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P.O. BOX 2370 RESTON, VIRGINIA TELEPHONE 703-620-4646

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DCCR CANCER INFORMATION SYSTEM PROGRAM RENEWED FOR THREE MORE YEARS; TWO DROPPED, TWO ADDED

Two of the original Cancer Information Service contracts awarded by NCI's Div. of Cancer Control & Rehabilitation to 17 comprehensive cancer centers have been terminated following merit review conducted by the division. The other 15 have been renewed for three more years,

(Continued to page 2)

In Brief

HEW APPROVES PATENT REQUEST FROM U. ARIZONA; CALIFANO STILL PONDERING BIOASSAY PROGRAM FATE

HEW FINALLY has agreed to permit the Univ. of Arizona to file a patent application on the process developed by Sydney Salmon and his associates to clone human tumor stem cells. This was one of the 29 patent applications requested by NIH grantees and contractors, most of them NCI's, which had been held up by the HEW general counsel and occasioned the outburst by Sen. Robert Dole (***The Cancer Letter***, Aug. 11). Salmon told ***The Cancer Letter*** that at least one firm is "quite interested" in the process and was willing to help support its development if its investment could be protected with some exclusive patent arrangement. . . . **SECOND DAY** of the Oct. 27-28 meeting of the Div. of Cancer Biology & Diagnosis Board of Scientific Counselors will be closed (the meetings list last week said both days would be open) to review personnel of the intramural Laboratory of Immunodiagnosis. . . . **NATIONAL CONFERENCE** on Breast Cancer is scheduled March 5-8 in Atlanta. The conference will emphasize the team approach and involvement of various specialties in problem areas, including high risk benign disease, minimal breast cancer, radiation risks, detection programs, invasive cancers, relationship of gynecological disease and breast disease, and rehabilitation. Contact American College of Radiology, 6900 Wisconsin Ave., Chevy Chase, Md. 20015, phone 301-654-6900. . . . **PERSISTENT RUMOR:** Atty. Gen. Griffin Bell and OMB Chief James McIntyre will step down, HEW Secretary Joseph Califano will take one of those jobs and retiring Congressman Paul Rogers, chairman of the House Health Subcommittee, will take over at HEW. . . . **CALIFANO IS STILL** kicking around various options that involve NCI's Bioassay Program. Director Arthur Upton feels NCI must retain its role in identifying carcinogens and hopes he has convinced Califano that carcinogenesis research and testing cannot be separated. Upton is pressing for greater coordination among the research and regulatory agencies rather than consolidating all toxicity testing into one. . . . **ELMER BOBST**, philanthropist and former chairman of Warner-Lambert Pharmaceuticals who died recently, was named to the National Cancer Advisory Board by his friend Richard Nixon when the Board was established in 1972. Bobst also was a national chairman of the American Cancer Society executive committee.

CIS MAJOR WEAKNESSES: NO EMPHASIS ON PREVENTION, REHAB INTERVENTION

(Continued from page 1)

and two additional centers have been brought into the program.

The new contracts in the $7.5 million program went to the comprehensive centers at Ohio State and UCLA. The centers there were not recognized as comprehensive when the program started three years ago. The program is limited to comprehensive centers.

Contracts were not renewed with the Univ. of Alabama Comprehensive Cancer Center and the Colorado Regional Cancer Center. Directors of both of those centers have indicated they will reapply. Carl Larson, assistant program director for cancer centers outreach and CIS project officer, said he feels the deficiencies cited by merit reviewers will be corrected and the two centers brought back into the program.

The only other comprehensive center is the newly recognized Cancer Center of Metropolitan Detroit, which has not yet had an opportunity to submit a CIS application.

The first and most urgent goal of the CIS program when it was established in 1975 was to provide health professionals and the public with access to the latest and most accurate information on cancer. Eleven tasks were required:

1. Establishment of a toll free phone system.
2. Development of up to date cancer resource directories—local, state, national.
3. Provide the public with current, accurate information about cancer.
4. Assess the need for, to plan and conduct appropriate educational programs directed toward selected target audiences.
5. Provide health professionals access to up to date accurate information about cancer.
6. Assess the need for, plan and conduct appropriate educational programs directed toward selected health professional groups.
7. Provide health professionals with access to defined channels of communication for professional advice and consultation.
8. Provide information and materials available upon request to NCI staff.
9. Cooperate with NCI and other comprehensive cancer centers in program development and the exchange of materials and reports.
10. Work and cooperate with appropriate cancer concerned institutions, groups and organizations in program development.
11. Design and implement evaluation procedures to provide feedback for necessary program development and improvement and assessment of the total program.

