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HEW RULING LIMITS DISTRIBUTION OF CHEMICALS FROM REPOSITORY TO CONTRACTORS, GOVERNMENT

With the unprecedented growth of cancer research since 1971, NCI has become an increasingly important supplier of critical research materials to investigators around the country. The National Cancer Act specifically authorizes NCI to supply "biological materials and therapeutic agents" to qualified investigators. That authority has permitted the institute to become the primary source for viruses and for experi-

(Continued to page 2)

In Brief

ADJUVANT CHEMOTHERAPY STANDARD PRACTICE FOR BREAST CANCER AT MILAN, BONADONNA SAYS

GIANNI BONADONNA was asked by science writers at the annual seminar sponsored by the American Cancer Society if he shared James Holland's enthusiasm for the breast cancer post operative chemotherapy regimen Bonadonna has been testing in Italy (Holland wrote in the *New England Journal of Medicine* that the results of Bonadonna's study plus those of other NCI-supported clinical studies headed by Bernard Fisher are so promising that adjuvant chemotherapy should be standard practice when evidence of metastasis is present). Bonadonna's response: "I don't have a message for the whole world. In our institution (in Milan), it has been adopted as standard treatment, with positive nodes." Bonadonna said another trial under way for about two years involves segmental surgery, with removal of about one-fourth of the breast followed by radiotherapy, and chemotherapy with positive nodes. So far, the recurrence rate has been no higher than with the traditional mastectomies . . . **NCI DIRECTOR** Frank Rauscher and Div. of Cancer Cause & Prevention Director James Peters probably will be telling their side of the Saffiotti story (see Saffiotti's statement inside) to Congressman L.H. Fountain's Subcommittee on Intergovernmental Relations. Fountain's staff has been studying the Cancer Program for quite some time and may be ready for hearings soon. . . . **FDA REVIEW** of investigational new drug applications should be done by non-government scientists similar to the NIH grant peer review process, says Emil (Jay) Freireich, chief of Developmental Therapeutics at M.D. Anderson. "The way the system is now, with government employees deciding whether or not a drug will be approved, will never work. They have their careers and their pensions to think about. They know they'll never get into serious trouble by disapproving a drug; the only danger to their careers comes when they approve a drug that doesn't work out. The safest thing to do is not to approve any drugs." Outside reviewers would not have those pressures and would be more inclined to approve a drug without some of the unreasonable demands FDA places on sponsors, Freireich believes.

NCI DENIES CHEMICALS WITHHELD TO AID STAFF SCIENTISTS; HEW RULING BLASTED

(Continued from page 1)

mental drugs for scientists and clinical investigators, whether or not they are supported by NCI grants or contracts. Literally thousands of such requests are filled each year, free of charge.

That section of the Act does not include chemicals as materials that may be distributed freely by NCI. As the Cancer Program has grown, however, so has the need by investigators for chemicals available only through NCI. Until recently, NCI chose to interpret the Cancer Act to include authority to distribute chemicals, and requests were filled on that basis. Again, it made no difference if the investigator had any connection with an NCI grant or contract.

The HEW general counsel failed to see it that way. He has ruled that the Act does not authorize NCI to distribute chemicals to any investigators other than those performing research under an NCI contract. Even NCI grantees are excluded. Other agencies of the federal government may still receive them.

That decision has prevented NCI from filling hundreds of requests for chemicals and may have contributed to the feeling by some non-NCI investigators that NCI staff scientists are taking advantage of the situation.

Although grantees may not now receive chemicals directly, NCI has found that some of them are affiliated with institutions which do have at least one contract with the institute, or with another federal agency. Requests through those sources are filled.

But hundreds of other requests go unfilled. When those investigators see their own research stymied because they can't get the proper materials, and then see publications by NCI scientists who have been able to complete the same research because they did have the chemicals, the resentment can be fierce.

Some have charged that NCI was deliberately withholding the chemicals, to give its staff members an edge. Harry Gelboin, chief of the Chemistry Branch in NCI's Carcinogenesis Program, denied that that was ever done when the distribution was handled through his office.

"No one was ever turned down while I was distributing chemicals," Gelboin said. "We sent out hundreds and hundreds of samples." Gelboin said NCI then viewed chemicals as biological materials, in the context of what was perceived as the intent of Congress in the National Cancer Act, and offered them to all qualified investigators.

