seems unlikely in the present study, as TIS subjects were not aware of a colorectal cancer increase among ARC employees at the time of the survey, nor did employees express any concern, before or during the survey, about colorectal cancer occurrence in C500 as a whole or in particular C500 buildings.

Both heredity and lifestyle factors have been implicated in the etiology of colorectal cancer. Among widely accepted environmental risk factors are diet, sedentary lifestyle and smoking (22, 23,43,53). A few studies of workers in the chemical and petrochemical industry have suggested elevated rates of colon cancer (14,26) or of colorectal cancer (34). However, none has provided persuasive evidence of a causal association. Excesses of colorectal cancers and adenomatous colorectal polyps have been reported inconsistently in polypropylene manufacturing workers and workers in industries that use polypropylene (1-3,29,31,32,58-60). This is of possible interest because some of the research carried out in C500 focused on polypropylene production. However, only two of the colorectal cancer cases among men employed in building 501 appear to have been involved in polypropylene research, whereas eight worked on diverse projects dealing with petroleum additives and inorganic intermediates.

We interviewed all of the colorectal cancer cases (or a family member) identified in this study and obtained information on pre-ARC work history and on personal and family medical history. Interviews indicated that nine of the 14 colorectal cancer cases in C500 employees and eight of the 11 cases in building 501 had worked at BP Amoco's Whiting refinery before coming to the ARC. Ten of the 11 cases employed in the 501 building were chemists or technicians before or during their tenure at the ARC; the other was a pipefitter. The history of employment

at Whiting is of interest because a previous investigation reported a small excess of rectal cancer among maintenance and operations workers with routine exposure to oil refinery operations at this refinery (37). We do not have data on previous work at Whiting for all C500 subjects, but we do know that many employees transferred from that facility to the ARC in the 1970s and early 1980s. The ostensibly high proportion of former Whiting employees among colorectal cancer cases in the 501 building may simply reflect a high frequency of a Whiting work history among all 501 subjects.

Information on personal and family medical history indicated that, of the 11 colorectal cancer cases who had worked in building 501:

- five had had a colorectal polyp before developing cancer but did not have family history of colorectal cancer;
- one had a family history of colon cancer, but no personal history of colorectal polyps;
- one had both a personal history of colorectal polyps and a family history of colon cancer.

This occurrence of a history of colorectal polyps and of a family history of colon cancer is similar to the occurrence of these factors among colorectal cancers occurring in the general population (47,53).

#### Strengths and limitations

This study has several strengths. Because of the focus on incident, rather than decedent, cases, we were able to examine cancer patterns in a young study group among which few deaths were experienced prior to the study closing date. Furthermore, the use of incidence data allowed us to focus on associations with disease, rather than on factors that may be correlates of survival. Another strength was the standardized procedure used to collect data and to classify subjects according to their work in C500 and to the buildings therein. This classification was made without regard to whether a respondent reported the existence of any medical condition and

before the TIS questionnaires were examined to determine whether any medical condition reported warranted follow-up.

This study was one component of a five-part investigation. Although each part of the overall project involved somewhat different study groups and designs, results observed in one study can be compared, or contrasted, with those obtained in the other research components to obtain a more complete picture of overall cancer mortality and morbidity patterns at the ARC. For example, our study of cancer incidence that was based on record linkage with the ISCR evaluated cancers only, was restricted to the time period of 1986 through 1997 and did not have complete data on work in specific buildings. The present investigation of C500 employees addressed all of these limitations. It evaluated cancer and benign tumor incidence, covered the time period of 1970 through approximately the end of 1998 and assessed incidence patterns for all C500 employees, as well as for employees in particular C500 buildings.

The present study had several important limitations. As in the other studies of ARC employees, the study group was young, and expected numbers of cancers among subjects with many years since hire and with long employment duration was low. Limited data from our pilot TIS indicated that seven (33%) of 21 participants classified provisionally as not having worked in C500 reported having worked there part-time (N=2) or intermittently (N=5). In addition to our having failed to include some part-time and intermittent C500 employees who worked for the ACC, we also probably missed some short-term C500 employees who worked for AOC or AC.

Although overall TIS participation of 84% was higher than for many survey studies, the 16% nonparticipation limits our ability to generalize our findings to the entire C500 study group. Another important limitation was the lack of information on potential confounders such as smoking and socioeconomic status. In addition, although we obtained information on many

types of benign tumor, we confirmed only a low proportion of the self-reported cases of tumors other than benign intracranial tumors, and we conducted a formal analysis only for the latter category.

Conclusions

This study found that the all-cancer incidence rate of C500 employees was 15% lower than the rate of the SEER general population. The favorable cancer incidence experience of C500 employees was due largely to fewer than expected cases of lung and bladder cancers. For several common forms of cancer, the incidence rate among C500 employees was similar to the general populations rate. The overall C500 group had a statistically significant threefold increase in brain cancer, limited to white men. White men in the 503 building had a statistically significant sevenfold increase in brain cancer, an increase somewhat higher than that reported previously (15). This association is not likely to be due to bias and may be attributable to an unidentified occupational exposure. Also, chance remains a possible but unlikely reason for the increased brain cancer incidence in the 503 building. The incidence of benign intracranial tumors was elevated among C500 employees, but the increase was not concentrated in any particular building and may have been due to chance, bias or both. Other results included an excess of colorectal cancer cases among white men who had worked in building 501. Factors related to certain aspects of lifestyle or an unknown occupational exposure may explain this increase.

## REFERENCES

1. Acquavella J, Douglass T, Phillips S. Evaluation of excess colorectal cancer incidence among workers involved in the manufacture of polypropylene. *J Occup Med* 30:438-442, 1988.
2. Acquavella J, Owen C, Bird M, Yarborough C, Lynch J. An adenomatous polyp case-control study to assess occupational risk factors following a workplace colorectal cancer cluster. *Am J Epidemiol* 133:357-367, 1991.
3. Acquavella J, Owen C. Assessment of colorectal cancer incidence among polypropylene pilot plant employees. *J Occup Med* 32:127-130, 1990.
4. Arnetz B, Raymond L, Nicolich M, Vargo L. Mortality among petrochemical science and engineering employees. *Arch Environ Health* 46:237-248, 1991.
5. Belli S, Comba P, De Santis M, Grignoli M, Sasco AJ. Cancer mortality patterns among laboratory workers. *Lancet* 335: 1597-1598, 1990.
6. Berleir M, Cordier S. The role of chemical, physical or viral exposures and health factors in neurocarcinogenesis: implications for epidemiologic studies of brain tumors. *Cancer Causes Control* 6:244-256, 1995.
7. Boice J, Land C, Preston D. Ionizing radiation. In Shottenfeld D, Fraumeni J (Eds). *Cancer Epidemiology and Prevention* (2<sup>nd</sup> ed). New York: Oxford University Press, 1996.
8. Bond G, McLaren E, Cartmill J, Wymer K, Sobel W, Lipps T, Cook R. Cause-specific mortality among male chemical workers. *Am J Ind Med* 12:353-383, 1987.
9. Carpenter L, Beral V, Roman E, Swerdlow AJ, Davies G. Cancer in laboratory workers. *Lancet* 338:1080-1081, 1991.