The Alabama center was unable to establish the toll free phone service, although that was considered to be the first priority. The State Medical Assn., fearing that it would lead to disruption of referral patterns, withheld its cooperation. Although DCCR permitted the center to proceed with the program without the phone service "and thus this couldn't have been the main reason for not renewing the contract," Larson said, "I suppose it did make a difference."

Alabama now plans, if its new application is approved, to operate a phone system through local American Cancer Society offices and expects the State Medical Assn. to approve.

The problem at Colorado, according to the merit reviewers, centered around the emphasis there toward the public relations and media aspects of the program.

Not enough attention was given to professional and public education, the reviewers said. The center is in the process of restructuring its staff "to do some real work in education," Larson said.

Larson described the program and summarized the merit review findings for members of the DCCR Advisory Committee.

"Presently the CIS toll-free telephone systems are serving 20 states in which better than half the people in the country live. New territory continues to be added to the network in an orderly manner. Volunteers, for the most part, handle the telephone lines, but receive backup assistance from regular members of the staff. All volunteers complete a comprehensive training program in preparation for their service. They have at their disposal easily retrievable materials to help them answer questions. Intelligent and well prepared volunteers have given satisfactory service but turnover continues to be a problem and necessitates frequent volunteer training and preparation sessions.

"Unfortunately, the Cancer Information Service is thought of only as a toll-free telephone service," Larson said. "While the telephone is a very important part of CIS, the contract called for the completion of other important tasks. Public education programs are conducted through pamphlets, brochures, featured news and magazine articles, and news releases. Newsletters, brochures and pamphlets are used as the major written sources of cancer education to health professionals. Public service announcements and other methods are used to promote CIS programs.

"The comprehensive cancer centers, through their cancer information service offices, provide the means through which the government can transmit important information to the public. The DES and thyroid alerts are examples. The CIS staffs responded with enthusiasm to Secretary Califano's call to get the word out to the public on asbestos."

Strengths of the program as identified by the merit review committee included:

1. The development of such a large scale social action program in such a short period of time.

2. The establishment of the necessary linkages among the American Cancer Society, other voluntary cancer-related agencies, a number of health care resources, and the various centers themselves.

3. The recruitment, training and management program for volunteers.

4. The development of the sense of the network among the contractors.

5. The resource support the program has been able to obtain from a variety of sources.

6. Development and implementation of the toll-free telephone system.

"While the committee noted that firm indicators had not been established, most members expressed the belief that there had been substantial impact," Larson said. "Many callers have received information which they have shared with others. There had been substantial impact through the promotion of the cancer centers and their outreach activities. There is ample evidence of the establishment of good working relationships among the cancer related organizations in the community."

Major weakness of the program, reviewers said, has been the lack of emphasis in prevention and rehabilitation intervention areas. They were concerned about the question of evaluation and suggested that because of the limited availability of evaluation expertise at the local level, including the inherent biases in self-evaluation, a national evaluation effort should be considered. Careful evaluation of the volunteer also should be made.

Reviewers also said a need exists for stronger educational program development directed toward allied health professionals and specific high risk minority target audiences.

Total cost of the program during the first three years was about $5 million. Larson said DCCR plans to allocate approximately $7.5 million to it over the next three years.

What does the public want to know about cancer?

Coordinators of the CIS programs analyzed 50,000 call record reports. They found that a majority of the callers are women, white middle class with mre than average knowledge of cancer, and about 45% are cancer patients, or relatives or friends of patients. Callers are interested in their own personal risks to cancer. They want to know if their risks are related to their places of work or to carcinogens in the air, water or food. Each new disclosure in the media stimulates questions. They also ask about familial risks.

