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Second Irregularity In NSABP Data Found; Fisher Takes Leave As Group's Chairman

An on-site investigation by NCI found a second irregularity in data submitted to the National Surgical Adjuvant Breast & Bowel Project.

NCI officials said they found that NSABP had known about the latest problem for six months, but failed to alert federal officials.

Accusing NSABP of delays in conducting audits and failure to report irregularities, NCI demanded that the Pittsburgh-based cooperative research group install a new administrative structure, remove Bernard Fisher from

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In Brief

Ross Retires From Bristol-Myers, Forms Own Consulting Service; Obey Wins Key Post

BRUCE ROSS, a Bristol-Myers Squibb Co. executive who played a key role in the development of the drug Taxol, has retired from the company. Accepting an early retirement package extended to all employees, Ross, senior vice president for policy planning and development of the pharmaceutical group, will retire effective April 1. Ross, 53, said he plans to launch a database on utilization of oncology drugs and to consult for pharmaceutical and biotechnology companies. He will remain on the board of directors of Fox Chase Cancer Center and has recently joined the board of Cytogen Corp. Ross joined Bristol Laboratories 27 years ago and has served as general manager of the oncology division of Mead Johnson and Bristol-Myers. On the Taxol project, Ross oversaw the production of the drug as well as the company's negotiations of the development and pricing agreements with NCI. He was also in charge of defending those agreements on Capitol Hill. . . . **REP. DAVID OBEY** (D-WI) won day-to-day control of the House Appropriations Committee last week. The committee's chairman, the ailing Rep. Bill Natcher (D-KY), will retain his titular role. . . . **RODRIGUE MORTEL**, of the Hershey Medical Center at Pennsylvania State Univ., was inducted as president of the Society of Gynecologic Oncologists and the society's annual meeting last month in Orlando, FL. **Stephen Curry**, of Hartford Hospital, was elected president-elect of the society. Other officers of the society are: David Gershenson, president-elect II; Larry Copeland, vice president; William Hoskins, secretary-treasurer; and Kenneth Hatch, secretary-treasurer-elect. Newly elected members to the society's Council are Hervy Averette, Michael Berman, Daniel Clarke-Pearson, and Edward Partridge.

Fisher On Leave From NSABP Following Second Irregularity

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his position as the prinicipal investigator, and temporarily halt the enrollment of patients.

Following the NCI demand, officially delivered to NSABP on March 28, Fisher requested administrative leave from the position he has held since 1967. The Univ. of Pittsburgh appointed Donald Trump, deputy director of the Pittsburgh Cancer Institute, as interim chairman of the NSABP.

Two Weeks of Crisis

The discrepancy in the controversial Breast Cancer Prevention Trial was the latest development in a crisis touched off two weeks ago by a revelation of falsification of data in NSABP studies.

On March 13, NCI and NSABP were publicly confronted with the falsifications in the data submitted by Roger Poisson of St. Luc Hospital in Montreal (**The Cancer Letter**, March 18). The latest discrepancy was found last week in data submitted by St. Mary's Hospital Center, an affiliate of McGill Univ.

NCI officials said they could not determine the significance of the latest discrepancy. However, several observers expressed concern that the latest controversy could damage public confidence in the Breast Cancer Prevention Trial, the NSABP's $60 million study of the potential of the drug tamoxifen to prevent breast cancer in asymptomatic women. Since its initiation two years ago, the prevention trial has been condemned by activists concerned about the health risks of the drug.

Over the past two weeks, NCI and NSABP have been overwhelmed by a tidal wave of outrage from Congress and consumer groups.

- Rep. John Dingell (D-MI), chairman of the House Committee on Energy and Commerce and its Subcommittee on Oversight and Investigations, scheduled a hearing April 13 to examine NCI's actions.
- The National Women's Health Network, a group that has spearheaded opposition to the prevention trial, urged NCI to end that trial as a result of the latest developments.
- The National Breast Cancer Coalition renewed its call for an independent investigation of NSABP.

Responding to the controversy surrounding NSABP, NCI said it will review its procedures for oversight of clinical trials. Separately, the National Cancer Advisory Board has formed a subcommittee to review the NSABP actions and NCI's response.