10. Central Brain Tumor Registry of the United States: 1996 Annual Report. Central Brain Tumor Registry of the United States, Chicago, IL, 1997.
11. Chiazze L, Wolf P, Ference L. An historical cohort study of mortality among salaried research and development workers of the Allied Corporation. *J Occup Med* 28:1185-1188, 1986.
12. Cordier S. Risk of cancer among laboratory workers. *Lancet* 335:1097, 1991.
13. Cowles S, Tsai S, Gilstrap E, Ross C. Mortality among employees at a plastics and resin research and development facility. *Occup Env Med* 53:782-786, 1996.
14. Dell L, Teta M. Mortality among workers at a plastics manufacturing and research and development facility. *Am J Ind Med* 28: 373-384, 1995.
15. Delzell E, Beall C, Rodu B, Lees P, Breysse P, Cole P. Case-series investigation of intracranial neoplasms at a petrochemical research facility. *Am J Ind Med* 36:450-458, 1999.
16. Delzell E, Beall C, Rodu B, Sathiakumar N. Mortality among employees at the Amoco Research Center. Report dated September 10, 1999.
17. Delzell E, Beall C, Rodu B, Sathiakumar N. Cancer incidence among employees at the Amoco Research Center. Report dated September 24, 1999.
18. Delzell E, Beall C, Rodu B, Sathiakumar N. A case-control study of intracranial tumors among employees in the 500 building complex of the Amoco Research Center. Report dated October 3, 1999.
19. D.H.H.S. National Death Index User's Manual. D.H.H.S. Publication No. (PHS) 90-1148, Hyattsville, MD, 1990.

20. Divine B, Barron V. Texaco mortality study: II. Patterns of mortality among white males by specific job groups. *Am J Ind Med* 10:371-381, 1986.
21. Dolecek T, Howe H, Snodgrass J. Illinois cancer statistics review: Incidence 1986 to 1995; Mortality 1986-1996. Illinois Department of Public Health, Springfield, IL, 1998.
22. Giovanucci E, Colditz G, Stampfer M, Hunter D, Rosner B, Willett W, Speizer F. A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U.S. women. *J Natl Cancer Inst* 86:192-199, 1994.
23. Giovanucci E, Rimm E, Stampfer M, Colditz G, Ascherio A, Kearney J, Willett W. A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U.S. men. *J Natl Cancer Inst* 86:183-191, 1994.
24. Gold E. Epidemiology of pituitary adenomas. *Epidemiol Rev* 3:163-183, 1981.
25. Greenwald P, Friedlander BR, Lawrence CE, Hearnest T, Earle K. Diagnostic sensitivity bias: an epidemiologic explanation for an apparent brain tumor excess. *J Occup Env Med* 23:690-694, 1981.
26. Hoar S, Pell S. A retrospective cohort study of mortality and cancer incidence among chemists. *J Occup Med* 23:495-501, 1981.
27. Hunter W, Henman B, Bartlett D, LeGeyt I. Mortality of professional chemists in England and Wales, 1965-1989. *Am J Ind Med* 23:615-627, 1993.
28. Inskip P, Linet M, Heineman E. Etiology of brain tumors in adults. *Epidemiol Rev* 17:382-414, 1995.
29. Lagast H, Tomenson J, Stringer DA. Polypropylene production and colorectal cancer: a review of the epidemiological evidence. *Occup Med* 45:69-74, 1995.

30. Land CE. Carcinogenic effects of radiation on the human digestive tract and other organs. In: Upton AC, Albert RE, Burns FJ, Shore RE (Eds). *Radiation Carcinogenesis*. Elsevier, New York, 1986, pp. 347-378.
31. Lewis RJ, Lerman SE, Schnatter AR, Hughes JJ, Vernon SW. Colorectal polyp incidence among polypropylene manufacturing workers. *J Med* 36:174-181, 1994.
32. Lewis RJ, Schnatter AR, Lerman SE. Colorectal cancer incidence among polypropylene manufacturing workers: an update. *J Med* 36:652-659, 1994.
33. Maekawa A, Mitsumori K. Spontaneous occurrence and chemical induction of neurogenic tumors in rats—influence of host factors and specificity of chemical structure. *Crit Rev Toxicol* 20:287-310, 1990.
34. Maher K, Defonso L. A historical cohort study of mortality among chemical researchers. *Arch Environ Health* 41:106-116, 1986.
35. Marsh G, Youk AO, Stone RA, Sefcik S, Alcorn C. OCMAP-Plus: A program for the comprehensive analysis of occupational cohort data. *J Occup Environ Med* 40:351-362, 1998.
36. National Academy of Sciences, Committee on the Biological Effects of Ionizing Radiations. *Health Effects of Exposure to Low Levels of Ionizing Radiation (BEIR V)*. Washington, D.C., National Academy Press, 1990.
37. Nelson N, Van Peenen P, Blanchard A. Mortality in a recent oil refinery cohort. *J Occup Med* 29:610-612, 1987.
38. O'Berg M, Burke C, Chen J, Walrath J, Pell S, Gallie C. Cancer incidence and mortality in the DuPont Company: an update. *J Occup Med* 29:245-252, 1987.

39. Olin GR, Ahlbom A. Cancer mortality among three Swedish male academic cohorts: chemists, architects, and mining engineers/metallurgists. *Ann NY Acad Sci* 381:197-201, 1982.
40. Olin GR, Ahlbom A. The cancer mortality among Swedish chemists graduated during three decades: a comparison with the general population and with a cohort of architects. *Environ Res* 22:154-161, 1980.
41. Olin GR. The hazards of a chemical laboratory environment -- a study of the mortality in two cohorts of swedish chemists. *Am Ind Hyg Assoc J* 39:557-562, 1978.
42. Olsen G, Lacy S, Cartmill J, Kravat B, Chamberlin S, Sadacene N, Lipps T. Half-century of cause-specific mortality experience of chemical manufacturing employees. *Am J Ind Med* 26:203-219, 1994.
43. Potter J, Slattery M, Bostick R, Gapstur S. Colon cancer: a review of the epidemiology. *Epidemiol Rev* 15:499-545, 1993.
44. Preston-Martin S, Mack W. Neoplasms of the nervous system. In Shottenfeld D, Fraumeni J (Eds). *Cancer Epidemiology and Prevention* (2<sup>nd</sup> ed). Oxford University Press, New York, 1996.
45. Preston-Martin S, Mack W, Henderson B. Risk factors for gliomas and meningiomas in males in Los Angeles County. *Cancer Res* 49:6137-6143, 1989.
46. Preston-Martin S, Thomas D, Wright W, Henderson B. Noise trauma in the aetiology of acoustic neuromas in men in Los Angeles County, 1978-1985. *Br J Cancer* 59:783-786, 1989.