"When the program started, speculation was that the cancer information lines would be used as 'hot lines' or crises intervention lines," Larson said. "This has not occurred. Speculation also was that considerable counseling would take place over the telephone. While almost all calls contain an element of counseling, they do not involve counseling in the traditional sense of the word.

"The early fears were that CIS would likely intervene in community referral practices. This concern has not manifested itself as few callers expressed a need for a change in doctor or wanted volunteers to give the name of a cancer specialist.

"The most frequent question asked about lung cancer is the relationship of lung cancer to smoking. Other questions asked are: What are the symptoms? What is the treatment? What is the prognosis for lung cancer?

"The questions most frequently asked about colon-rectum cancer are: What are the symptoms? What diagnostic tests are available, where can I go to obtain a test? Some questions were asked about the kind of diet a person should follow to avoid cancer.

"On uterine and cervical cancer among the most frequently asked questions were: Where can I get a Pap test? What does the classification of the Pap test mean? Many questions about uterine and cervical cancer related to the availability of local services. This type of question does not seem to occur as frequently for other sites.

"Most of the questions about skin cancer related to what it looks like and how one can keep from getting it.

"Many of the questions on breast cancer centered around treatment and symptoms. Many of the calls were made by patients, members of the family, or other relatives. Generally, the callers wanted to know if the treatment being received was the best available and did it fall into the category of 'recommended treatment?' The mammography issue ranked high in frequency. This again reflects news stories about dangers from radiation. Few questions were asked about breast self-examination and rehabilitation and reconstruction. Also, evidently psychosocial concerns are not important to callers. Questions about the one stage, two stage procedure relating to breast surgery were not frequently asked.'

UPTON SAYS FLEXIBILITY OK IN PAYING GRANTS, BUT WITH 'CORPORATE' REVIEW

NCI Director Arthur Upton clarified his position on flexibility in awarding grants, as expressed in an interview with ***The Cancer Letter*** (Aug. 25).

Upton had said that grants would be paid strictly according to priority scores. Division directors and program managers would be permitted to skip over grants with higher priority scores (as determined by study sections) to fund grants they feel are more urgently needed only if they can find extra money out of that allocated to their divisions for contracts.

That would appear to be a significant change from the practices of the Div. of Cancer Research Resources & Centers (now the Div. of Extramural

Affairs), which administered and awarded most NCI grants before this year's reorganization. DCRRC program managers have been permitted to skip over grants by as much as 10 to 15 points in the priority scores. They have had to justify it in writing each time, but this practice has been frequently used and rarely, if ever, challenged.

The NIH Div. of Research Grants has recommended that institutes be permitted to skip over by as much as 40 points, if it can be justified.

Upton said he would not object to skipping (and to paying grants out of money allocated for grants) when valid reasons are presented. "We will continue that degree of flexibility." A significant difference in how that will work will be that NCI's "corporate body," as Upton refers to senior executives of the institute, will have to approve each variation from priority scores.

"In the past, this was a decision that was kept within DCRRC," Upton said. "I think now that when there are exceptions, we will want the program areas to justify them to all of us. I can foresee there will be some juggling, but I do not want to see it get out of hand. Any departure from strict priority scores will have to be justified and brought to the attention of the corporate body. We intend to monitor it and maintain the integrity of priority rankings."

GORI GOES TO HOPKINS PART-TIME, WILL RETAIN JOB AS DCCP DEPUTY

The problem of what NCI is going to do with Gio Gori has been resolved, at least for the present.

Gori, deputy director of the Div. of Cancer Cause & Prevention, will spend most of his time during the next academic year starting Sept. 5 in Johns Hopkins Univ.'s master of public health program. He will continue to hold his title as DCCP deputy director and will return full time in that role next June.

Gori's position at NCI has been anything but secure since the change of DCCP directors last year. Gregory O'Conor, the new director, would like to be able to select his own deputy. Gori also had headed the nutrition and smoking programs, which were largely contract supported. With the reorganization emphasizing grants, management of those programs has been transferred to the Extramural Programs Branch, headed by Thaddeus Domanski. The Smoking & Health Program is now under the Physical & Chemical Carcinogenesis Section, headed by Thomas Owen.

