THE CANCER LETTER

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CENTERS, CONTROL TO BE IN NEW DIVISION; UPTON MOVES FINK UP; TERRY ACTING DIRECTOR OF DCCR

Arthur Upton finally dropped the other shoe on NCI's reorganization after deliberating for the last 16 months on what to do about the Centers Program and Cancer Control. The answer: put them together.

Here's how this latest shakeup will change NCI's structure:

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In Brief

UPTON SAYS DELANEY CLAUSE IS NEEDED: CPSC DROPS EFFORT TO SET POLICY ON CARCINOGENS

"WE MUST not abandon the Delaney Clause . . . without equally effective safeguards," NCI Director Arthur Upton said at the annual ACS science writers seminar. That provision in the law requires FDA to ban food additives proven carcinogenic in animals. "There is . . . no scientific way to arrive at quantitative and precise risk estimates for humans based on extrapolating from animal data and therefore no scientific basis for accurately and confidently weighing the benefits of a particular substance against its risks as a potential carcinogen. If we are to be serious about preventing cancer for future decades, we must continue to identify these substances which may jeopardize human health and lives and either minimize human exposure to them or learn to counteract their effects" . . . . **NATIONAL TOXICOLOGY** Program within five years will develop and validate a series of tests "of increasing complexity, duration and expense," David Rall, NTP and NIEHS director, said at the same seminar. "If a compound passes the initial stages of this sequential series of tests with flying colors, it generally will be presumed not to pose an unreasonable risk of injury to health. My estimate is that 80-85% of chemicals will pass the first stages of the sequential series. Suspicious results would require further testing, culminating in full scale, two year, two species lifetime rodent tests. Let me add, however, that I believe that any chemical which is produced in large quantities, or any chemical to which a significant human population will be exposed, should promptly undergo full scale testing." . . . **CONSUMER PRODUCT** Safety Commission has withdrawn its "interim statement of policy" on the classification, evaluation and regulation of carcinogenic substances in consumer products. Implementation of the policy was blocked by a U.S. district court order (***The Cancer Letter***, Jan. 19). CPSC was unsuccessful in getting the court order lifted. The agency said in its announcement it was abandoning the interim policy statement; that it was joining with FDA and EPA in developing a document describing the scientific bases for identifying potential carcinogens and estimating the risks. The document will be published soon for notice and comment. Anyway, "the commission has ample authority under the statutes it administers to regulate suspected carcinogens on a case by case basis," CPSC said.

NEW PREVENTION DIVISION WILL INCLUDE PARTS OF CONTROL PROGRAM, DCCP

(Continued from page 1)

• The Div. of Cancer Control & Rehabilitation will be dismantled. It its place would be created:

1. A new division, to be named something like the Div. of Cancer Resources, Centers & Community Programs. It would include all existing DCCR programs except those related to prevention; the Cancer Centers Program; facilities (construction); the manpower training efforts and the organ site programs.

2. Another new division, the Div. of Cancer Prevention. It would include the present DCCR prevention programs and certain elements of the Div. of Cancer Cause & Prevention—probably the Bioassay Program, perhaps parts of the epidemiology, field studies and chemoprevention programs, and maybe the Smoking & Health Program.

The new lineup would give NCI five operating divisions—the two new ones, the Div. of Cancer Cause & Prevention (which would have to get a new name), the Div. of Cancer Biology & Diagnosis and the Div. of Cancer Treatment. The sixth division is the Div. of Extramural Activities (still officially known as the Div. of Cancer Research Resources & Centers, much to everyone's confusion), which is responsible for the review of grants and contracts.

When he announced the proposed changes, Upton also announced that DCCR Director Diane Fink had been appointed to a new position as associate director (of NCI, assigned to Upton's office) for medical applications of cancer research. Her job will be "the continuing identification of NCI's research findings that are ready for application in medical practice," Upton said.

Fink assumed the new position Monday. William Terry, who has been acting director of the Centers Program, also will be acting director of DCCR. Upton emphasized that Terry will hold that position on an "interim" basis, and that a search committee will be organized to find a permanent director for the new division.