47. Rex DK, Lehman GA, Hawes RH, Ulbright TM, Smith JJ. Screening colonoscopy in asymptomatic average-risk persons with negative fecal occult blood tests. *Gastroenterology* 100:64-67, 1991.
48. Ries LAG, Kosary CL, Hankey BF, Miller BA, Edwards BK (Eds). *SEER Cancer Statistics Review, 1973-1995*. National Cancer Institute, Bethesda, MD, 1998.
49. Ron E, Modan B, Boice JD, Alfandary E, Stovall M, Chetrit A, Katz L. Tumors of the brain and nervous system after radiotherapy in childhood. *N Engl J Med* 319:1033-1039, 1988.
50. Sasco AJ. Risques pour la sante dans les laboratoires de recherche biologique et medicale. *Med Sci* 5:489-498, 1989.
51. Satin K, Wong O, Yuan L, Bailey W, Newton K, Wen C, Swencicki R. A 50-year mortality follow-up of a large cohort of oil refinery workers in Texas. *J Occup Env Med* 38:492-506, 1996.
52. Schneider AB, Shore-Freedman E, Ryo UY, Bekerman C, Murray F, Pinsky S. Radiation-induced tumors of the head and neck following childhood irradiation. *Medicine* 64:1-15, 1985.
53. Schottenfeld D, Winawer S. Cancers of the large intestine. In Schottenfeld D, Fraumeni J (Eds). *Cancer Epidemiology and Prevention* (2<sup>nd</sup> ed). Oxford University Press, New York, 1996.
54. Searle CE, Waterhouse JAH. Epidemiological study of the mortality of British chemists. *Br J Cancer* 38:192-193, 1978.

55. Sznajder L, Abrahams C, Parry DM, Gierlowski TC, Shore-Freedman E, Schneider AB. Multiple schwannomas and meningiomas associated with irradiation in childhood. *Arch Intern Med* 156:1873-1878, 1996.
56. Teta M, Ott M, Schnatter A. An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. *J Occup Med* 33:45-51, 1991.
57. Teta M, Schnatter A, Ott M, Pell S. Mortality surveillance in a large chemical company: the Union Carbide experience, 1974-1983. *Am J Ind Med* 17:435-447, 1990.
58. Vobecky J, Caro J, Devroede G. A case-control study of risk factors for large bowel carcinoma. *Cancer* 51:1958-1963, 1983.
59. Vobecky J, Devroede G, Caro J. Risk of large-bowel cancer in synthetic fiber manufacture. *Cancer* 54:2537-2542, 1984.
60. Vobecky J, Devroede G, Lacaille J, Watier A. An occupational group with a high risk of large bowel cancer. *Gastroenterology* 75:221-223, 1978.
61. Waxweiler R, Alexander V, Leffingwell S, Haring M, Lloyd J. Mortality from brain tumors and other causes in a cohort of petrochemical workers. *J Natl Cancer Inst* 70:75-81, 1983.

TABLES

Table 1. Response, participation and eligibility (ever v. never in the 500 Complex) of ARC cohort members included in the questionnaire survey of employees initially classified as definitely or possibly having worked in the 500 Complex

Subject group	N	%
Total ARC subjects	6955	100%
Included in questionnaire survey	2595	37*
Respondents	2214	85†
Participants	2172	98‡ (84)†
Ever in the 500 Complex	1847	85§
Ever full- or part-time	1735	94¶
Intermittent, only	112	6¶
Never in the 500 Complex	325	15§
Nonparticipants	42	2‡
Nonrespondents	381	15†

\* Per cent of total ARC subjects.

† Per cent of subjects included in the questionnaire survey.

‡ Per cent of respondents.

§ Per cent of participants.

¶ Per cent of subjects in the 500 Complex.

Table 2. Number or selected median characteristics of subjects included in the questionnaire survey of definite or possible 500 Complex (C500) employees, by response/participation status and final C500 employment status

Characteristic	Survey participants			Survey nonrespondents and nonparticipants N (% of total)
	C500 full/part-time N (% of total)	Intermittent N (% of total)	Not in C500 N (% of total)	
Total	1735 (100) ‡	112 (100)	325 (100)	423 (100)
Pre-survey C500 employment classification				
Definitely in C500	1449 (84)	17 (15)	11 (3)	204 (48)
Possibly in C500	286 (16)	95 (85)	314 (97)	219 (52)
Employment status				
Active at the ARC	394 (23)	18 (16)	28 (9)	26 (6)
Active elsewhere, Amoco	209 (12)	28 (25)	47 (14)	24 (6)
Retired	282 (16)	15 (13)	21 (6)	31 (7)
Other inactive	850 (49)	51 (46)	229 (70)	342 (81)
Usual company				
ACC	1446 (84)	61 (55)	208 (64)	314 (74)
AOC	38 (2)	8 (7)	42 (13)	18 (4)
AC	248 (14)	43 (38)	75 (23)	90 (21)
Other	3 (0)	0 (0)	0 (0)	1 (0)
Vital status*				
Alive	1669 (96)	110 (98)	305 (94)	378 (89)
Deceased	65 (4)	2 (2)	20 (6)	25 (6)
Unknown	1 (0)	0 (0)	0 (0)	20 (5)
Race/gender				
White men	1107 (64)	75 (67)	201 (62)	230 (54)
Nonwhite men	136 (8)	10 (9)	25 (8)	79 (19)
White women	444 (26)	23 (21)	90 (28)	89 (21)
Nonwhite women	48 (3)	4 (4)	9 (3)	25 (6)
Age, median †	47	44	44	44
Year of hire, median				
At ARC	1978	1982	1978	1979
At Amoco	1977	1980	1977	1978
Years worked, median				
At ARC	6.8	5.0	1.8	2.2
At Amoco	9.5	10.5	3.7	3.0

\* As of the survey response date for participants; as of 10/01/97 for nonrespondents and nonparticipants.

† As of the survey response date for living participants; as of 01/01/98 for living nonrespondents and nonparticipants; as of death date for decedents.

‡ Per cents may not sum to 100 because of rounding.