Gori also has been in hot water over his publication of conclusions drawn from the development of less hazardous cigarettes stimulated by the Smoking & Health Program. Gori contends that certain low tar and nicotine brands now can be smoked in limited amounts with no danger to health.

Although Gori included several strong and clear disclaimers, insisting that no smoking at all was safer than even limited smoking of the less hazardous brands, his remarks riled both NCI Director Arthur Upton and HEW Secretary Joseph Califano.

Upton's objection was primarily to the use of the word "tolerable" by Gori in describing the effects of the low tar and nicotine cigarettes when compared to the brands in existence before 1960.

"Dr. Gori's goal was to call attention to those brands, and to tell the public that if you have to smoke, smoke these," Upton said. "That was a worthwhile goal, but that message got lost in the word 'tolerable.' Those brands have not been proven safer, although the data suggest it. His comparisons were hypothetical. It has created confusion. I know people who had stopped smoking but started again when they heard a Cancer Institute scientist say that smoking certain brands was tolerable. That certainly was not Dr. Gori's objective."

Gori has received considerable support from the press in the controversy. An editorial in the *Washington Star* applauded him for the success of his program which has resulted in dramatic reductions of hazardous substances in a growing number of cigarette brands, and for publicizing that fact. Columnist James Kilpatrick blasted Gori's critics who he said were discouraging government employees from telling the truth.

Upton is aware that Gori's semisabbatical will be viewed by some as an exile. He was careful to point out, and Gori confirmed, that the plans for him to go to Hopkins were in the works before the cigarette controversy erupted. The transfer of the Smoking & Health Program also antedated that flap.

Upton said he expected Gori to continue to provide scientific guidance to the smoking program but that he feels it is "inappropriate" for programs to be managed by division directors or their deputies.

Upton told ***The Cancer Letter*** that when Gori returns fulltime to NCI next June, he will do so as the deputy director of DCCP and in fact will continue to hold that title while he is at Hopkins.

DCCP, SHORN OF ADVISORY COMMITTEES, NOW HAS BOARD OF SCIENTIFIC COUNSELORS

NCI's Div. of Cancer Cause & Prevention, for the first time, has a Board of Scientific Counselors.

The Div. of Cancer Biology & Diagnosis and Div. of Cancer Treatment, both of which have large intramural programs as well as responsibility for major extramural research activities, have had Boards of Scientific Counselors for several years. Consisting of nongovernment scientists, they serve as advisors in the review of scientific concepts and program direction. They also provide what is the only outside peer review for the intramural laboratories.

DCCP's outside advisors had been the advisory committees and groups for the major programs—carcinogenesis, viral oncology, nutrition, and smoking. All of those were eliminated last year when the

Carter Administration forced a cutback in the number of advisory committees.

The new DCCP Board will advise on all the division's programs, Director Gregory O'Conor said.

Ten scientists have accepted invitations to serve on the Board and have been approved:

Philip Cole, Dept. of Epidemiology, Harvard; Charlotte Friend, director of the Center for Experimental Cell Biology at Mt. Sinai School of Medicine; Seymour Jablon, director of the Medical Follow-up Agency of the National Academy of Sciences; Jenifer Kelsey, Dept. of Epidemiology & Public Health, Yale; George Klein, head of the Dept. of Tumor Biology, Karolinska Institute, Stockholm; Peter Magee, director of Fels Research Institute, Temple Univ.; Lloyd Old, associate director for research of Memorial Sloan-Kettering Cancer Center; Louis Siminovitch, chairman of the Dept. of Medical Cell Biology, Univ. of Toronto; James Watson, director of Cold Spring Harbor Laboratory of Quantitative Biology; and Bernard Weinstein, director, Div. of Environmental Sciences at Columbia's Institute of Cancer Research.

Thre others have agreed to serve but have not yet been formally approved—Ingegerd Hellstrom, professor of microbiology and immunology, Fred Hutchinson Cancer Research Center; Warren Nichols, assistant director of the Institute for Medical Research, Camden, N.J.; and G. Barry Pierce, professor of pathology, Univ. of Colorado Medical Center.

No chairman has been designated yet. The Board will hold its first meeting at NIH Oct. 17-18.