Interim or not, Terry will have the responsibilities and authority of a division director and will have something to say about the $12 million worth of DCCR contract and grant proposals pending or undergoing review or in the process of being generated by RFPs and RFAs. The DCCR Advisory Committee had been scheduled to meet next week to take a final look at how the division's fiscal 1979 money is allocated and to discuss projects to be funded with 1980 money. That meeting was canceled, after the new reorganization was revealed.

Terry and Upton were both out of the country this week and not available for comment. Another NCI executive told ***The Cancer Letter*** that Terry probably would review all pending projects and might well decide to postpone or drop some of them, following consultation with Upton, Fink and the advisory committee. One of those pending is the new Community Oncology Program.

None of the organizational changes can be implemented until they are approved by HEW. Upton hopes to submit the entire reorganization package to Secretary Joseph Califano by June. Until it is approved, the various elements marked for new divisions will remain where they are. Terry will be responsible only for DCCR as it now exists and the Centers Program. He also will continue in his permanent position as head of the Immunology Program in DCBD.

Upton named Robert Hoover, chief of the Environmental Studies Section of the Environmental Epidemiology Branch in DCCP to head a task force which will make recommendations on organizing the new prevention division. A search committee also will be established to find a director for the division.

This latest stage in Upton's reorganization of NCI addressed two major concerns and sources of criticism:

• The complaints by cancer center directors and others that cancer control efforts should be more closely coordinated and perhaps supported through the centers. Centers executives resented the fact that certain mandates for control and outreach efforts had been imposed on them, particularly the comprehensive centers, while all too often funds to carry out those mandates were not available. At the same time, they saw DCCR supporting a wide variety of control programs independently of centers, some of which the centers people regarded as frivolous.

• The complaints by prevention advocates that NCI's efforts in that direction were undersupported and diffuse. One critic, Samuel Epstein, called for a Div. of Cancer Prevention in his testimony before Sen. Kennedy's Health Subcommittee.

Epstein also said that prevention should command at least 50% of the NCI budget; it is not likely the new division will get anything close to that, although with the reorganized DCCP prevention will still receive a substantial share of NCI's money.

The new prevention division probably will pick up about $24 million in DCCR prevention activities. The remainder of its $30-35 million budget would come from DCCP programs.

Although the new setup will please most of those connected with centers, it has left others—especially those involved with existing DCCR programs—with some uneasiness. Members of the Assn. of Community Cancer Centers debated a resolution at their annual meeting opposing any dismemberment of DCCR. The resolution was not approved, but the discussion made it clear that some did fear a possible deemphasis of programs unrelated to larger centers.

Because of the disaffection of center directors, difficulties in drawing a line between cancer control and cancer treatment research, misconceptions on

what cancer control should include, over-expectations by many, and perhaps other factors, DCCR probably absorbed more criticism than all other NCI divisions combined. Fink, who headed the division since it was established in 1974, bore the brunt of that criticism.

She went to that job from the Clinical Investigation Branch, where she worked with the Cooperative Groups in protocol development. She had built a reputation there as a hard worker, and she continued it at DCCR, putting in long hours and frequently taking armloads of work home.

Fink's major problem as an administrator seemed to be in building and keeping a professional staff. The turnover among her branch chiefs and program directors was continuous. The complaint invariably was that she would not delegate responsibility.

The support of allegedly frivolous projects was at least as much the fault of DCCR advisory groups as it was Fink's.

Fink also took a lot of heat over the Breast Cancer Detection Demonstration Project, which she inherited from DCBD with all its deficiencies. But she saw it through, organized the successful effort to reduce mammogram doses, set up the consensus meeting which resulted in plans for exploiting the data coming out of the project, and seems to have it running smoothly.

Fink handled two interagency assignments well, chairing task forces on DES and terminal care.

"I consider this a promotion," Fink told ***The Cancer Letter.*** "It involves the things I like to do." She said her five years at DCCR "was an exciting, professionally rewarding experience. I think we had a lot of accomplishments."

Upton sent a memo to NCI staff members describing the changes and proposed changes:

"I am pleased to be able to tell you of several important staff appointments and of plans for completion of the reorganization of the institute.