John Cooper, deputy director of the Carcinogenesis Program, said he was not aware of any effort to deliberately withhold materials to benefit staff members conducting intramural research. "I'm not going to say that someone in one of the labs may not be sitting on something to gain an advantage," Cooper told *The Cancer Letter.* "But if I find out about it, I'll put a stop to it immediately."

Gelboin no longer is responsible for distributing chemicals, that task having been transferred to the Chemical Repository established by NCI in a contract awarded last year to IIT Research Institute in Chicago. About 130 compounds, all carcinogens or carcinogen analogs, are available.

Main purpose of the repository is to provide reference samples, analyzed and well characterized, so that research will have the same starting point. Investigators obtain compounds in quantities required for experiments from other sources, or synthesize them themselves. NCI intends eventually to provide some chemicals in sufficient quantitites for experiments when they are not available commercially.

But the repository's usefulness will be limited until the restriction against grantees and non-NCI-funded investigators is lifted. "That has caused unending amounts of grief," Marcia Litwack, project officer for the repository, told *The Cancer Letter.* She estimated that hundreds of requests have had to go unfilled.

When grantees apply, they are advised to submit their requests through the project officer of other agencies if their institution happens to have a contract with one. The same advice is offered to investigators with no NCI funding. "But the whole thing is stupid," Litwack said. "There are many smaller schools and commercial organizations which don't have contracts. Many of these compounds are not for sale anywhere. It means simply that they are not able to go ahead with their research."

NCI's plans to offer the compounds to all investigators now probably will have to await some action by Congress. The Cancer Act will be up for renewal next year, and it seems logical that adding chemicals to the distribution authorization would not be a problem. That would be a delay of more than a year, however. Faster action would require a special bill, probably not much of a possibility unless a case can be made for the immediate need.

In the meantime, investigators at other government agencies and NCI contractors may request compounds by writing to Litwack, Manager of Information, Resources Segment, NCI, Landow Bldg A306, Bethesda, Md. 20014. Phone requests are not being accepted. Include with the request a statement describing the intended use, quantity required, and contract number or agency affiliation.

MEMO OF MEETING BETWEEN OFFICIALS OF NCI, NIH AND FDA ON IND PROBLEMS

An anonymous staff member of the Food & Drug Administration, apparently stung by criticism of his agency in *The Cancer Letter,* sent a copy of a memo describing the meeting between NCI and NIH executives with FDA leaders. Accompanying it was a note which said, "The Cancer Letter can regain some of its lost credibility by publishing this."

Such an opportunity could not be passed up. Here is the memo, complete and unedited:

"Participants: National Institutes of Health: Dr. Donald Fredrickson, Director; Dr. Frank Rauscher, National Cancer Institute; Dr. Ronald W. Lamont-Havers, Deputy Director, NIH; Dr. DeWitt Stetten, Deputy Director for Science, NIH; Dr. Joseph Perpich, Associate Director for Program Planning and Evaluation, NIH; Dr. Vincent T. DeVita Jr., Director, Division of Cancer Treatment, National Cancer Institute, Dr. Leon Jacobs, Associate Director for Collaborative Research.

"Food and Drug Administration: Dr. Alexander M. Schmidt, Commissioner; Mr. Sherwin Gardner, Deputy Commissioner; Mr. Sam D. Fine, Associate Commissioner for Compliance; Dr. Mark Novitch, Acting Associate Commissioner for Science; Dr. J. Richard Crout, Director, Bureau of Drugs; Dr. Carl Levanthal, Deputy Director, Bureau of Drugs; Dr. Paul Parkman, Deputy Director, Bureau of Biologics; Mr. Roger Barnes, Office of the Associate Commissioner for Medical Affairs; Mr. Gary Dykstra, Office of the Associate Commissioner for Compliance.

"Subject: Compliance With IND Regulations by the National Institutes of Health.

"This meeting was called for the purpose of discussing IND requirements and their application to clinical research conducted or supported by the National Institutes of Health (NIH) and specifically the National Cancer Institute (NCI).

"Dr. Crout began the discussion by discussing his observations of the IND process and how it relates to the type of work being done by NCI. He stated that, historically, NCI had a very well established drug development program and that FDA, over the years, had accepted much IND information on faith rather than fact, presumably because of the confidence we had in their program. Dr. Crout stated that recent events have forced him and FDA to take a different position with regard to NCI. These events were:

"1. The recent upsurge in NCI activities.