CLEARINGHOUSE FINDS SEVEN COMPOUNDS ARE CARCINOGENIC, THREAT TO HUMANS

Seven of 28 chemicals tested in NCI's Bioassay Program were found to be carcinogenic with potential risk to humans by the Clearinghouse on Environmental Carcinogens Data Evaluation/Risk Assessment Subgroup following review of the test data.

Seven additional chemicals were found to be carcinogenic by the subgroup but no determination was made on human risk. Ten of the 28 were not carcinogenic, according to test data, subgroup reviewers found, although a number of deficiencies clouded results in some cases. Enough deficiencies existed in tests of the remaining four chemicals that no conclusions were drawn on their carcinogenicity.

Carcinogenic with potential risk to humans:

3-amino-9-ethylcarbazole (hydrochloride); an intermediate in the manufacture of dyes. Reviewer Michael Shimkin noted that in addition to a statistically significant incidence of liver tumors in both treated rats and mice, several other tumor types were found at increased rates in rats, including lung tumors.

Sulfallate, used as a herbicide on vegetable crops. Reviewer Louise Strong found some experimental shortcomings but that the conclusion that it was carcinogenic in both rats and mice was still valid.

Aniline hydrochloride, a dye intermediate. Reviewer Arnold Brown pointed out that it was carcinogenic in treated rats; there was marked hemosiderosis in the renal tubular epithelium and in the liver of treated rats but none was reported in treated mice.

2-aminoanthraquinone, a dye intermediate. Shimkin said the compound was found to induce hepatocellular carcinomas in male rats and in both sexes of mice. Female rats also died of nephrotoxicity, and Shimkin said that in addition to its potential carcinogenic risk to humans, nephrotoxicity also may pose a human hazard.

1,5-napthalenediamine, a dye intermediate. Brown reported that it was carcinogenic in treated female rats and in both sexes of mice. Although a deficiency existed in that the study was conducted in a room in which other compounds were under test, Brown said the findings suggested the compound may be a carcinogenic risk to humans.

Pivalolactone, an intermediate chemical used in making polymers. Reviewer David Clayson agreed with the conclusion that the compound was carcinogenic in treated rats. He expressed surprise that it also was not carcinogenic in treated mice and conjectured that it may have hydrolyzed to an innocuous substance by the time it was administered to the mice, thus accounting for its lack of carcinogenic activity. He said it hydrolyzes to propionic acid in the presence of water. Other deficiencies included the small control group size and the route of exposure, but the chemical should be considered a potential carcinogenic risk to man, Clayson said.

Para-cresidine, used in preparation of dyes. Reviewer Paul Nettesheim said the nature of tumors in treated rats and mice clearly indicated they were treatment related. He noted that p-cresidine was dissolved in acetone but that there was no acetone control group. That shortcoming should not interfere with the conclusion that the compound was carcinogenic and would appear to be a risk to humans, Nettesheim said.

Carcinogenic, with no determination on risk to humans:

5-nitro-o-anisidine, a dye intermediate. Brown agreed that it was carcinogenic in both mice and rats, although there were a number of experimental deficiencies.

Chlorobenzilate, an agricultural pesticide. Nettesheim agreed that it was carcinogenic in treated mice, and said the evidence in treated rats was only suggestive of a carcinogenic effect. He was critical of the high doses administered which necessitated the intermittent treatment of the animals. He also was critical of the small number of control mice.

Chlorothalonil, an agricultural fungacide and also an ingredient in paints. Strong said the compound was carcinogenic in treated rats but was not clearly

carcinogenic in treated mice. She was critical of the limited number of matched control animals and pointed out that the occurrence of certain tumors in treated rats and mice may have taken on greater significance had control groups been larger. Other deficiencies included use of different batches of the compound and poor animal survival. Despite the shortcomings, she said that the kidney tumors in both the treated male and female rats appeared to be biologically significant.

1-amino-2-methylanthraquinone, a dye and a dye intermediate. Shimkin said the compound induced liver tumors in both sexes of treated rats and in female mice. It also induced kidney tumors in male rats and was nephrotoxic in mice. He said the hepatic effect in male mice may have been masked by the high spontaneous incidence of liver tumors in this sex. He noted the negative trend for mammary tumors in treated female rats.