"First, effective immediately, Dr. Diane Fink, who has headed DCCR since 1974, will assume important new responsibilities in my office as associate director for medical applications of cancer research. In this position, Dr. Fink will be responsible for the continuing identification of NCI's research findings that are ready for application in medical practice. She will follow research activities and existing information in cancer prevention, screening, diagnosis, treatment, rehabilitation and continuing care, as well as trends in medical practice and issues of general public concern. Her activities will include the coordination of scientists, practitioners, other interested parties and the public to examine these issues in a consensus form for the development of recommendations on practice ready methods and techniques.

"Second, Dr. William Terry will immediately become acting director of DCCR. He will continue as acting associate director for the Cancer Centers Program in DCBD. His appointment is of an interim nature.

"I have asked Dr. Terry to begin work in his new dual capacity to develop a detailed plan for a new resources division which will ultimately encompass much of the DCCR program, the Centers Program, and other cross cutting activities of the institute such as our professional education, construction, and organ sites programs. However, at the present time, none of these latter organizational changes are to be made. It will be necessary for Dr. Terry to develop a detailed plan for the new division and for us to obtain HEW approval before the new division can be created. Meanwhile, Dr. Terry's dual role as acting director of DCCR and acting associate director for the Centers Program will facilitate coordination of these two activities in anticipation of more extensive organizational change.

"As soon as possible, there will be formed a third committee to identify a director for the new division.

"Third, I have asked Dr. Robert Hoover, chief of the Environmental Studies Section in DCCP, to head a task force charged with preparing for me in the next 30 days a detailed recommendation for creation of a new prevention division. I would anticipate that this plan will recommend transfer to the new prevention division of some activities now located in DCCP and DCCR. Based on the recommendations of the task force, I will also seek HEW approval for creation of the new prevention division along with any changes to be made in other divisions.

"As soon as possible, a search committee will be formed to identify a director for the new prevention division.

"No changes in organization and no other changes in personnel assignments are being made at this time. As soon as such further changes are to be made, I will keep you informed of them."

PITOT NCAB CHAIRMAN; WOGAN, SCHRIER REAPPOINTED; FOUR NEW MEMBERS NAMED

Henry Pitot, director of the McArdle Laboratory for Cancer Research at the Univ. of Wisconsin, is the new chairman of the National Cancer Advisory Board.

Pitot has been a member of the Board since 1976 and is chairman of the Subcommittee on Environmental Carcinogenesis. He replaces Jonathan Rhoads, who had served as NCAB chairman since it was created by the National Cancer Act of 1971. Rhoads' term as a Board member and also as chairman expired last year, but he has continued to serve while the Carter Administration took its time making the new appointments.

There have been six vacancies on the Board since May, 1978, and they were filled with the Presidential appointments this week which accompanied Pitot's appointment as chairman. Gerald Wogan, professor of

toxicology in the Dept. of Nutrition & Food Science at MIT, was reappointed. Morris Schrier, vice president of MCA Inc., also was reappointed, filling one of the lay positions on the Board.

New members are Maureen Henderson, an epidemiologist and assistant vice president for health affairs at the Health Sciences Center of the Univ. of Washington; Janet Rowley, geneticist and associate professor at the Univ. of Chicago School of Medicine; Irving Selikoff, director of the Environmental Sciences Laboratory at Mt. Sinai School of Medicine; and Sheldon Samuels, director of the health, safety, and environmental industrial union department of the AFL-CIO. Samuels was named to one of the lay positions.

One of the issues in the new appointments was the amendment to the Cancer Act last year which requires that at least five members of the Board be persons knowledgeable in the environmental and occupational causes of cancer and in nutritional aspects of cancer. Henderson, Selikoff and Samuels meet those criteria, as do Pitot, Wogan and holdover members Bruce Ames and Philippe Shubik, giving the environmentalists a dominating seven of the 16 voting positions on the Board, including the chairman.

Leaving the Board, in addition to Rhoads, are Laurance Rockefeller, David Hogness and Frank Dixon.