"2. The ever increasing pressure upon FDA to apply IND standards in a consistent manner.

"3. Major staffing changes within FDA and NIH.

"Dr. Crout made it clear that the recent hold-up of cancer drug INDs was not because of a single medical officer or bureaucratic problems. He said the INDs were held because of a real concern about the safety decisions which could not be resolved because of insufficient data.

"Dr. DeVita explained in much detail the systems used by NIH and NCI to assure adequate safety both before and during clinical trials. He admitted that there was a problem with reports necessary to meet FDA requirements. Many of these required reports are delinquent due mainly to staffing problems. An effort is being made currently to resolve this problem.

"Dr. Schmidt entered the discussion at this time and said that the reason he thought it necessary to discuss this situation because of the visibility being given to FDA's responsibilities. These responsibilities extend to all drug research whether conducted by private industry or the Federal Government. He said he felt it better to have this type of discussion prior to a hearing rather than as a result of a hearing.

"Dr. Schmidt went on to say that he and FDA do not question the scientific integrity of NIH or NCI. In his opinion, this is not at issue here. What is at issue is FDA's ability to do its job. Part of that job is the review and approval of IND protocols. In order to accomplish this objective, certain information is needed whether it be from private industry or NCI. FDA can no longer operate on good faith in this area. Our decisions must be well founded and subject to the closest scrutiny. Dr. Schmidt further stated that not only will FDA be looking more closely at NIH data sent to us, but our trained investigators will be inspecting clinical investigators working on NCI projects.

"Dr. Schmidt also stated that if the NCI program is unique, these differences must be agreed upon by all concerned so that the differences are fully understood by everyone including the public at large.

"At this point, Dr. Rauscher told Dr. Schmidt and Dr. Crout that if an IND submission is forwarded from NCI with insufficient data to approve the project, FDA should turn it down. NCI will then provide the additional information and if this is impossible, the submission will be withdrawn.

"Dr. Crout stated that there should be guidelines governing clinical testing. Dr. DeVita expressed his displeasure at the idea of guidelines; however, he said that the recent guidelines he reviewed were reasonable and he could live with them.

"At this point, Dr. Schmidt asked if there were any problems concerning IND submissions from the institutes other than NCI. Dr. Crout responded in the negative and went on to say that because of the uniqueness of NCI projects, a formal agreement is needed to spell out exactly what will be done by FDA and NCI regarding IND submissions. Dr. Fredrickson said that it may be premature to begin work on such an agreement until such time as all the reporting is up to date and some conclusions can be drawn about the current system. He asked Dr. DeVita when this work would be complete and received a reply of July 1, 1976. At this point, the participants agreed that on or soon after July 1, 1976, negotiations will begin concerning the formal agreement mentioned above. This consensus ended the meeting."

The memo (but not the anonymous note) was signed by Dykstra.

The Cancer Letter asked DeVita to review the memo to determine if it accurately reflected the discussions. His reply:

"It is a very limited description of the discussion of some complex problems, but accurate as far as it went."

Neither DeVita nor Rauscher, who also was shown the memo, commented further on the meeting. But ***The Cancer Letter*** has learned that the discussions also included NCI's complaint about FDA's nitpicking over terminology, and unnecessary, unrealistic and duplicative paperwork demands.

The conference also dealt with the IND application for hycanthone, an anti-infectious disease drug which investigators at M.D. Anderson wanted to include in a protocol for cancer patients. FDA did not act on the application because it could not decide if it should be reviewed by the Oncology Division or Anti-Infectious Drug Division (***The Cancer Letter,*** March 19). It was decided at the conference to refer it to the latter.

ORGAN SITE REPORT FAVORABLE TO PANCREAS PROJECT, BCTF

The report of the National Cancer Advisory Board Subcommittee on National Organ Site Programs is concluded here. The portion published last week covered the Prostatic Cancer Project and the Lung Cancer Task Force.

The report here on the Pancreatic Cancer Project and Breast Cancer Task Force includes the recommendations that the funding cutoff of all organ site project applications be brought more closely into line with that of regular grants; and that contracts awarded by BCTF be given a second review by NCAB.