3-(chloromethyl) pyridine hydrochloride, an intermediate in the manufacture of pharmaceuticals, veterinarian and agricultural chemicals. Reviewer Verne Ray agreed with the conclusion that it was carcinogenic under the conditions of the test.

Cupferron, an analytical reagent. Reviewer Verald Rowe agreed that it was carcinogenic in rats and mice, although suggesting that hemosiderosis detected in several organs should be further evaluated. Rowe commented on the wide temperature variation in the animal rooms, on the fact the mice were housed in a room in which other chemicals were under study, and on the lack of data on the stability and concentration of the compound in the diet. He questioned the basis for selecting the chronic dose levels since it did not correspond with the criteria described in the protocol. Rowe said the study's shortcomings cast doubt on its validity, and that the data do not allow an assessment of human risk.

Bioassay Program Director Richard Griesemer said that the test was too limited to allow an interpretation of the hemosiderosis problem and noted that it did not appear to interfere with the survival of treated animals.

5-nitro-acenaphthene, used in manufacture of pharmaceuticals. Ray agreed that it was carcinogenic in treated female mice and both sexes of rats. Poor survival of treated male mice precluded an analysis of this group.

Chemicals found not to be carcinogenic

2,3,5,6-tetrachloro-4-nitroanisole, a fungacide and acaricide. Clayson noted an increased although not statistically significant incidence of hepatic neoplasms among treated rats and lymphomas and leukemias among treated mice. Although the results indicated that the animals were administered maximum tolerated doses of the compound, Clayson expressed surprise that the levels were so low given the nature of the substance. He suggested that the low dose levels imposed by the toxicity may have limited the expression of a higher tumor rate at those sites at which an increased incidence was observed. Despite the apparent adequacy of the study, Clayson felt that some additional testing was appropriate. He suggested that short term in vitro assays might provide useful information.

Anilazine, a fungacide. Rowe agreed with the conclusion that it was not carcinogenic in treated rats or mice. He commented on the small number of control animals and low dose levels administered. Results from the subchronic study indicated that higher dosages should have been used in the chronic phase, and these experimental flaws detracted from the value of the bioassay, Rowe said.

4-nitroanthranilic acid, a dye intermediate. Shimkin agreed that it was not carcinogenic in rats or mice, that the experimental design was adequate, and pointed out that there was a negative trend in several tumor types among treated animals.

Mexacarbate, an agricultural pesticide. Clayson said that although the report concluded it was not carcinogenic under the conditions of the test, the incidence of hepatocellular carcinomas in the high dose treated male mice was statistically significant when compared with matched controls. However, the incidence was not statistically significant when compared with historical controls. Clayson said use of historical control data sometimes provides fallacious comparisons for commonly occurring tumor types, especially for those that may be influenced by dietary contaminants.

3-nitro-p-acetophenetide, a dye intermediate. Rowe agreed with the conclusion that it was not carcinogenic in treated rats or female mice but did induce a statistically significant incidence of liver tumors in treated male mice. Rowe noted several flaws that detracted from the study—analyses were not done to confirm identification of the compound, its stability, or concentration in the diet, and the study was conducted in a room in which other compounds were under test.

Griesemer said the compound was obtained from the manufacturer of the chemical. He suggested that further consideration of the report be deferred until a sample of the reference could be analyzed for identity and stability, and the subgroup agreed.

Triphenyltin hydroxide, a fungacide which is also used for insect control. Clayson agreed that it was not carcinogenic in rats or mice, although the control groups were smaller than the optimal size.

1-phenyl-2-thiourea. This compound has an interesting dual use: It is used as a research substance in testing the sense of taste; it is also a rat killer. Rowe agreed that it was not carcinogenic under the conditions of the test, although there were deficiencies in the experimental design, he said. Among those were inadequate control group size, lack of analytical data on the dietary concentration of the test substance, the conduct of the study in a room in which other

chemicals were under test, and an improperly run subchronic study.