CLEARINGHOUSE FINDS THREE COMPOUNDS ARE CARCINOGENIC, THREAT TO HUMANS

The Clearinghouse on Environmental Carcinogens may be on its way out due to the transfer of carcinogenesis testing authority to the National Toxicology Program, but the Clearinghouse Data Evaluation/Risk Assessment Subgroup still has a lot of clout in the eyes of some.

The Subgroup considered Bioassay Program reports this week on three widely used compounds and found them all to be carcinogenic in animals and two of them potential carcinogenic threats to humans. The ramifications of those findings brought an overflow crowd of spectators to the NIH meeting room, including national media representatives and network television crews.

Most of the interest centered on reserpine, the drug used by thousands of Americans to control hypertension. It (and perhaps other agents) have been credited with contributing to the dramatic decrease in deaths from stroke and heart disease.

The reserpine bioassay was conducted through the Carcinogenesis Testing Program by Southern Research Institute, initially under direct contract to NCI and then under a subcontract to Tracor Jitco, the program's prime contractor. The chronic studies in rats and mice were conducted from October 1975 to October 1977.

The summary of the program's report on the study:

"A bioassay for possible carcinogenicity of reserpine was conducted by administering the test chemical in feed to F344 rats and B6C3F1 mice. Groups of 50 rats and 50 mice of each sex were administered reserpine at two doses, 5 ppm or 10 ppm, for 103 weeks and then observed for an additional two weeks. Matched controls consisted of groups of 50 untreated rats and 50 untreated mice of each sex. All surviving animals were killed and necropsied at the end of 104 or 105 weeks.

"The significant effects that could be related to administration of reserpine at the doses used were decreased body weight and increased tumor formation in dosed male rats and in mice of both sexes. Dosed male rats had an increased incidence of adrenal medullary pheochromocytomas. Among dosed mice, some males developed undifferentiated carcinomas of the seminal vesicals, which rarely occur in control mice, and females had an increased incidence of mammary cancer.

"It was concluded that under the conditions of the bioassay, reserpine was carcinogenic in male rats and in mice of both sexes producing three different kinds of cancers. Reserpine was not carcinogenic for female rats but they may not have received a high enough dose for maximum test sensitivity."

CIBA-GEIGY, the manufacturer, predictably disagreed with the conclusion. Robert Diener, executive director for toxicology/pathology, presented a statement in which he contended the data in the bioassay report in fact confirms the premise that reserpine is not a carcinogen.

"The summary of that report is, however, inconsistent with its data, and conclusions are lifted out of context from observations reported and presented therein," Diener said. He offered what he said were examples of inconsistencies.

"In addition," Diener continued, "a detailed evaluation of the histopathology of crucial organs was conducted by CIBA-GEIGY pathology personnel, including Dr. S.W. Thompson, a diplomate of the American College of Veterinary Pathologists. This evaluation further confirmed the non-carcinogenic nature of reserpine. The examination of tissue slides revealed that many histological lesions were either overlooked or overinterpreted and that the denominators for rat adrenal medullas were misrepresented. Furthermore, 'diagnosis of convenience' were employed for the adrenal gland and seminal vesicle tumors which are not consistent with accepted histological criteria.

"Finally, CIBA-GEIGY cannot agree with the statement made in the report's discussion section which states that, 'present study in rats and mice strongly indicates a possible increased risk to humans.' Even if mouse mammary tumors were increased, the results cannot be extrapolated to man according to the FDA Toxicology Advisory Committee which in its report on antipsychotic drugs (in

1977) stated, 'There are major differences in hormonal and reproductive physiology between rodents and humans, including some related to the role of prolactin. At present the committee feels there is insufficient evidence to extrapolate from mice and rats to humans with respect to the role of prolactin in mammary carcinogenesis. It is, therefore, the opinion of the advisory committee that the rodent studies are not relevant to a determination of the magnitude of the potential for human risk from mammary cancer.'

"Due to the discrepancies mentioned above," Diener continued, "and the questionable scientific validity of crucial histopathologic diagnoses, it is the opinion of CIBA-GEIGY that the reserpine bioassay should be reevaluated. To accomplish this in a scientific and unbiased manner, the histopathologic reexamination of crucial organs should be performed by several distinguished pathologists with recognized experience in the type of tumors found in this experiment and who are mutually acceptable to NCI and CIBA-GEIGY."