PANCREATIC CANCER PROJECT

Merit. This project is the newest of the organ site projects, awarded Jan. 1, 1975. It was thought useful to conduct a review even though only 10 months had elapsed. As of the end of October, 1975, 160 inquiries and 57 grant applications had been received. The rate of accretion of grant applications is far greater than that experienced by the other three projects during their first year. At the time of the review, 16 applications had been approved, but only one has been funded and it had not been in operation long enough to permit judgment. Applications had been received in the areas of epidemiology, experimental biology, diagnosis, immunology, treatment, and multidisciplinary research. No applications for pathology research had been submitted although letters expressing interest had been received. The weighting in favor of laboratory studies probably reflects the state of clinical research in pancreatic cancer at this time.

Review. The project follows the same review procedures as the others and its approval rate of 47% is lower than the average for NIH and substantially lower than the other organ site projects. Although the sample was small, the lower approval rate indicates either more rigorous review or a higher proportion of poor quality applications; or perhaps a little of both. If the quality of some of the applications is poor, then the working cadre deserves credit for not approving such applications.

Historically some of the organ site projects have funded approved applications to a somewhat lower payline than the regular grants at NCI. The Bladder, Large Bowel, and Prostate Projects have funded a total of 15 (7.1%) applications with priority scores poorer than 275. In FY '75 the traditional programs funded grants down to priority scores of 260-280, depending on the program. This situation in the organ site projects may reflect the need to foster research in relatively neglected areas and the need to obtain data through research projects which are essential but not particularly imaginative. An analysis subsequently provided by NOSP staff demonstrated that the 47% approval rate for the pancreas working cadre was lower than the average for all the organ site projects (60%), but the percentage of approved applications recommended for funding (94%) was slightly higher than the average for all the projects (91%). The average priority score of approved applications recommended for funding was 206 for all the projects and identical for the pancreas project. When informed of the subcommittee's concern, the pancreas working cadre voted that the project director not recommend for funding approved applications with priority scores poorer than 300.

Planning. At the time of the review the working cadre had not yet established priorities within its plan, even though this was an item of concern at the November 1974 discussion of the project. However, a discussion of priorities was scheduled for the working cadre meeting on Dec. 1, 1975, and a priority statement is being developed.

Dissemination of Information. Shortly after being activated, the project mailed an announcement of its objectives to 1300 scientists throughout the country. An announcement has appeared in six scientific journals and a newsletter is planned. The 160 inquiries received in the first 10 months indicate that interested scientists are being made aware of the project. An announcement in *Science* on behalf of all the organ site projects drew 50 replies, 22 of which expressed interest in all four projects. Eight of the 28 requests for individual project information were for the pancreas project.

Administration. Although the project appears to be coping reasonably well with its work load, concern was expressed that an assistant scientific director had not been appointed. In view of the planning, analysis, evaluation, and integration expected of an organ site project, and in view of the very large number of applications being received, the director cannot be expected to perform effectively without substantial assistance.

Budget. Based on the costs requested for applications in hand, anticipated applications, and the Headquarters operational budget, the project requested a ceiling for its second year of operation of

$2.7 million. This is slightly higher than the originally approved ceiling of $2.5 million.

Subcommittee Evaluation: The National Pancreatic Cancer Project is still in its formative stages and therefore it is too early for a complete assessment. The subcommittee is pleased with the rate of accretion of grant applications. The subcommittee wishes the funding cutoff of all organ site project applications to be brought more closely into line with that of regular grants. The subcommittee also expects the working cadre to address the question of areas of emphasis in its plan and to develop a priority statement.

BREAST CANCER TASK FORCE

Organization and Procedure. The overall activities of the BCTF are directed by a steering committee chaired by Pietro Gullino of the NCI Div. of Cancer Biology & Diagnosis; detailed planning and operations are guided by four technical committees. The Breast Cancer Virus Segment Working Group of the Div. of Cancer Cause & Prevention works in close association with these four technical committees and uses BCTF funds for some of its contracts. The present chairmen and executive secretaries, as well as some members of the technical committees are employees of NCI; a small number of the committee members are employed in other institutes of NIH. However, most committee members are scientists drawn from the biomedical community

The technical committees review the activities of their contractors and recommend new ideas for RFPs; the NCI and NIH employee members serve as project officers or co-project officers on the committee's contracts. The steering committee approves ideas for new RFPs, coordinates the activities of the technical committees, and recommends budgetary allocations for their activities.

Overlap of Contract and Grant Activities. Questioning by subcommittee members elicited the opinion from BCTF staff that there is relatively little grant-supported research directly concerned with breast cancer.