Table 3. Number of incident cancers and of benign intracranial tumors among 1735 survey participants who were full- or part-time in the 500 Complex (C500), 111 survey participants employed only intermittently in C500, 325 survey participants confirmed as never in C500 and 423 nonrespondents/nonparticipants, by case confirmation source

	Cancers		Benign intracranial tumors		Other tumors	
	N	%#	N	%	N	%
<b>Participants full- or part-time in C500</b>						
Total reported cases	103§	100%	6	100%	131§	100%
Not confirmed	3	3	0	0	48	37
Confirmed, not a case†	8§	8	0	0	25	19
Confirmed cancer/tumor, total*	92	89 (92)	6	100	58§	44 (70)
Medical record confirmed diagnosis	83		6		58	
ISCR only or ISCR+DC‡	6		0		0	
DC only‡	3		0		0	
<b>Participants intermittently, only, in C500</b>						
Total reported cases	9	100	2	100	11	100
Not confirmed	1	11	0		5	46
Confirmed, not a case†	1	11	0		0	0
Confirmed cancer/tumor, total*	7	78 (88)	2		6	55 (100)
Medical record confirmed diagnosis	7		2		6	
<b>Participants never in C500</b>						
Total reported cases	19	100	2	100	16	100
Not confirmed	0	0	0	0	11	69
Confirmed: not a case†	1	5	0	0	2	13
Confirmed cancer/tumor, total*	18	95 (95)	2	100	3	19 (60)
Medical record confirmed diagnosis	14		2		3	
ISCR only or ISCR+DC‡	2		0		0	
DC only‡	2		0		0	
<b>Nonrespondents/nonparticipants</b>						
Confirmed cancers, total*	16		0	0	0	
ISCR only or ISCR+DC‡	12		0	0	0	
DC only‡	4		0	0	0	

\* Confirmed nonmelanotic skin cancers are counted as "other" tumors.

† Medical records indicated that the subject did not have cancer, other than nonmelanotic skin cancer; or did not have a benign intracranial tumor; or did not have another type of tumor.

‡ Diagnosis confirmation source: ISCR, Illinois State Cancer Registry; or DC, death certificate, only.

§ Includes three cases confirmed as nonmelanotic skin cancers and also counted as "other" tumors.

# Numbers not in parentheses are per cents of all reported cases. Numbers in parentheses are per cents of all reported cases for whom we obtained confirmation.

Table 4. Number of subjects employed in the 500 Complex (C500) by gender, race, employment status and vital status

	Men		Women		Total					
	White		Nonwhite		Nonwhite					
	N	%†	N	%	N	%				
<b><u>Full- or part-time in C500</u></b>	1107	100	136	100	444	100	48	100	1735	100
Employment status*										
Active at ARC	259	23	46	34	77	17	12	25	394	23
Active elsewhere at Amoco	135	12	24	18	44	10	6	13	209	12
Inactive	713	64	66	49	323	73	30	63	1132	65
Vital status*										
Alive	1050	95	134	99	437	98	48	100	1669	96
Deceased	56	5	2	1	7	2	0	0	65	4
Unknown	1	<1	0	0	0	0	0	0	1	<1
<b><u>Intermittent in C500</u></b>	75	100	10	100	23	100	4	100	112	100
Employment status*										
Active at ARC	14	19	2	20	2	9	0	0	18	16
Active elsewhere at Amoco	16	21	2	20	8	35	2	50	28	25
Inactive	45	60	6	60	13	57	2	50	66	59
Vital status*										
Alive	73	97	10	100	23	100	4	100	110	98
Deceased	2	3	0	0	0	0	0	0	2	2

\* As of January 1, 1998.

† Per cents may not sum to 100 because of rounding.

Table 5. Selected median characteristics of subjects and total and median person-years of follow-up by gender and race

Characteristic	Men		Women		Total
	White	Nonwhite	White	Nonwhite	
Age (years)*	49	48	44	39	47
Year of hire*					
In C500	1978	1984	1983	1986	1979
At ARC	1976	1981	1981	1985	1978
At Amoco	1976	1981	1980	1985	1977
Years worked*					
In C500	4.4	4.3	2.8	2.5	3.6
At ARC	8.2	7.0	5.1	5.3	6.8
At Amoco	12.5	9.5	6.5	5.7	9.5
Person-years of follow-up					
Total	20160	2102	7031	668	29962
Median	19.6	14.2	15.0	12.1	18.2

\* Median value: as of death date for decedents; as of response date for other subjects.

Table 6. Number of subjects, median years worked and median hire year by mutually exclusive building

Building	Number (%)*		Median years worked			Median hire year		
	In building		501	502	503	501	502	503
	501 only	472	(27)	2.3	—	—	1978	—
502 only	310	(18)	—	2.8	—	—	1978	—
503 only	445	(26)	—	—	2.8	—	—	1981
501 + 502	116	(7)	3.6	3.8	—	1981	1981	—
501 + 503	181	(10)	3.5	—	2.2	1983	—	1985
502 + 503	85	(5)	—	3.0	3.5	—	1987	1983
501 + 502 +503	105	(6)	2.0	1.6	1.4	1981	1985	1984
Unknown	21	(1)	—	—	—	—	—	—

\* % in building, proportion of the total study group of 1676 subjects.

Table 7. Number of subjects and of person-years and selected median characteristics of subjects ever in buildings 501, 502, and 503

	Men		Women		Total
	White	Nonwhite	White	Nonwhite	
<b>Ever 501</b>					
Subjects	571	69	210	24	874
Person-years, total	10074	953	3151	268	14446
Person-years, median	18.8	12.6	14.2	8.5	17.0
501 hire year, median	1978	1985	1983	1989	1980
501 years worked, median	2.9	3.6	1.6	1.9	2.5
<b>Ever 502</b>					
Subjects	356	55	182	23	616
Person-years, total	5940	835	2773	320	9867
Person-years, median	17.2	15.9	14.8	11.6	16.3
502 hire year, median	1980	1982	1983	1986	1981
502 years worked, median	2.7	4.0	2.2	1.7	2.7
<b>Ever 503</b>					
Subjects	541	60	200	15	816
Person-years, total	8792	884	2836	157	12669
Person-years, median	15.5	12.6	12.6	11.5	14.1
503 hire year, median	1982	1985	1985	1986	1984
503 years worked, median	2.7	3.5	1.9	2.1	2.5

Table 8. Observed/expected numbers of cancers, SIRs and 95% CIs by gender and race, full- or part-time C500 employees, SEER comparison