DDT, TDE and p,p-DDE, insecticides. Nettesheim agreed that the study did not provide firm evidence for the carcinogenicity of DDT in rats or mice; that TDE may be carcinogenic in the treated rats as evidenced by an increased incidence of thyroid tumors; and that p,p-DDE was not carcinogenic in treated rats but did appear to be a hepatocarcinogen in mice. Nettesheim said that caution should be exercised in interpreting the results in view of the studies' shortcomings. Among the experimental limitations were the small matched control groups, the fact that the study was conducted in a room in which other chemicals were under test, the numerous dosage changes during the course of the chronic study, and the variations in the pathology protocol. He said it was not possible to assess human risk on the results of the study.

NCI staff member Cipriano Cueto commented that other studies have demonstrated the carcinogenicity of some of these test compounds in mice. He said that the data from this study probably reflected a difference in response that exists between species and strains. Any consideration on retesting the compounds would be based, in part, on a review of all published data.

3-chloro-p-toluidine, a dye intermediate and an avacide. Strong agreed that it was not carcinogenic. She pointed out that the compound was obtained from the commercial producer and was analyzed for purity and stability, both over time and in the dietary mixture. Although she noted the small control group sizes and dosage changes during the chronic phase, Strong said she still considered the study valid.

1-phenyl-3-methyl-5-pyrazolone, a dye intermediate. Nettesheim said the study was "straightforward" and agreed that the compound was not carcinogenic in rats or mice.

No conclusion was reached on the carcinogenicity of four chemicals.

Azinphosmethyl, an organophosphorous cholinesterase inhibitor used as an insecticide. Strong said that although the neoplasms of the thyroid and pancreatic islets in treated male rats were only suggestive evidence of carcinogenicity, the experimental design was sufficiently flawed as to preclude any definite conclusions being drawn. The study was particularly deficient due to the small number of matched controls and limited number of organs examined, she said. She questioned the practice used for concluding that a tumor incidence, observed in treated animals, was within the spontaneous range. Because of the inadequacies of the bioassay, she said that no conclusion could be drawn regarding the carcinogenicity of the compound. She suggested that it be tested in short term in vitro assays, and if found positive, that it be considered for retest in a long term animal assay.

Allyl chloride, a general chemical intermediate. Ray said that the study should be considered inadequate for drawing any conclusion about the compound's carcinogenicity. He said that poor survival in the high dose treatment groups precluded an evaluation of the carcinogenicity. Griesemer said the compound would be considered by the Chemical Selection Working Group for retesting.

Clonitralid, a molluskacide. Ray said the study should not be considered definitive, although it failed to establish the carcinogenicity of the compound. He noted the finding of mammary adenocarcinomas in both treated and control female rats as well as in treated male rats. Ray concluded that the evidence was insufficient to declare the compound carcinogenic but said he was concerned that the study "may not have been definitive."

2,5-toluenediamine sulfate, a dye intermediate. Brown said that although a carcinogenic response was not demonstrated, the evidence was suggestive that the compound may have a carcinogenic potential. He recommended that it be considered for retest. He noted several experimental flaws, including the use of animals from different shipments, the conduct of the subchronic study in a different mouse strain than used in the chronic phase, and the start of the high dose rats on test some months after the initiation of the low dose animal group. Brown said the compound warranted further retesting because of the experimental design and study conduct deficiencies, as well as the fact that the compound had been shown to be positive in the Ames assay.

CLEARINGHOUSE RATES 11 CHEMICALS AS PROSPECTS FOR BIOASSAY PROGRAM

The Clearinghouse Chemical Selection Subgroup reviewed 11 compounds as candidates for testing in the Bioassay Program and assigned priority scores to each. The subgroup's recommendations, along with those of the Chemical Selection Working Group, are presented to NCI staff for consideration. About 200 chemicals a year are entered into the program.

The candidates were rated on a scale of 1-10, with 10 being highest rating:

Phenolphthalein, 7.7; 4-hydroxyacetanilide, 7.0; 6-methylcoumarin, 6.7; gibberellic acid, 6.0; hydroquinone, 6.0; p-quinone, 6.0; carvone, 5.3; catechol, 4.3, *y*-butyrolactone, 4.0; hematoxylin, 3.7; and 3,4-dihydrocoumarin, 2.7.