"The main issue for us is to settle the question of the credibility of NSABP ourselves," Bruce Chabner, director of NCI's Div. of Cancer Treatment, said to **The Cancer Letter**. "I firmly believe the results of the studies are correct and there is enough corroborating evidence to support the conclusions."

Second Hospital In Montreal

The latest discrepancy was discovered when NCI sent a team of investigators to Pittsburgh last week to review all data from NSABP studies to which Poisson had submitted falsified data.

Poisson was found by the NIH Office of Research Integrity more than a year ago to have committed 115 instances of scientific misconduct in data from 99 patients enrolled in 14 NSABP studies, including the B6 study of lumpectomy and three studies of tamoxifen as adjuvant therapy for breast cancer.

"We found a series of reports that had not been filed on time," Chabner said to **The Cancer Letter**. NSABP had found the discrepancy six months ago, but had not reported it to NCI, violating the group's guidelines, he said. Chabner refused to name the hospital or the NSABP trial involved because NCI turned over the investigation to the Office of Research Integrity.

However, **The Cancer Letter** has learned that the discrepancy was found in the file of a St. Mary's patient who was enrolled in the Breast Cancer Prevention Trial.

NCI auditors had found one irregularity involving the date on a chart of a patient enrolled in the

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prevention trial, Pamela Pavlik, director of communications at St. Mary's, said to **The Cancer Letter**. She declined to characterize the discrepancy.

St. Mary's is one of six Montreal hospitals that enroll patients in the Breast Cancer Prevention Trial.

NCI and NSABP staff were in Montreal this week auditing the records of all 200 patients the hospital had enrolled in NSABP studies, Pavlik said.

"Our files are completely open to the NSABP and NCI representatives," Pavlik said. "They have been given the fullest cooperation."

In a statement issued this week, NCI said patients currently enrolled in NSABP studies will continue to receive treatment and follow-up. The group will not be allowed to resume accrual of patients until the Institute completes its review.

NCI: No Cause For Concern

"The Institute strongly believes there is no cause for concern regarding the current practice of medicine, and in particular, the care of breast cancer patients," NCI said in a statement last week. "The Institute has confidence in the standard breast cancer treatments now in use and in clinical trials that are currently in progress."

According to the statement NCI intends to:

- Conduct an independent review of the major contributors to the B6 lumpectomy study, and review all data on NSABP
- Examine the compliance of all clinical cooperative groups to data quality assurance standards.
- Conduct a review of the Institute's internal oversight procedures.
- Create a Clinical Trials Monitoring Branch to oversee group compliance with NCI guidelines.
- Add a provision to the funding mechanism for cooperative groups to require prompt publication of revised research data following a federal finding of scientific misconduct.
- Place information about the problem in the Physician's Data Query information system, a computerized information system, and on CancerFax, accessible to anyone with a fax machine.

In addition, NCI said NSABP is preparing a manuscript that will be submitted to the New England Journal of Medicine.

Fisher has been given the opportunity to present the reanalysis at the meetings of the American Association for Cancer Research and the American Society of Clinical Oncology in April and May.

NCI's Div. of Cancer Treatment provides $7 million a year to fund NSABP. The cooperative group receives funding from the Div. of Cancer Prevention & Control for the prevention trial.

Erosion of Public Trust?

"The important thing is to identify the errors immediately and correct them, and then put it behind us," said Paul Calabresi, chairman of the NCAB, who formed a subcommittee of the board to review the NSABP. The six-member committee, headed by Samuel Wells, will meet with NCI Director Samuel Broder in April.

"Our immediate goal is to have the investigators publish immediately the corrected data from the NSABP trials," Calabresi said. "The second goal is to establish stringent auditing and monitoring systems for the NSABP, and third, to identify and take prompt action on any additional discrepancies or falsified data."

Fran Visco, a member of the President's Cancer Panel and president of the National Breast Cancer Coalition, said the actions planned by NCI and the NCAB were insufficient.

"I think the public trust has been eroded to such an extent that what is needed now is an independent investigation," Visco said to **The Cancer Letter**. "Consumers must be involved in the investigation, oversight, the reporting mechanism—at every level of the process.