The question of whether RFPs are reaching a sufficiently wide audience in terms of scientists capable of, and interested in, participating in the work of the BCTF, was answered by the comment that six RFPs recently stimulated 485 responses.

Review Procedures. Proposals submitted in response to RFPs are sent to all members of the technical committee, two of whom are designated as primary reviewers. After discussion of the written reviews provided by the primary reviewers, a written ballot is used to determine ranking of proposals. A proposal must be favored by 50% of the committee to be considered. Those proposals receiving the highest rankings are project site visited, then ranked again based on the site visit findings and an assessment of how well each proposal matches the priority areas established by the technical committees. There is no system for review of contracts at the NCAB level comparable to the review of study section actions on grant proposals. Lists of contracts awarded are available to the Board, but no documentation analogous to the "pink sheet" is submitted to the Board prior to award, and the Board is not required to concur with contract approvals as it does with grant approvals.

Subcommittee Evaluation: Based on verbal responses and written materials submitted in advance, the BCTF appears to be effectively organized and administered. The research, as described, was found to be useful, directed at worthwhile problems, and interesting. The work presented by four of the contractors is of high calibre.

The BCTF appears to be making good use of the available mechanisms for informing the biomedical community of RFPs. Apparently some attempts at coordination of activity between BCTF and DCRRC have been made, but results are not completely satisfactory to either staff.

The subcommittee believes that the system for developing RFPs and the primary review of contract proposals is adequate and the method for the selection of contractors is proper. However, the subcommittee members were concerned about the lack of a second review by the NCAB, before award.

FULL TEXT OF SAFFIOTTI'S STATEMENT ON REASONS FOR HIS RESIGNATION

Last week's issue of ***The Cancer Letter*** went to press before the complete text of Umberto Saffiotti's memo explaining his resignation as director of NCI's Carcinogenesis Program was available. The article last week reporting on the resignation was based on ***The Cancer Letter's*** conversation with Saffiotti.

James Peters, director of the Div. of Cancer Cause & Prevention, will take over as acting director of the Carcinogenesis Program until a new director is appointed.

Saffiotti's complete statement, with limited editing to conserve space, follows:

On April 14, I notified the NCI director of my decision to submit my resignation as associate director for Carcinogenesis, while retaining the position of chief of the Experimental Pathology Branch. By this action, I will separate my responsibilities completely from the direction of the program and return to a research and study activity through which I hope to continue my professional contribution to the field of carcinogenesis and cancer prevention.

I believe that this for me is the only course of action compatible with the scientific and policy criteria under which I have directed the Carcinogenesis Program for eight years and developed it to its present level of scientific ahcievement and as a widely recognized national resource. A well-motivated resignation as associate director is the only action that I can consider taking to reaffirm clearly my position in these matters to all concerned. For three years I have expressed in strong terms the state of crisis of the Carcinogenesis Program due to lack of support. I have warned time and time again that lack of personnel and policy support would inevitably lead to a breakdown of the program's accomplishments. In my judgment, this has now taken place.

I believe it is my duty to explain clearly the reasons for my decision to all those who have participated with me in the development of the Carcinogenesis Program. These reasons can be summarized as follows: (1) Lack of manpower to operate a rapidly expanding program of major national importance; (2) Inadequate support for carcinogen bioassay operations and for cancer prevention; (3) Inadequate partici-

pation offered to staff scientists in the development of NCI policies in this field; (4) Removal of integral components from the program with resulting fragmentation of program direction; and (5) Administrative actions and management policies.

The accomplishments of the past eight years of joint effort speak for themselves. I wish every success to those who will assume the burden of leadership that I am now relinquishing. The NCI director has kindly expressed his appreciation of my scientific activities and his desire that I continue to serve in the NCI not only as a laboratory chief but also as an individual scientific expert and advisor. I am greatly looking forward to a period of renewed scientific research activity and study in a field to which I have devoted my career for almost 25 years.

For the members of my staff, who have worked so valiantly and enthusiastically at all levels for the progress of carcinogenesis, I have such a profound gratitude that I can only express it with one word: Thanks. To all the colleagues in science who have devoted their intellectual energies, their enthusiasm and their efforts to a truly monumental accomplishment in scientific collaboration as investigators, advisors, and reviewers, and to their staffs, I wish to express my thanks for having made it all possible and for allowing me to share with them the excitement of advancing a major field of science and public health towards the prevention of cancer.