Subgroup members were not persuaded. Louise Strong, the primary reviewer, said that the experiment was well conducted. "I can't comment on the disagreement among pathologists. I can only comment on what is in the report. There certainly was an increase in the total number of tumors." Morton Levitt, one of the NCI staff members responsible for evaluating the experiment, said that there was evidence the seminal vesical lesions were primary tumors and "there was no disagreement whatever, no question, that they were malignant."

"Based on these comments," Strong said, "and that the study was well conducted, with no flaws, I move we accept the report as written, with the comment on potential human risk."

Subgroup member Sheldon Samuels said that CIBA-GEIGY "is challenging the competence of NCI. I think we should base our decision on the bioassay report." Samuels said he had no objection to a review by an independent panel, provided the company pays for it.

Clearinghouse member Kenneth Wilcox supported the conclusion that it was carcinogenic in animals. "As for the significance to humans, the doses people get may not make it practical to determine human risk." But he seconded Strong's motion anyway.

Subgroup member Michael Shimkin commented that "since there are thousands of people who are getting this drug, we ought to be sure before implying any danger." He asked Program Director Richard Griesemer if the staff would have any objection to a review "by a presumably objective group, not necessarily one CIBA-GEIGY would agree to. If so, I suggest we withhold our conclusion until we receive the new report."

"We're looking for the truth, just as you are, and would welcome any review," Griesemer said.

Subgroup member Joseph Highland said he disagreed with Samuels and Shimkin on an independent review. "It's important that we look at information in the Bioassay Program report. It is not appropriate to bring in outside reports. We're trying to deal here with what the Bioassay Program has reported." Highland said the CIBA-GEIGY arguments were "misleading."

Samuels said he agreed that the Subgroup's evaluation should not await a new pathology report. "Our job is to review the report and base our conclusion on it. If there is a question of competence of the staff, they can resolve that at CIBA-GEIGY's expense."

Clearinghouse and Subgroup Chairman Arnold Brown argued that it was not a question of staff competence, but that seminal vesical tumors "are highly unusual. I don't feel I have to accept the staff's conclusion, and it is not an issue of their competence. I would like to look at the tumors."

After the slides of the seminal vesical tumors were shown, Strong agreed to add to her motion a provision for outside pathology review. Clearinghouse member David Clayson objected, saying, "It would be a degradation of the report. I try to put myself in the position of someone at FDA (trying to read the Subgroup's conclusion)."

Strong agreed to split the motion, permitting separate votes on acceptance of the report and approving an independent pathology review. The Subgroup voted unanimously to accept the report, with the comment that reserpine did pose a human carcinogenic threat. The vote was 3-1 on approving the pathology review, with Strong, Wilcox and Samuels supporting it and Highland opposed.

When Highland asked if the motion should say whether the government or company should pay for the review, Brown said, "I'm not sure we should be concerned about that. The government will request funds from the company if it feels that is appropriate.

"Industry is asking for cuts in budgets to support this kind of work. They can't at the same time add to the costs. The time has past for Uncle Sam to pay for free lab service for industry," Samuels said.

Brown said the motion would not contain any reference to who pays, "but our comments are on the record."

Brown commented to reporters after the meeting that while there was no doubt of reserpine's carcinogenicity in animals, "the possible threat to humans is far outweighed by the benefits to the thousands of people who use the drug."

The Subgroup took a much tougher stand on methapyrilene, an ingredient in dozens of over-the-counter sleeping aids and antihistamines.

The bioassay has not yet been completed, yet the overwhelming evidence of liver tumor inducement has caught the attention of FDA, which sent a representative to the meeting to inform the Subgroup that

the agency was considering action against products containing the compound.

It also caught the attention of the Environmental Defense Fund, a consumer activist organization which has filed a petition with FDA demanding immediate removal of those products from the market.

The test is being conducted by William Lijinsky's group at Frederick Cancer Research Center. It is not under the direction of the NCI Carcinogenesis Testing Program but is supported by NCI through its contract with Litton Bionetics for the operation of FCRC.