Type of cancer		Men		Women		All Subjects
		White	Nonwhite	White	Nonwhite	
All cancer	Obs/Exp	75/82	2/5.0	14/20	1/1.0	92/108
	SIR	91	40	71	97	85
	95% CI	72-114	5-144	39-119	2-543	69-104
Digestive system*	Obs/Exp	19/15	0/1.3	0/2.3	0/0.1	19/19
	SIR	127	-	-	-	102
	95% CI	77-199	-	-	-	62-159
Colon	Obs/Exp	8/6.0	0/0.4	0/1.1	0/0.1	8/7.5
	SIR	133	-	-	-	107
	95% CI	57-262	-	-	-	46-210
Rectum	Obs/Exp	6/3.2	0/0.2	0/0.5	0/0.0	6/3.9
	SIR	186	-	-	-	152
	95% CI	68-406	-	-	-	56-331
Respiratory System	Obs/Exp	8/16	0/1.2	1/2.0	0/0.1	9/20
	SIR	49	-	-	-	46
	95% CI	21-97	-	-	-	21-87
Lung	Obs/Exp	6/14	0/1.0	1/1.9	0/0.1	7/17
	SIR	42	-	-	-	41
	95% CI	16-92	-	-	-	16-84
Melanoma of the skin	Obs/Exp	4/4.0	0/0.0	0/1.1	0/0.0	4/5.1
	SIR	100	-	-	-	78
	95% CI	27-255	-	-	-	21-199
Breast	Obs/Exp	-	-	8/7.0	1/0.4	9/7.4
	SIR	-	-	114	-	121
	95% CI	-	-	49-224	-	55-230
Prostate and testis	Obs/Exp	21/19	1/0.8	-	-	22/20
	SIR	111	-	-	-	111
	95% CI	68-169	-	-	-	70-168
Prostate	Obs/Exp	19/17	1/0.8	-	-	20/18
	SIR	109	-	-	-	110
	95% CI	66-171	-	-	-	67-171

Table 8. Observed/expected numbers of cancers, SIRs and 95% CIs by gender and race, full- or part-time C500 employees, SEER comparison

Type of cancer		Men		Women		All Subjects
		White	Nonwhite	White	Nonwhite	
Bladder and kidney	Obs/Exp	2/7.9	0/0.3	1/0.6	0/0.0	3/8.9
	SIR	25	-	-	-	34
	95% CI	3-91	-	-	-	7-99
Bladder	Obs/Exp	1/5.3	0/0.1	0/0.3	0/0.0	1/5.7
	SIR	19	-	-	-	17
	95% CI	1-106	-	-	-	0-97
Central nervous system	Obs/Exp	6/1.7	0/0.1	0/0.3	0/0.0	6/2.1
	SIR	359	-	-	-	287
	95% CI	132-781	-	-	-	105-624
Brain†	Obs/Exp	6/1.6	0/0.1	0/0.3	0/0.0	6/2.0
	SIR	376	-	-	-	302
	95% CI	138-819	-	-	-	111-657
Non-Hodgkin's lymphoma	Obs/Exp	5/4.1	1/0.3	0/0.6	0/0.0	6/5.1
	SIR	121	-	-	-	118
	95% CI	39-283	-	-	-	44-258
Leukemia	Obs/Exp	3/2.2	0/0.1	0/0.4	0/0.0	3/2.7
	SIR	137	-	-	-	112
	95% CI	28-400	-	-	-	23-327
Other cancer‡	Obs/Exp	7/12	0/1.0	4/5.4	0/0.3	11/19
	SIR	58	-	74	-	58
	95% CI	23-119	-	20-189	-	29-104

\* Includes, in addition to colon and rectal cancers, cancers of the esophagus (1 case), stomach (1) gallbladder (1) and pancreas (2).

† The observed number for white men and for the total study group includes one subject recorded in a population-based cancer registry as having primary brain cancer but found, by pathology review of material obtained after the original diagnosis, to have melanoma of an unknown primary site.

‡ Includes soft tissue sarcoma (1), Hodgkin's disease (2), multiple myeloma (1), and cancers of the buccal cavity and pharynx (1), ovary (1), endometrium (1), thyroid (2), adrenal gland (1) and unknown primary site (1).

Table 9. Observed/expected number, SIR and 95% CI for selected cancers, all race/gender groups combined and white men, by years since hire and years worked, full- or part-time C500 employees, SEER comparison

Years since hire	Years worked	Obs/Exp	All race/gender groups combined					White men				
			All cancer	Colon cancer	Rectal cancer	Brain cancer	All cancer	Colon cancer	Rectal cancer	Brain cancer		
<10		13/19	1/1.1	1/0.6	0/0.6	9/12	1/0.8	1/0.5	0/0.4			
	SIR	67	91	157	0	72	127	211	0			
	95% CI	36-114	2-506	4-870	0-671	33-137	3-705	5-1185	0-900			
10+		5/8.6	1/0.6	1/0.4	1/0.2	4/6	1/0.5	1/0.3	1/0.2			
	SIR	59	169	289	504	65	219	364	621			
	95% CI	19-136	4-944	7-1591	13-2785	18-166	6-1211	9-2063	16-3481			
<5		34/27	3/1.8	1/0.9	1/0.5	27/19	3/1.4	1/0.7	1/0.4			
	SIR	128	171	110	212	144	223	141	276			
	95% CI	89-179	35-501	3-612	5-1185	95-209	46-650	4-785	7-1547			
5+		40/54	3/4.1	3/2.1	4/0.8	35/45	3/3.4	3/1.8	4/0.7			
	SIR	75	74	147	521	78	87	170	602			
	95% CI	53-102	15-216	30-428	142-1330	54-108	18-256	35-498	165-1552			

Table 10. Observed/expected numbers of cancers, SIRs and 95% CIs by building (ever), all race/gender groups combined, full- or part-time C500 employees, SEER comparison

Type of cancer		Ever 501	Ever 502	Ever 503
All cancer	Obs/Exp	47/51	35/41	28/45
	SIR	92	85	62
	95% CI	68-123	59-118	41-90
Digestive system	Obs/Exp	13/8.8	5/7.0	2/7.8
	SIR	149	71	26
	95% CI	79-254	23-166	3-92
Colon	Obs/Exp	6/3.5	1/2.9	1/3.1
	SIR	170	-	32
	95% CI	62-370	-	1-179
Rectum	Obs/Exp	5/1.9	2/1.5	0/1.7
	SIR	269	-	-
	95% CI	87-629	-	-
Lung	Obs/Exp	2/8.0	4/6.6	1/7.1
	SIR	25	61	14
	95% CI	3-90	17-155	0-78
Melanoma of the skin	Obs/Exp	2/2.5	3/1.8	1/2.2
	SIR	-	166	-
	95% CI	-	34-486	-
Breast	Obs/Exp	4/3.2	5/3.6	2/3.1
	SIR	127	138	64
	95% CI	35-324	45-322	8-232
Prostate and testis	Obs/Exp	12/9.4	6/7.3	7/8.3
	SIR	127	82	85
	95% CI	66-222	30-178	34-175
Prostate	Obs/Exp	11/8.6	6/6.9	5/7.5
	SIR	128	87	66
	95% CI	64-229	32-190	22-155