1. Lack of manpower to operate a rapidly expanding program of major national importance — Since three years ago, I have clearly indicated to the NCI director, and to the National Cancer Advisory Board that the Carcinogenesis Program was in a serious crisis for lack of manpower and of policy support. The director assured me that he would help to resolve the problems. We agreed that the intramural research staff and resources, already heavily committed to program development, scientific monitoring and management, should not be further cut back or dismantled, so that an effective nucleus of scientific expertise in carcinogenesis could be retained.

The intention to support program needs was repeatedly expressed by the director, even recently in his testimony to the House of Representatives; yet assignment of new resources to the Carcinogenesis Program in this fiscal year was once again insignificant. In fact, since 1973 the situation has considerably deteriorated: fiscal responsibilities continued to increase at a rapid rate, while the number of staff positions remained essentially the same for three years and is now projected to fall to a grand total of 123 full-time positions, the lowest level since 1971. Most of these positions are committed to the laboratories, so that program planning, direction, monitoring and management are all done with a skeleton crew which is totally insufficient. The carcinogenesis staff has worked with a tremendous energy in the past three years, against increasing odds, to maintain a high level of scientific integrity and of responsible program accomplishments. Under the present circumstances, I believe that this can no longer continue.

Several senior scientists in the staff, affected by the lack of personnel and resources and by an increasing burden of assignments, have left and could not be replaced with new staff of comparable experience and scientific stature. Several working groups of great importance for the accomplishment of the program had to be phased out.

Other outstanding scientists could have been attracted to join in program leadership positions, but lack of adequate support made these recruitments impossible. Some outstanding young investigators left the staff when it became impossible to provide them with the necessary support, in spite of the fact that they had worked most intensively and effectively for the development of the total program.

The scientific staff works both in direct research and in developing, leading, and monitoring a collaborative program which includes outstanding scientists and unique resources in this country and abroad.

It is my firm conviction that we cannot coordinate and maintain an effective national program in carcinogenesis and cancer prevention requiring a complex interdisciplinary science basis and affecting technology, economy, and public health policy at the national and international level, without adequately supporting a top level scientific staff highly qualified in the key disciplines involved in the field.

The continuing lack of personnel support, together with the mounting pressures of fiscal and scientific responsibilities have caused serious damage to the morale and possibly the health of members of the staff who worked so exhaustively to achieve major accomplishments towards the prevention of cancer.

Lack of competent staff in directing such a wide and complex program means one of two things: either a phasing out of activities or a compromise on quality standards. Several very important areas of program were already phased out and the program operates at a bare minimum. A compromise on scientific quality standards is unacceptable to me.

2. Inadequate support for carcinogen bioassay operations and for cancer prevention — Particularly affected by the lack of policy and personnel support are the carcinogen bioassay operations, where high quality standards of experimental design, pathology and data analysis were achieved by the Carcinogenesis Program after much hard effort.

It is well known that the likelihood of detecting the carcinogenic effects of a test chemical by animal bioassay is proportional to the extent and quality of the bioassays: setting high quality standards for these bioassays becomes therefore a crucial policy issue, as clearly shown in hearings recently held by Senator Kennedy on the issue of "sloppy tests". In fact, it is almost axiomatic that if bioassays are used to claim a negative finding for regulatory purposes, the sloppier the test the "safer" will the product appear—unless one investigates the adequacy of the procedures used.

The major contribution our program has made in the area of bioassays has been that of establishing high quality standards, which have now been widely accepted. A large bioassay operation was established in the early 1970's to provide a much needed national resource capable of conducting long-term animal tests on hundreds of substances under closely monitored conditions. This undertaking, widely reviewed and approved by the NCI and its advisory bodies, was not backed up in time with sufficient staff assignments. Only by the strenuous efforts of the available staff did we succeed in establishing the logistics, the experimental protocols, the data systems, the diagnostic pathology criteria and the statistical analysis methods which have now made it possible for the first time to fulfill the need for publication of fully documented reports of carcinogenesis bioassays. The first volumes of the new NCI Carcinogenesis Technical Report Series are evidence of this accomplishment.

Lack of staff support and a load of other assignments imposed on the staff to respond to requests from NCI and other agencies have led to the inevitable build-up of a backlog of pathology review and data analysis.

There are now over 200 bioassay results still awaiting to be reviewed and published, while no substantial support to staff is provided and key staff members are taken away from this task.