"This is a serious problem in the National Cancer Program, and all of us working together need to find a way to correct it immediately," she said. "I really believe the investigation has to be from someone like the Institute of Medicine. I don't believe it should be an entity connected to NCI."

Cindy Pearson, program director for the National Women's Health Network, said the network has been concerned about the Breast Cancer Prevention Trial from the trial's beginning.

"Now to find out that the NSABP can't even guarantee the quality of the recordkeeping and the adherence to this trial, this adds insult to injury," she said. "We are delighted that NCI has stopped enrollment to all NSABP trials. We hope NCI won't just look at adherence, but take a step back and look at the risk-benefit ratio for the prevention trial and consider stopping it permanently."

Harmon Eyre, executive vice president of the

American Cancer Society, agreed that a review of the clinical trials monitoring process is warranted. "As a clinical oncology community we need to affirm the policing and self reporting of clinical trials," he said. "We hope the lessons learned will result in more rapid reporting so we don't lose the trust of the public."

However, Eyre added, "To the best of my knowledge, in spite of the fraud, I have yet to see anyone question the interpretation of the results of the trials." ACS grants fund some pilot NSABP studies.

Lack of Rigorous Auditing?

Clinical researchers contacted this week said NSABP's delay in publishing the reanalysis following the Poisson case may have been the result of the group's inability to keep up with its rapid expansion.

"The group was very busy with getting the Breast Cancer Prevention Trial running," one source said. "They got behind the eight-ball. They need to reorganize their operations office."

A more disturbing question is why the Poisson falsifications were not discovered for as long as 13 years, several observers said.

Sources said NSABP's data auditing procedures were not as stringent as those at other cooperative groups.

"They had a nurse who was on the road five days a week going from hospital to hospital," a researcher involved in auditing for one cooperative group said to **The Cancer Letter**. "She spent most of the time copying information from patient charts, and then would take that back to headquarters."

In contrast, some of the other groups have a committee of physicians and data managers who conduct detailed site visits involving direct comparison of patient records with the records submitted to headquarters, the source said. This scrutiny, by a panel of their peers, by itself would deter most investigators from attempting to falsify data, the source said.

"Dr. Fisher has the highest ethical standards," a researcher involved in another cooperative group said. "These were bizarre, isolated episodes."

Instances of scientific impropriety are relatively rare, researchers said. In an article published last July in the Journal of the American Medical Association, auditors for the Cancer & Leukemia Group B, a group considered to have the most rigorous on-site auditing process, found two instances of improprieties in 11 years of audit reports on 691 institutions. Both instances occurred before 1984.

Another question is the motivation to falsify data. A lawyer for Poisson said the researcher was motivated by a desire to enter more patients onto studies because he believed they received better treatment, not for any financial reasons (**The Cancer Letter**, March 18).

Sources noted that NSABP, unlike most other groups, pays its member institutions on a per-patient basis. Member institutions of other groups depend primarily on grant support, and while a few high-accruing institutions get modest funding from cooperative groups, many hospitals receive no funding.

"In NSABP, everyone gets paid to put patients on trials," a source said. "That's how Fisher gets so many patients on studies so quickly. Nobody else can match him."

Fisher On Administrative Leave

Cancer researchers around the country said they were saddened by the controversy surrounding Fisher, one of the founders of NSABP, who is widely respected for having designed and led innovative studies that changed the standard treatment for breast cancer.

"This is devastating to one of our most prestigious clinical trialists," said Robert Cooper, an NSABP member at the Bowman Gray School of Medicine. "I know there is criticism of NSABP for not reporting this promptly, and I agree with that. But I don't think these events have led to the improper treatment of patients. One or two investigators cannot change the outcome of a study."

Ross McIntyre, chairman of the Cancer & Leukemia Group B, said researchers should not let a few instances of fraud paralyze the clinical trials system. "I find it distressing that this problem has occurred," McIntyre said. "But I feel the public needs to keep this in perspective. There is a tendency to believe the whole system is rotten. We can't let an event like this cause a large diversion of resources from research that moves the treatment of disease forward."

Others called for the swift publication of an NSABP paper reexamining the results of breast cancer trials. "I hope Bernie will soon publish a reanalysis so this whole thing can be put to rest," said Sharon Murphy, chairman of the Pediatric Oncology Group. "We are all pretty sad."