Lijinsky's interim report on his test included this summary:

"The widely used over-the-counter antihistaminic drug methapyrilene has not, as far as can be determined, been subject to a long term chronic toxicity test. For this reason it was selected by NCI for a bioassay for possible carcinogenicity. It was assigned for test to FCRC because of a previous positive, though not entirely adequate, test carried out by Lijinsky and Taylor in the Biology Div., Oak Ridge National Laboratory. The compound was administered to rats in combination with sodium nitrite because of a suspicion that it could react with nitrous acid in vivo to form the potent carcinogen nitrosodimethylamine. Methapyrilene was one of a series of drugs that are nitrosatable amines and have not been adequately tested, although widely sold.

"Examination of the structure of methapyrilene shows no relationship to the structure of any known carcinogen. Comprehensive testing in a large number of strains of Salmonella, provided by Ames, revealed no mutagenic activity, with or without activation by a rat liver microsomal fraction. Neither did prior reaction with nitrous acid give rise to a mutagenic response (as was the case with several other tertiary amines) with metabolic activation. Methapyrilene hydrochloride did not transform hamster embryo cells in vitro, with or without activation by rat liver microsomes; however, transformed colonies were seen when the drug was reacted with nitrous acid and the product was subjected to metabolic activation.

"A subchronic toxicity test in Fishcer 344 rats involved feeding methapyrilene hydrochloride in powdered food at concentrations of 2,000, 1,000, 500, 250 and 125 parts per million for 26 weeks. Histopathological examination of the liver of animals killed at 10, 15 and 26 weeks revealed progressive liver lesions, which appear neoplastic at the two highest doses.

"In the chronic test 50 male and 50 female Fischer rats were given powdered food containing 1,000 ppm of methapyrilene hydrochloride ad libitum, starting at eight weeks of age. Another similar group of rats of both sexes was given the drug combined with 2,000 ppm of sodium nitrite in the diet. Average consumption of food has been 20 grams per day by females and 30 grams per day by males, corresponding to a dose of 20 and 30 milligrams, respectively, per day of methapyrilene hydrochloride and double that dose of sodium nitrite in those animals so treated.

"These animals are now at the 64th week of treatment. In the group given methapyrilene alone nine rats have died with massive liver tumors, the first succumbing at the 43rd week. Of the rats given methapyrilene plus nitrite nine have died with the same large liver carcinomas, the first at the 55th week. Untreated control rats of our colony when sacrificed at 2.2 years of age have an incidence of one liver tumor in 100 animals. Of a group of 40 rats given 2,000 ppm sodium nitrite in powdered food for life, four have died after two years treatment and none had liver tumors.

"Chemical analysis of the methapyrilene hydrochloride samples show them to be of high purity (exceeding 99%) and to contain no identifiable carcinogenic impurities (particularly nitrosamines).

"It is concluded that methapyrilene is a liver carcinogen in rats of considerable potency, at daily doses below those recommended for people (50 milligrams per day), and that it must be considered a potential carcinogenic risk to man, even though its chemical structure, and the results of tests in two standard in vitro tests do not suggest a suspicion of adverse biological effects."

Brown was the primary reviewer of the report. "Despite the preliminary nature of the report, it must be noted that the compound is carcinogenic in animals. The structure is different than other carcinogens, but it is highly carcinogenic. It must be regarded as possibly carcinogenic to humans."

Brown moved that the preliminary report be accepted as written until a final report is written.

"What does that mean?" Shimkin asked.

"It means we're accepting this as written, but expect a final report," Brown answered.

"It's not a matter of accepting a report. Look at the data. This stuff is hot," Shimkin said.

"We accept the conclusion that this compound is carcinogenic and a possible risk to humans," Brown said.

"You waffled in your motion, adding 'until the report is completed,'" Shimkin said. "I think we can say flat out that this compound is carcinogenic."

Shimkin's motion that "data presented to the Clearinghouse on methapyrilene sufficiently demonstrates it is a potent hepatocarcinogen and poses a potential human risk" was accepted unanimously.

Selenium sulfide, an ingredient in a number of hair shampoos, was the third widely used compound which the Subgroup agreed at this session was carcinogenic in animals.