Table 10. Observed/expected numbers of cancers, SIRs and 95% CIs by building (ever), all race/gender groups combined, full- or part-time C500 employees, SEER comparison

Type of cancer		Ever 501	Ever 502	Ever 503
Bladder and kidney	Obs/Exp	1/4.3	3/3.3	0/3.7
	SIR	24	90	0
	95% CI	1-131	19-263	0-100
Central nervous system	Obs/Exp	3/1.0	2/0.7	5/0.9
	SIR	298	-	562
	95% CI	62-871	-	182-1311
Brain*	Obs/Exp	3/1.0	2/0.7	5/0.9
	SIR	314	-	592
	95% CI	65-917	-	192-1381
Non-Hodgkin's lymphoma	Obs/Exp	5/2.5	0/1.8	5/2.2
	SIR	203	-	228
	95% CI	66-474	-	74-533
Leukemia	Obs/Exp	0/1.3	3/1.0	0/1.1
	SIR	-	308	-
	95% CI	-	64-901	-
Other cancers	Obs/Exp	5/10	4/8.1	5/8.8
	SIR	50	49	57
	95% CI	16-116	13-126	19-133

\* The observed number for 501 and for 502 includes one subject recorded in a population-based cancer registry as having primary brain cancer but found, by pathology review of material obtained after the original diagnosis, to have melanoma of an unknown primary site.

Table 11. Observed/expected number of cancers, SIRs and 95% CIs by building (ever), white men, full- or part-time C500 employees, SEER comparison

Type of cancer		Ever 501	Ever 502	Ever 503
All cancer	Obs/Exp	40/40	26/29	24/34
	SIR	101	89	71
	95% CI	72-137	58-130	45-105
Digestive system	Obs/Exp	13/7.2	5/5.3	2/6.1
	SIR	181	94	33
	95% CI	96-309	31-220	4-118
Colon	Obs/Exp	6/2.9	1/2.2	1/2.4
	SIR	206	-	-
	95% CI	76-449	-	-
Rectum	Obs/Exp	5/1.6	2/1.2	0/1.3
	SIR	323	-	-
	95% CI	105-754	-	-
Lung	Obs/Exp	2/6.8	3/5.2	1/5.7
	SIR	29	58	17
	95% CI	4-106	12-169	0-97
Melanoma of the skin	Obs/Exp	2/2.0	3/1.3	1/1.8
	SIR	-	226	-
	95% CI	-	47-662	-
Prostate and testis	Obs/Exp	12/9.1	6/7.0	6/7.9
	SIR	132	85	76
	95% CI	68-231	31-186	28-166
Prostate	Obs/Exp	11/8.3	6/6.6	4/7.2
	SIR	133	91	56
	95% CI	67-239	33-198	15-143

Table 11. Observed/expected numbers of cancers, SIR and 95% CI by building (ever), white men, full- or part-time C500 employees, SEER comparison

Type of cancer		Ever 501	Ever 502	Ever 503
Bladder and kidney	Obs/Exp	1/3.8	2/2.9	0/3.3
	SIR	26	-	0
	95% CI	1-145	-	0-114
Central nervous system	Obs/Exp	3/0.8	2/0.6	5/0.7
	SIR	364	-	701
	95% CI	75-1065	-	228-1636
Brain*	Obs/Exp	3/0.8	2/0.5	5/0.7
	SIR	382	-	735
	95% CI	79-1117	-	239-1716
Non-Hodgkin's lymphoma	Obs/Exp	4/2.1	0/1.4	4/1.8
	SIR	196	-	225
	95% CI	53-501	-	61-576
Leukemia	Obs/Exp	0/1.1	3/0.8	0/0.9
	SIR	-	398	-
	95% CI	-	82-1163	-
Other cancers	Obs/Exp	3/6.9	2/4.9	5/5.8
	SIR	43	40	86
	95% CI	9-126	5-146	28-201

\* The observed number for 501 and for 502 includes one subject recorded in a population-based cancer registry as having primary brain cancer but found, by pathology review of material obtained after the original diagnosis, to have melanoma of an unknown primary site.

Table 12. Observed/expected number, SIR and 95% CI, all cancer and selected cancers, all race/gender groups combined and white men, by building (ever), years since hire and years worked, full- or part-time C500 employees, SEER comparison

Building	Years since hire	Years worked	All race/gender groups combined					White men				
			All cancer	Colon cancer	Rectal cancer	Brain cancer	All cancer	Colon cancer	Rectal cancer	Brain cancer		
Ever 501	<10	Obs/Exp	11/11	1/0.7	2/0.4	2/0.3	9/7.4	1/0.5	2/0.3	2/0.2		
		SIR	98	150	525	653	122	211	706	860		
		95% CI	49-175	4-831	64-1900	78-2329	56-232	5-1185	86-2579	105-3139		
	5+	Obs/Exp	2/3.6	0/0.3	1/0.2	0/0.1	1/2.8	0/0.2	1/0.1	0/0.1		
		SIR	55	0	664	0	35	0	786	0		
		95% CI	7-199	0-1419	17-3713	0-4613	1-197	0-1677	19-4285	0-5271		
	10+	Obs/Exp	20/16	2/1.1	1/0.6	0/0.3	17/12	2/0.8	1/0.4	0/0.2		
		SIR	128	188	179	0	147	245	227	0		
		95% CI	78-197	23-681	5-995	0-1318	86-236	30-880	6-1266	0-1677		
	5+	Obs/Exp	14/20	3/1.5	1/0.8	1/0.3	13/18	3/1.4	1/0.7	1/0.3		
		SIR	69	195	131	346	72	214	144	384		
		95% CI	38-115	40-569	3-723	9-1921	38-123	44-626	4-796	10-2142		
Ever 502	<10	Obs/Exp	6/9.8	0/0.6	0/0.3	0/0.2	4/5.9	0/0.4	0/0.2	0/0.2		
		SIR	61	0	0	0	67	0	0	0		
		95% CI	22-135	0-625	0-1085	0-1604	18-173	0-923	0-1538	0-2306		
	5+	Obs/Exp	1/2.8	1/0.2	0/0.1	0/0.1	1/1.9	1/0.1	0/0.1	0/0.0		
		SIR	36	517	0	0	53	709	0	0		
		95% CI	1-201	13-2932	0-3355	0-6150	1-298	18-3979	0-4613	0-9225		
	10+	Obs/Exp	11/14	0/1.0	0/0.5	0/0.2	6/9.3	0/0.7	0/0.4	0/0.2		
		SIR	80	0	0	0	65	0	0	0		
		95% CI	40-143	0-388	0-769	0-1757	24-141	0-535	0-1054	0-2306		
	5+	Obs/Exp	17/15	0/1.1	2/0.6	2/0.2	15/12	0/0.9	2/0.5	2/0.2		
		SIR	113	0	355	1009	122	0	423	1204		
		95% CI	66-181	0-327	43-1289	121-3610	68-202	0-397	51-1536	142-4247		