The day after NCI issued its demand that he step

down as the principal investigator, Fisher requested an administrative leave from NSABP.

"Excessive administrative demands at this time interfere with my ability to devote sufficient time to my research and with my availability to respond to inquiries about the scientific aspects of NSABP clinical trials," Fisher said in a March 29 statement.

"I am requesting administrative leave from the chair of the NSABP so that I can continue my investigations which relate to breast cancer and which are so important to the women of this country.

"I assure the public that the published conclusions from the NSABP's breast cancer studies remain valid and are not compromised by any of the recent developments," Fisher said. "I believe that the audit process will fully confirm that. I look forward to my continuing relationship with NSABP."

Fisher will continue as Distinguished Service Professor at Univ. of Pittsburgh, the university said.

"All of us interested in the NSABP studies share the objective of maintaining public trust in science, particularly when the public's health is concerned," said Thomas Detre, senior vice chancellor for health sciences at the university. "I applaud Dr. Fisher's decision to take the time necessary to respond to the concerns raised about the NSABP's management of clinical trials. The Univ. of Pittsburgh stands fully behind Dr. Fisher and recognizes his integrity and commitment to science and women's health."

In 1968, Fisher's research demonstrated the efficacy of lumpectomy, a less radical surgery for breast cancer. In 1989, his publications in the New England Journal of Medicine demonstrated the value of chemotherapy for women with hormone receptor negative breast cancer and the value of tamoxifen for women with hormone positive breast cancer.

Fisher has served on the National Cancer Advisory Board and is a past president of the American Society of Clinical Oncology.

Biotech Group Endorses Bills Changing Orphan Drug Act

A measure introduced in the House and Senate last week is likely to end the controversy over the Orphan Drug Act of 1983.

The amendments introduced in the House by Henry Waxman (D-CA) and in the Senate by Nancy Kassebaum (R-KS) received an endorsement from the Biotechnology Industry Organization, which has opposed similar amendments for over six years.

Under the measure, co-sponsored in the House by Gerry Studds (D-MA) and in the Senate by Edward Kennedy (D-MA) and Howard Metzenbaum (D-OH), agents that qualify for the orphan drug designation would receive four-year exclusivity, down from seven years guaranteed by current law.

As a result of negotiations between BIO, the bill's sponsors and patient advocacy groups, the proposed legislation grandfathers drugs currently in clinical trials and on the market.

Also, the bill's sponsors have dropped the provision that removed exclusivity rights as soon as gross sales of a product reached $150 million. That threshold, recommended in the legislation lasst year, ran into opposition from the industry.

As introduced, the most recent version of the bill calls for removing exclusivity as soon as the population treated by the drug reaches 200,000 people.

The bill gives FDA the option to extend the exclusivity period if regulators determine that the drug in question has a "limited commercial potential." Exclusivity could also be granted to two companies if they develop a drug simultaneously.

"Retroactivity and a sales cap were both proposals which we have vigorously opposed," said Carl Feldbaum, president of BIO. "It's our hope that this legislation will end the uncertainty about enactment of retroactive amendments to the Orphan Drug Act and allow the biotechnology industry to focus on health care reform."

Salick Is First To Contract For Fixed-Price Services

Salick Health Care Inc. of Los Angeles became the first company to make a contract for a full range of oncology services at fixed prices, the company said.

Under the deal, SalickNet Inc., a subsidiary, will become the preferred provider of oncology services for Capp Care, a national managed health care company that insures 3.4 million lives. The deal also includes other Salick services, including home infusion and dialysis.

The SalickNet agreement provides Capp Care with all of its services at a fixed price which would cover physician fees, medical supplies and products as well as labor, facility and room charges.

"This is the first time a company has been able to provide a 'carved-out' catastrophic disease-specific program, including practice guidelines, outcomes

analysis and case management," said Bernard Salick, chairman and CEO of Salick Health Care.

"Our organization is able to directly provide the services under such a carved out program in inpatient, outpatient and home care settings, thereby effectively controlling both the quality and cost of care," Salick said.

Capp Care, based in Newport Beach, CA, provides managed health care services through networks that include more than 75,000 providers and 3,000 facilities.