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. Their addresses, all followed by NIH, Bethesda, Md. 20014, are:

Biology & Diagnosis Section – Landow Building
Viral Oncology & Field Studies Section – Landow Building
Control & Rehabilitation Section – Blair Building
Carcinogenesis Section – Blair Building
Treatment Section – Blair Building
Office of the Director Section – Blair Building
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CP-VO-91001-66

Title: *Large scale tissue culture virus production for cancer research*
Deadline: *Oct. 5*

Produce, purify, characterize and distribute a variety of different RNA type-C retroviruses and selected tissue culture cell lines. This is a continuation of an ongoing project. Electro-Nucleonics Laboratories Inc., Bethesda, Md. is the incumbent. It is essential to the task that the contractor's principal investigator and staff have a demonstrated base of knowledge and experience in the areas of tumor viruses, replication of viruses in tissue culture, propagation of cells in tissue culture, concentration of viruses by various means, and quality control characterization.

Types of viruses to be produced may include, but not be limited to: AKR murine leukemia virus in the AKR mouse embryo fibroblast cell line; NZB murine leukemia virus (NZB ME C1 35) in the New Zealand black mouse embryo cell line; Kirsten murine sarcoma virus pseudotype of either NZB murine leukemia virus (NZB-MuLV, 232) or NIH murine leukemia virus (NIH-MuLV, BC232) both grown in the human rhabdomyosarcoma cell line (A673); NIH murine leukemia virus (ATS-124) in the RD human rhabdomyosarcoma cell line; BALB virus-1 in Swiss mouse embryo cells (NIH 3T3); BALB virus 2 (BC-177) in the A673 cell line; Gross leukemia virus, passage A, in the NIH 3T3 cell line; and Moloney leukemia virus (SNE 81) in the NIH 3T3 line.

On a weekly basis, 110 liters of virus-containing cell culture fluid will be produced. The government will not accept offers limited to subsection, smaller elements, or portions of the overall work.

Contract Specialist: Clyde Williams
Viral Oncology
301-496-1781

RFP NCI-CM-87227

Title: *Conduct in vitro cell culture screening of new materials for cytotoxicity*
Deadline: *Oct. 30*

The Developmental Therapeutics Program of the Div. of Cancer Treatment is seeking the services of organizations having the necessary scientific and technical personnel and physical facilities for this project. Assignments will encompass the propagation and maintenance of stock cell lines; preparation of test materials; recording, computation, and evaluation of results; and summarization and reporting of results as specified. Testing is performed according to protocols. Materials to be tested and initial stock lines will be supplied by NCI.

Candidate organizations must have the capability to conduct cell culture screening and demonstrate evidence of general experience in standard cell culture techniques as well as specific experience in tube assay screening of drugs for cytotoxicity utilizing the KB, L1210 and P 388 cell lines. Materials to be tested will include chemically hazardous or potentially carcinogenic compounds. Proposals must therefore include well qualified personnel with appropriate training and experience with hazardous materials.

To be considered for such a contract, organizations must demonstrate established competence and resources for cell culture screening at a minimum level of 5,000 tests per year. A test, as used here, means a single materia l tested at three to five dose levels, each dose level in duplicate, with appropriate controls. Proposals will be invited for a three year incrementally funded contract period at levels of 5,000, 10,000 or 15,000 tests per year. Respondents will be required to demonstrate capability to perform at the chosen level.

Contract Specialist: John Thiessen
Cancer Treatment
301-427-8125

NCI CONTRACT AWARDS

Title: Drug distribution and protocol monitoring system
Contractor: Value Engineering Co., $338,195.

Title: Maintain an animal holding facility and provide research services
Contractor: Pharmacopathics Research Laboratories Inc., Laurel, Md., $77,837.

Title: Lipid levels and cholesterol metabolism in relation to human breast cancer risk
Contractor: Kaiser Foundation Research Institute, $67,000.

Title: Study of morphology of normal/abnormal mammary tissue
Contractor: State Univ. of New York, $233,000.

Title: Lung cancer control detection and therapy–phase II, continuation
Contractor: Johns Hopkins Univ., $800,000.

The Cancer Letter –*Editor* JERRY D. BOYD

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