Table 12. Observed/expected number, SIR and 95% CI, all cancer and selected cancers, all race/gender groups combined and white men, by building (ever), years since hire and years worked, full- or part-time C500 employees, SEER comparison

Building	Years since hire	Years worked	Obs/Exp	SIR	95% CI	All race/gender groups combined					White men				
						All cancer	Colon cancer	Rectal cancer	Brain cancer	All Cancer	Colon cancer	Rectal cancer	Brain cancer		
Ever 503	<10	Obs/Exp	7/11	0/0.6	0/0.4	2/0.3	5/7.3	0/0.5	0/0.3	2/0.2	22-161	0-802	0-1367	110-3282	
		SIR	64	0	0	695	69	0	0	918					
		95% CI	26-131	0-577	0-1025	83-2490	22-161	0-802	0-1367	110-3282					
	5+	Obs/Exp	1/2.9	0/0.2	0/0.1	0/0.1	1/2.1	0/0.2	0/0.1	0/0.1	48	0-2460	0-4613	0-6150	
		SIR	34	0	0	0	48	0	0	0					
		95% CI	1-191	0-1845	0-3355	0-5271	1-265	0-2460	0-4613	0-6150					
10+	<5	Obs/Exp	9/14	1/1.0	0/0.5	1/0.2	9/11	1/0.8	0/0.4	1/0.2	85	3-723	0-923	13-2932	
		SIR	63	100	0	420	85	129	0	529					
		95% CI	29-120	3-557	0-724	11-2321	39-161	3-723	0-923	13-2932					
5+	<5	Obs/Exp	11/17	0/1.3	0/0.7	2/0.3	9/14	0/1.1	0/0.6	2/0.2	64	0-351	0-659	110-3282	
		SIR	65	0	0	796	64	0	0	920					
		95% CI	32-116	0-286	0-559	97-2888	29-122	0-351	0-659	110-3282					

Table 13. Observed/expected numbers of benign intracranial tumors by gender, full- or part-time C500 employees, CBTRUS\* comparison

Type of intracranial tumor		Men	Women	Total
Meningioma	Obs/Exp	2/0.4	0/0.3	2/0.7
Vestibular schwannoma	Obs/Exp	1/0.3	1/0.1	2/0.4
Pituitary adenoma	Obs/Exp	1/0.3	1/0.1	2/0.5
Total	Obs/Exp	4/1.1	2/0.5	6/1.6
	SIR	368	-	385
	95% CI	100-942	-	142-839

\* Central Brain Tumor Registry of the United States, 1990-1993.

Table 14. Observed/expected numbers of benign intracranial tumors by building (ever), all race/gender groups combined, full- or part-time C500 employees, CBTRUS\* comparison

Type of intracranial tumor		Ever 501	Ever 502	Ever 503
Meningioma	Obs/Exp	0/0.3	1/0.3	1/0.3
Vestibular schwannoma	Obs/Exp	1/0.2	0/0.1	1/0.2
Pituitary adenoma	Obs/Exp	1/0.2	1/0.2	0/0.2
Total	Obs/Exp	<del>1/0.7</del> 2/0.7	2/0.6	2/0.7

\* Central Brain Tumor Registry of the United States, 1990-1993.

Table 15. Number of confirmed and unconfirmed self-reported nonmelanotic skin cancers, cancers in situ (other than bladder cancer) and benign tumors (other than benign intracranial tumors) among subjects who worked full- or part-time or intermittently, only, in C500

Type of tumor	<u>Full-or part-time in C500</u>	<u>Intermittent in C500</u>
	Number of tumors	Number of tumors
<b>Confirmed tumors</b>	<b>58</b>	<b>6</b>
Breast cancer <i>in situ</i>	1	0
Melanoma <i>in situ</i>	2	0
Nonmelanotic skin cancer	27	4
Colorectal polyps	6	1
Benign connective/soft tissue tumors	4	0
Benign skin tumors	4	0
Benign breast tumors	3	0
Benign thyroid tumors	4	0
Hemangiomas	4	0
Benign tumors of the uterus and ovaries	3	0
Other benign tumors	0	1
<b>Unconfirmed tumors</b>	<b>48</b>	<b>5</b>
Nonmelanotic skin cancer	16	0
Colorectal polyps	0	2
Benign connective/soft tissue tumors	5	0
Benign skin tumors	0	0
Benign breast tumors	0	1
Benign thyroid tumors	0	1
Hemangiomas	0	0
Benign tumors of the uterus and ovaries	0	0
Other specified benign tumors	5	0
Benign tumors of an unspecified site	22	1

APPENDIX

SURVEY OF CURRENT AND FORMER EMPLOYEES AT THE  
AMOCO RESEARCH CENTER IN NAPERVILLE, ILLINOIS

**SURVEY OF CURRENT AND FORMER EMPLOYEES AT THE  
AMOCO RESEARCH CENTER IN NAPERVILLE, ILLINOIS**

By

**THE UNIVERSITY OF ALABAMA AT BIRMINGHAM**

For additional information contact Dr. Elizabeth Delzell, UAB School of Public Health, 209 Tidwell Hall, 720 South 20th Street, Birmingham, Alabama 35294-0008, telephone (205) 934-1200 (call collect).

**CONSENT TO PARTICIPATE IN SURVEY OF CURRENT AND FORMER  
EMPLOYEES AT THE AMOCO RESEARCH CENTER IN NAPERVILLE, ILLINOIS**

Date: \_\_\_\_\_

I agree to participate in the health study of employees of Amoco. I understand that, by signing this form, I am giving permission for the University of Alabama at Birmingham (UAB) to use my answers on the enclosed questionnaire regarding my employment at Amoco and about any tumors or cancers I may have had. This information will be used by UAB only for statistical purposes and for contacting physicians and hospitals that provided me with diagnostic and treatment services for cancers and other tumors, if I ever had such tumors. I understand that my cooperation is voluntary, and that I have the right to withdraw from the study at any time before its completion by contacting Dr. Elizabeth Delzell (call collect: 205-934-5857) at UAB. I further understand that the information I provide will be kept strictly confidential by UAB and that UAB will not release my answers to the questionnaire to Amoco or to any other individual or agency.