DCE Advisors OK New RFAs: Occupational Cancer, H. Pylori

Advisors to NCI's Div. of Cancer Etiology have given concept approval to two new Requests for Applications on the role of Helicobacter in cancer and in occupational cancer prevention and control research.

The DCE Board of Scientific Counselors also approved in concept the recompetition of two contracts supporting DCE Director Richard Adamson's office.

Following are the concept statements:

The Role of Helicobacter in Cancer. Proposed new RFA, first year funding (FY95) $1.5 million, four years. Program Director: Thomas Nightingale, DCE Biological Carcinogenesis Program.

Epidemiologic studies have consistently demonstrated an association between *Helicobacter pylori* and gastric cancer. A recent study of over 3,000 subjects from 13 countries showed a sixfold higher risk of gastric cancer in populations with *Helicobacter pylori* infection compared to populations with no infections. A longitudinal study of patients with gastric adenocarcinoma showed that *Helicobacter pylori* infection was a risk factor, and while the relationship between *H. pylori* and gastric lymphoma was only suggestive at that time, *H. pylori* has subsequently been confirmed as a risk factor for gastric lymphoma.

The goal of this proposed RFA is to stimulate research on defining the role of Helicobacter in the etiology of cancer. The types of studies could include: subtyping of Helicobacter strains to define those with a greater oncogenic potential; determination of the role and mechanism of Helicobacter virulence factors in carcinogenesis; and, potential novel approaches in carcinogenesis involving microorganisms. Investigators will be encouraged to assess the role of Helicobacter, H. *pylori,* and other related species as factors or co-factors in the etiology of cancer with the goal of developing short-term bioassays and early indicators of carcinogenesis.

Examples of studies that may be supported by this RFA include (1) defining the virulence factors of the Helicobacter species such as cytotoxin-associated factors with carcinogenic potential; (2) developing *in vitro* methods of culturing and propagating Helicobacter species without loss of animal pathogenicity; (3) developing reagents or markers for early detection of precancerous lesions in humans or animal models; (4) developing diagnostic tests and tools to isolate and identify Helicobacter serotypes and infections leading to cancer in humans; and, (5) characterizing relevant models that will reflect development of Helicobacter-related neoplastic changes seen in humans.

Occupational Exposure and Cancer Prevention/ Control Research. Proposed new RFA, first year funding (FY95): $2 million, four years. Program Directors: Richard Bragg, DCPC, and A.R. Patel, DCE Epidemiology & Biostatistics Program.

The purpose of this proposed RFA is to promote cancer control research activities among populations that may be occupationally exposed to potential carcinogenic substances. Special emphasis is placed on investigating minority populations and women, who have not been studied adequately in the past. This initiative is a collaborative effort between DCE and the Div. of Cancer Prevention and Control. The funds for this RFA come from the NCI cancer control budget.

The purpose of this proposed RFA is to stimulate epidemiologic studies of cancer in the workplace and to enhance related cancer prevention and control efforts. Innovative approaches that include new diagnostic or exposure measurements are particularly encouraged. Projects should be proposed as traditional R01s. Proposals that build upon ongoing research projects, utilizing already collected epidemiologic data or biospecimens, are encouraged.

One important goal of this initiative is to assess the extent that occupational exposures contribute to cancer incidence and mortality among minority populations, underserved groups, and women, and to develop effective means of cancer control in these special populations.

The initiative permits a wide range of epidemiologic investigations to identify the occupational determinants of cancer and to develop measures for cancer prevention and control in the workplace. Proposed studies must have components that provide cancer control activities, such as recommendations for substitute chemicals and for specific changes in work practices and engineering controls, informational and educational programs for workers, unions and management, and dissemination of results to regulatory agencies, and other interested parties from labor and industry.

Examples of areas of research that are considered to be responsive to this announcement:

1) Analytic epidemiologic studies to clarify the

relation of specific occupational exposures to specific tumors, and if possible to evaluate the impact of changing exposures on time trends in cancer incidence. Once discovered, the information must be disseminated to workers in the study, and to regulatory agencies, management unions, and other labor and industry associations.

2) Epidemiologic studies of occupational cancer that include molecular and biochemical components to more precisely identify previous exposures, intermediate outcomes or susceptibility states among particular groups of workers who are then targeted for cancer control interventions in the proposed research. The significance of biochemical or molecular analysis would be conveyed to the subjects along with suggested methods of reducing cancer risks.