The subgroup, however, did not make any statement on possible risk to humans, and neither did the bioassay report.

The bioassay of selenium sulfide was conducted by

Hazleton Laboratories America, initially under direct contract to NCI and currently under a subcontract to Tracor Jitco. The report summarized:

"A bioassay of selenium sulfide for possible carcinogenicity was conducted by administering this substance by gavage to F344 rats and B6C3F1 mice.

"Groups of 50 rats and 50 mice of each sex were administered selenium sulfide suspended in 0.5% aqueous carboxymethylcellulose five days per week for 103 weeks at either 3 or 15 mg/kg/day for rats and 20 or 100 mg/kg/day for mice. As vehicle controls, groups of 50 rats and 50 mice of each sex were administered only the 0.5% aqueous carboxymethylcellulose. Similar groups of untreated-controls also were used. All surviving rats and mice were killed and necropsied at week 104 or 105.

"The significant effects that could be related to administration of selenium sulfide at doses used were decreased body weight and increased tumor formation in female mice and in rats of each sex. Dosed rats and female mice had an increased incidence of hepatocellular carcinomas and adenomas. Dosed female mice also had an increased incidence of alveolar/bronchiolar carcinomas and adenomas.

"Under the conditions of this bioassay, selenium sulfide was carcinogenic for F344 rats and female B6C3F1 mice, inducing hepatocellular carcinomas in male and female rats and female mice and alveolar/-bronchiolar carcinomas and adenomas in female mice. Selenium sulfide was not carcinogenic for male mice; however, based on the absence of effects on survival and mean body weight, male mice may have been able to tolerate higher doses."

Strong, the primary reviewer, said she supported the conclusions, that under the conditions of the test it was carcinogenic in male and female rats and in female mice. The study was well conducted, she said, with adequate controls, although there may have been some inadequate dosing in meeting the maximum tolerated dose. "There was a dramatic increase in liver lesions in the high dose animals. Under the conditions of the study, the compound is a carcinogen," Strong said.

Clayson noted there was some increase in tumors among male mice, but not a statistically significant number. "But that should not detract from the significance of the tumors in the females," he said.

The motion to accept the report was approved unanimously.

The Subgroup agreed with bioassay reports that the garden insecticide malathion was not carcinogenic in the test; and that two more compounds—malaoxon and bis(2-chloro-1-methylethyl) either also were not carcinogenic to animals in the tests.

KENNEDY BILL WOULD EXTEND CANCER PROGRAM THREE YEARS, END BYPASS

A bill introduced by Sen. Edward Kennedy (S. 988) would provide new comprehensive authorization for biomedical research, including anew three year extension of the National Cancer Program.

Congress renewed the Cancer Program last year for two years, extending through the 1980 fiscal year which starts next Oct. 1. Kennedy's extension would take it through the 1983 fiscal year, with authorizations for NCI of $1.019 billion, $1.173 billion, and $1.349 billion, plus cancer control authorizations of $113.3 million, $124.6 million and $137 million.

The most notable and controversial change the measure would make would be to take away the independent budget authority NCI received in the National Cancer Act of 1971. That authority permits NCI to submit its budget directly to the White House without giving NIH and HEW any opportunity to change it. This has permitted NCI to carry arguments supporting its requests directly to the Office of Management & Budget and was a key factor in the early years of the program in securing big budget increases. OMB has not been receptive to increases in the last four years, but the independent authority still helps make NCI's budget requests more visible and open without appearing to be "disloyal" to the Administration. This in turn has helped generate support for cancer funds in Congress.

Kennedy conceded in his statement which accompanied introduction of the bill that dropping the budget bypass might not be something for which he would fight. "As part of our reauthorization of the National Cancer Institute, we have eliminated the budget bypass authority provided that agency," the statement said. "This amendment is proposed for the purposes of discussion, and we welcome comments on its potential effects on the National Cancer Program. Clearly, the President's Council for the Health Sciences (a new body the bill would create) will have to take into account the budget proposals of NCI in setting its plans and priorities for a five year period. Therefore, maintaining the bypass authority may make more difficult the work of the Council. However, we recognize that an alternative arrangement would have the budget of NCI forwarded both to the Council and to the President. This may have certain advantages during the period in which the Council is developing its capacity to plan and set budget policy. We look forward to hearing the research community's assessment of this and other alternative proposals."