Signature: \_\_\_\_\_

Street  
Address: \_\_\_\_\_

City: \_\_\_\_\_

State: \_\_\_\_\_ Zip Code: \_\_\_\_\_

Telephone Number: (\_\_\_\_) \_\_\_\_\_

**SURVEY OF CURRENT AND FORMER EMPLOYEES AT  
THE AMOCO RESEARCH CENTER IN NAPERVILLE, ILLINOIS**

**I. YOUR IDENTIFICATION**

1. Your name:

Last name (Surname) \_\_\_\_\_

First name \_\_\_\_\_

Middle name \_\_\_\_\_

Other name(s) while employed at Amoco (if you were an Amoco employee)  
\_\_\_\_\_

2. If you are a family member completing this form for an employee who cannot participate, please indicate your relationship to the Amoco employee (check one):

Spouse \_\_\_\_\_ Child \_\_\_\_\_ Brother/Sister \_\_\_\_\_

Other (please specify) \_\_\_\_\_

**II. EMPLOYMENT**

**Instructions.** Please provide the following information about your Amoco employment history. If you do not remember your exact dates of employment, please estimate the dates as closely as possible. Please indicate whether the dates provided are definite or approximate. If you do not know the dates circle "unknown". If you need additional space to answer any question, please use the space provided on page 6.

1. Years of employment with Amoco at any location:

(If your employment with Amoco was interrupted by lay-off, military leave, maternity leave or other type of absence, please list each employment period separately.)

Indicate if your answer is:

From 19\_\_\_\_ to 19\_\_\_\_ Definite / Approximate / Unknown

From 19\_\_\_\_ to 19\_\_\_\_ Definite / Approximate / Unknown

2. Dates of employment at the Amoco Research Center (ARC) in Naperville, Illinois:

(If there was more than one period of employment at the ARC, please list each period separately.)

Indicate if your answer is:

From \_\_\_\_\_ to \_\_\_\_\_ Definite / Approximate / Unknown  
month/year month/year

From \_\_\_\_\_ to \_\_\_\_\_ Definite / Approximate / Unknown  
month/year month/year

3. Did you ever occupy an office or laboratory in the "500 Complex" (buildings 501, 502 or 503) for at least 30 hours per week for one week or longer? The map insert shows the location of 500 Complex buildings.

YES / NO / UNKNOWN [circle one]

If NO, please skip to question 5.

If YES, please answer question 4.

4. Dates of work (at least 30 hours per week) in the "500 Complex" (buildings 501, 502 or 503). (Please list all time periods and buildings in which you worked in the 500 Complex. If you do not remember where you worked, please see question 7.)

Dates:	500 Complex Bldg no. (circle one)	Floor or Area:
From _____ to _____ month/year month/year	501 / 502 / 503	_____
From _____ to _____ month/year month/year	501 / 502 / 503	_____
From _____ to _____ month/year month/year	501 / 502 / 503	_____
From _____ to _____ month/year month/year	501 / 502 / 503	_____
From _____ to _____ month/year month/year	501 / 502 / 503	_____
From _____ to _____ month/year month/year	501 / 502 / 503	_____

5. Did you ever work fewer than 30 hours per week or occasionally in the "500 Complex" (buildings 501, 502 or 503)?

YES / NO / UNKNOWN [circle one]

If NO or Unknown, please skip to Section III.

If YES, please answer question 6.

6. Dates of work (less than 30 hours per week) in the "500 Complex". (Please list all time periods and buildings in which you worked in the 500 Complex. If you do not remember where you worked, please see question 7.)

Dates:	500 Complex Bldg.no.[circle one]	Floor:	No. hours per day(D)/week(W)/ month(M)[circle one]
From _____ to _____ month/year month/year	501 / 502 / 503	_____	_____ Hrs. per D / W / M
From _____ to _____ month/year month/year	501 / 502 / 503	_____	_____ Hrs. per D / W / M

Dates:		500 Complex Bldg. no. [circle one]	Floor:	No. hours per day(D)/week(W)/ month(M) [circle one]
From _____ month/year	to _____ month/year	501 / 502 / 503	_____	Hrs. per D / W / M
From _____ month/year	to _____ month/year	501 / 502 / 503	_____	Hrs. per D / W / M

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7. If you worked in the 500 Complex but do not remember where you worked, please provide any other information you recall, such as the name of the business group with which you worked or the lab supervisor with whom you worked.

[Turn to page 6 to record additional information]

Use the space below to provide additional employment information

Additional Amoco employment (other than at ARC) information:

Additional ARC employment information:

Additional 500 Complex employment information:

III. DIAGNOSIS OF CANCERS & OTHER TUMORS

**Instructions.** Please answer the following questions about cancers or tumors which you may have had. Other terms used for cancers or tumors include "malignancy," "neoplasm," or even "growth." If a physician ever told you that you had one of these diagnoses, please indicate this when we ask about "tumors."

1. Were you ever diagnosed as having a cancer or other type of tumor?

YES / NO / Don't Know [circle one]

If YES, please continue with questions 2-4.  
If NO or Don't Know, please sign the consent form and the questionnaire and return them in the envelope provided.

2. For each cancer or tumor that was diagnosed, please tell us the location in the body where the tumor was first found (for example, lung, prostate, breast, brain, blood, leukemia, lymph nodes, intestines, liver, etc.) and the date of diagnosis. If more than one cancer or tumor was diagnosed, please provide information on each. Use the back of page 7 if you need additional space.

Tumor location or type:	Diagnosis date:	Name of HOSPITAL or other place where diagnosis was made	Physician's name
_____	month/year _____	_____	_____
_____	month/year _____	_____	_____
_____	month/year _____	_____	_____

3. Please provide the name and address of any hospital / health care facility listed in question 2 above:

Name: \_\_\_\_\_

Address: \_\_\_\_\_

City and State: \_\_\_\_\_ Zip: \_\_\_\_\_

(2nd facility) Name: \_\_\_\_\_

Address: \_\_\_\_\_

City and State: \_\_\_\_\_ Zip: \_\_\_\_\_

4. Please provide the name and address of any physician listed in question 2:

M.D. Name: \_\_\_\_\_

Address: \_\_\_\_\_

City and State: \_\_\_\_\_ Zip: \_\_\_\_\_

(2nd physician) M.D. Name: \_\_\_\_\_

Address: \_\_\_\_\_

City and State: \_\_\_\_\_ Zip: \_\_\_\_\_

Date: \_\_\_\_\_

**Please return this questionnaire and the signed consent form in the enclosed, self-addressed envelope.**

If you worked in the 500 Complex, either full time or part time, were diagnosed as having a tumor and will give us permission to request medical records pertaining to the tumor diagnosis, please complete and sign the enclosed Consent to Release Medical Records.

Check here if you wish to receive summary of the survey, which we expect to be available by the end of 1998.