3) Intervention studies with chemopreventive agents or cancer screening modalities involving population groups previously exposed to occupational carcinogens.

4) Cancer control intervention studies to address the impact of occupational exposures to carcinogens on the minority populations of the United States.

5) Cancer surveillance activities to utilize existing occupational data resources to identify occupational cancer risks among minority populations and women.

6) Educational interventions to inform populations-at-risk about the potential consequences of exposures to occupational carcinogens, especially as they relate to minorities and women.

Cancer of the Prostate: Epidemiology and Etiology. Proposed Program Announcement. Program Directors: Kumiko Iwamoto, Extramural Programs Branch; and David Longfellow, Chemical and Physical Carcinogenesis Branch.

The purpose of this initiative is to stimulate innovative epidemiologic and interdisciplinary research into the origins of prostate cancer. Collaborations of several disciplines and research institutions are particularly encouraged. Whenever possible, research designs should utilize shared laboratory and specimen resources. Extension of an ongoing epidemiologic study by the addition of a laboratory component can be proposed. Projects will be evaluated on the basis of the potential for enhancing the understanding of prostate cancer etiology and strategies for prevention. DCE particularly encourages epidemiologic investigations using hormonal biomarkers that have been or are being evaluated for sensitivity, specificity, and intra and inter-individual variability. The initiative permits a range of epidemiologic and interdisciplinary investigations of prostate cancer including, but not limited to:

1. Biochemical epidemiologic studies to

—validate and compare prostate tissue levels of sex hormones (e.g., androgens, estrogens), their metabolites and their receptors with other sources of specimens such as serum and prostatic fluid;

—evaluate panels of circulating hormones (e.g., dihydrotestosterone (DHT) and its precursors, testosterone, DHEAS, DHEA, androstenedione and its metabolites such as DHT sulfate, DHT glucuronide, 3-alpha-diol) in racial/ethnic populations particularly at young ages (less than 50 years old);

2. Epidemiologic studies of

—the influence of lifestyle factors (e.g., smoking, alcohol), occupation (e.g., cadmium and zinc exposures, rubber industry, farming), dietary intake (e.g., fatty acids, vitamins A, D, and E), and xenoestrogens and their interaction on prostate cancer risk;

—the interrelationship of hormone levels, hormonal profiles, dietary variables, lifestyle factors, and occupational exposures and prostate cancer risk;

3. Analytic studies to identify risk factors (e.g., hormonal, lifestyle, environmental) that contribute to activation of latent carcinoma to clinically evident prostate cancer;

4. Molecular epidemiology studies exploring differences in genetic predisposition to prostate cancer due to variations in susceptibility genes, hormone metabolism, DNA repair activities, chromosome sensitivity to mutagens or other factors;

5. Epidemiologic studies to identify risk factors (e.g., environmental, hormonal, viral exposure, sexually transmitted diseases) associated with benign prostatic hypertrophy and to clarify its possible relation to prostate cancer;

6. Population-based studies of the relationship between prostatic intraepithelial neoplasia, dysplasia, atypical hyperplasia, and invasive prostate cancer.

Survey of Compounds Which Have Been Tested for Carcinogenic Activity: 1995-1998. Recompetition of a contract held by CCS Associates, small business set-aside, total $940,000 over four years. Project Officer: Thomas Cameron, DCE Office of the Director.

The "Survey of Compounds Which Have Been Tested for Carcinogenic Activity," commonly referred to as PHS-149, has been published by NCI since 1951. There are 18 published volumes, covering the years 1939 through 1990, and a cumulative index for all these years. The 1991-92 volume is being finalized by the current contractor who is also working on the compilation of the 1993-94 volume and a new cumulative index. Over the years, the size of these volumes has grown from 1,043 pages containing data on 574 chemicals and 646 citations in the 1974-75 volume to 2,134 pages covering 682 chemicals and 752 citations in the 1989-90 volume. The latest index contains 5104 CAS Registry Numbers covering over 21,000 chemical names and synonyms. The 1991-92 volume will cover 941 chemicals and contain more than 850 citations. To compile each one of these volumes, Current Contents, which covers over 1,200

journals worldwide, as well as all other pertinent databases such as CHEMLINE, TOXLINE, etc., are being screened. Any applicable journals, both domestic and foreign, not covered by Current Contents, are also being screened. In order to enhance the value of PHS-149 to its users, the expansion of the column headed "Detailed Information" was continued and authors' comments, explanatory notes, and references to other citations were included, where applicable.