Other changes the bill would make in NCI's authority include:

- Placing appointment of the NCI director back into the hands of the HEW secretary instead of the President. All other institute directors at NIH except the Heart & Lung Institute are HEW appointees. The 1971 Act made the NCI director a Presidential appointee specifically to give the director more prestige and clout. President Carter has unofficially returned that job to the secretary, but most Cancer Program advocates would like to see it continued as a direct White House appointment, even if in name only.

• Increase from $35,000 to $50,000 the maximum level of grant awards which can be made by the NCI director without approval of the National Cancer Advisory Board.

• Change appointment of NCAB members from the Presidential to HEW secretary level and reduce their terms from six to four years.

• Require that at least one member of the President's Cancer Panel also be a member of the National Cancer Advisory Board (a superfluous requirement, since Panel members sit as ex officio members of the Board anyway).

• Add to Cancer Control authority these mandates:

"The demonstration of, evaluation of, testing of, and the education of health professions in (A) effective methods for the primary prevention of cancer; (B) effective methods for the secondary prevention of cancer, including the early detection of cancer and the identification of individuals with a high risk of developing cancer; and (C) improved methods of patient referral to appropriate centers for early diagnosis and treatment of cancer."

In a jab at the slow pace of Secretary Joseph Califano and the White House in filling NCAB and Panel vacancies, the bill includes a requirement that such vacancies be filled within 90 days after they occur.

In another jab at the Administration, this time for its shortsighted policy of dragging its feet on chartering of peer review groups, the bill would take that authority away from HEW and place it directly in the hands of the NIH director. Kennedy said:

"In relation to peer review, I would like to make one additional point. It is a matter of intense concern to me and many of my colleagues that the number and size of initial review groups at NIH has remained almost unchanged over the last several years despite an effective doubling in the workload of those groups. This erosion of the capacity of our peer review system must not be permitted to continue. We have provided the NIH director with authority to appoint advisory councils, and we have done so with precisely this problem in mind. It is our specific intent that he use this authority to help bolster the peer review system by appointing new groups as the need arises."

Of course, if a President is determined to hold down the number of government advisory groups, he could order the NIH director not to create any new ones. But that could pose political problems for a President, and at least require him to more carefully consider such a policy.

HEW and the White House have indicated they will oppose the bill.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the contract officer or specialist named, NCI Research Contracts Branch, the appropriate section, as follows:
Biology & Diagnosis Section and Viral Oncology & Field Studies Section—Landow Building, Bethesda, Md. 20014; Control & Rehabilitation Section, Carcinogenesis Section, Treatment Section, Office of the Director Section—Blair Building, Silver Spring, Md. 20910.
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP CI-79-0383

Title: *Ames bioassay of exhaust soluble organics emissions*
Deadline: *See RFP*

Preliminary evidence suggests that vehicular exhaust from both gasoline and diesel engines contains potentially mutagenic compounds. Many of these organic compounds are associated with, or absorbed on, carbonaceous soot particles which can be trapped by filtering during vehicle or engine testing. It is the intent of the EPA to have tested the organic emissions from various vehicles, engines and control devices over a range of operating conditions for genetic activity via the Ames test. This contract involves: (1) a simple solvent extraction of the organic compounds from a matrix composed of particulate material and filter media, and (2) Ames testing of this organic extract to determine biological activity, if any. The Environmental Protection Agency will supply 188 samples per year in the form of the above mentioned matrix of particulate and filter media.

Negotiated Contracts Branch
Contracts Management Div
Environmental Research Center
Environmental Protection Agency
Cincinnati, OH 45268

NCI CONTRACT AWARDS

Title: Studies of mammalian cell transport systems
Contractor: Hebrew Univ., Jerusalem, $62,225.

Title: Procurement of melanoma cell vaccine
Contractor: Litton Bionetics, $183,885.

Title: Additional renovation/upgrading project at Frederick Cancer Research Center, modification
Contractor: Litton Bionetics, $953,381.

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