The contractor will continue the screening of applicable computerized databases and pertinent journals; relevant data will be extracted, edited, and formatted according to the established headings prescribed for this publication. Camera-ready copies and tapes or floppy disks will be delivered to NCI. For the sake of continuity, it is proposed to retain the two-year cycle. The concept statement, therefore, covers two volumes over a four-year period plus a new cumulative index.

Resource to Support the Chemical, Economic, and Biological Information Needs of the Div. of Cancer Etiology. Recompetition of a contract held by Technical Resources Inc., total $3.625 million over five years. Project Officer: Thomas Cameron, DCE Office of the Director

This project is the major source of support to the Office of the Director, DCE, for the development of information in the areas of environmental and occupational cancer. The project was initiated over 17 years ago and has been recompeted three times since. The present contract began in September 1990 and consists of four major tasks.

Task I supports NCI's Chemical Selection Working Group in selecting and nominating chemicals to the National Toxicology Program for its carcinogenicity bioassay program. One of the primary functions of the contractor in support of NCI's Chemical Selection Working Group is to gather information and prepare summary sheets on candidate chemicals. Summary sheet preparation has averaged 86 professional hours, 59 semi-professional hours, and 51 support staff hours per summary sheet.

Task II provides support for the International Agency for Research on Cancer. NCI/DCE provides the major collection of data and the preparation of first drafts of Section 1: Exposure Data (Nomenclature, Chemical and Physical Properties, Technical Products and Impurities, Analysis, Production, Use, Occurrence [Natural, Occupational and Environmental], and Regulations and Guidelines) of the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Many reference sources, both on-line and hard copy, are routinely searched to obtain this information. Contract support for a typical IARC Working Group meeting has averaged 152 professional hours, 600 semi-professional hours, and 307 support staff hours.

Task III deals with the development and maintenance of data for the Chemical Carcinogenesis Research Information System. This is an evaluated and fully referenced database containing carcinogenicity, mutagenicity, tumor promotion, and tumor inhibition test results.

Task IV. Under this task, Bioassay Report Summaries are prepared from the NTP Technical Reports for inclusion in the Bioassay Report Summary Handbook, which is distributed to 50 Federal and State government agencies and is available through the National Technical Information Service.

NCI Biomarker Registry Seeks Information From Researchers

NCI has established a biomarker registry comprised of information that may be useful to investigators when biomarkers are being considered as intermediate endpoints or as outcome measures in prevention trials.

In an effort to collect information on biomarkers, NCI seeks cooperation from the extramural scientific community on a voluntary basis. Information may be submitted by anyone currently engaged in biomarker research. The following characteristics of biomarkers are of interest:

1. Biological Characteristics: The description should include, but is not limited to, the spontaneous biological rate of progression and/or regression, site-specificity, histology, chromosomal aberrations, epigenetic changes, mutations, histologic correlation, and the phase, i.e., whether the marker in question occurs at an early, intermediate, or late stage of the carcinogenesis process.

2. Outcome Association: Provide information on population, subjects, sites, intermediate endpoints, and the rate of regression of intermediate endpoints in a given time frame in response to the intervention (e.g., 50 percent regression in two months). In the case of chemoprevention trials, also provide the name of the chemopreventive agent, dose (including toxicity data), preclinical efficacy, preclinical safety, clinical safety, and the clinical efficacy, if known.

3. Epidemiological Characteristics: Provide information on (1) types of marker: (a) biomarkers of susceptibility, (b) biomarkers of exposure, (c) biomarkers of biological effects, (d) biomarkers of disease cancer; (2) source of variability: sampling variability, inter- and intra-individual variability, inter- and intra-observational variability, and time-dependent variability; (3) study design: case-control, prospective cohort, or randomized trial. Provide the material for the choice of the endpoint and sample size in your study.

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