I cannot accept any longer a situation which in fact deprives the regulatory agencies, industry, labor, consumers and the scientific community of data of urgent public health value: it is people who are now exposed to toxic agents and who are not protected because the necessary support was not provided in time.

Evaluation of carcinogenesis bioassay results is not a mechanical operation: it needs professional skills, competence and experience which are notoriously scarce. Not to support the unique team we have assembled for this effort is, in my judgment, a tragic policy. At this time, most of pathology material and raw data on this backlog of tests has been assembled with high quality standards. Several detailed reports have been already published; all it takes now to speed up the publication of the full documentation (by a pattern that has been already well established) is specialized manpower and a fully supportive policy. Reassignments and disruption in the current staff appear to me to lead to further delays in the publication of well-documented evidence of cancer hazards. I cannot endorse such policy.

Because of the lack of a single focus of responsibility in the coordination of carcinogenesis work in NCI, a great deal of critical staff time was, in my view, wasted in an excessive number of meetings of committees and interagency groups, which have contributed little to constructive work and documentation in the areas of real high need and priority.

3. Inadequate participation offered to staff scientists in the development of NCI policies in this field — I came to the NCI in 1968 as the Associate Scientific Director for Carcinogenesis; in 1973 the title was changed to Associate Director for Carcinogenesis, DCCP, and in 1975 to Associate Director, Carcinogenesis Program, DCCP. These apparently trivial changes in a title, occurring while the leadership responsibilities were increasing at a very fast rate, are perhaps symbolic of the decreasing participation offered to senior staff scientists in the development of NCI policies, at least in our field.

At the present time, carcinogenesis has acquired an essential role in the whole cancer field with major involvement and impact on national and international public health policies. There are very few scientists experienced in chemical and physical carcinogenesis with working expertise also in the field of occupational and environmental health. Their knowledge is an essential basis for the formulation of wise and effective national policies for the prevention of cancer. Experts in carcinogenesis are in fact among the top government advisors in several major countries. It is indeed most encouraging to me to see that other agencies of the government have recently appointed good scientists with experience in these fields to key policy positions. In the NCI, judging from

my own experience and that of my colleagues with an international reputation in science, there have been at best only a few opportunities to discuss and participate in major policy decisions at the institute level. In many cases major policy decisions directly affecting our field and our work have been taken without adequate participation or even discussion with the expert staff. The establishment of a Clearinghouse on Environmental Carcinogenesis, recently announced by the NCI director, is a case in point.

In 1972 Dr. Rauscher asked the senior staff for their individual views and recommendations for the organization of the institute. I pointed out the growing importance of the Carcinogenesis Program, its close interactions with other agencies and departments and its role in providing a scientific basis for major national and international policy decisions in regulatory and public health matters. I expressed my strong belief that such a program should be placed organizationally immediately under the institute director, without the intermediate layer of a broader division with many other commitments, that the scientific leadership in carcinogenesis should be an integral part of the NCI policy-making staff, and that it should have direct and close access to the institute director, providing him with a single focus of science and policy advice and documentation.

This proposal was made long before the present division director was appointed and bears no reference to personality connotations. I have always hesitated to state this view more widely, as it may have appeared motivated by a desire for personal advancement. Now that I am stepping out of the line of command, I feel free to express again this strong personal view. NCI, I believe, needs a unified and coordinated effort in carcinogenesis, under a strong scientific leadership capable of providing scientific quality monitoring and creative scientific direction towards the identification of human cancer hazards and their prevention. Such unified effort should be fully supported by all means of research support (intramural, grants, and contracts). It should be provided with adequate staff and facilities and should receive long-term commitments of support and of supportive policy for its work which is necessarily of a long-term nature.

4. Removal of integral components from the program with resulting fragmentation of program direction — Carcinogenesis, by its very nature a multifaceted interdisciplinary field, must be developed through a coordinated interaction of its component parts. The fact that many cancer causative agents have been discovered to be environmental contaminants simply requires that research on the sources, distribution, exposure and activity of these environmental agents be included in the development of the field. The mode of exposure of people to these agents will need to be studied in relation to occupational and environmental conditions, and the opportunities for control and prevention will closely relate to societal actions. This does not mean to me that we can artificially separate environmental carcinogenesis studies and documentation from the whole field of carcinogenesis research. A separation can in fact deprive each side of an important perspective in the other. An office of the scientific coordinator for environmental carcinogenesis was established in my immediate office in 1972, to provide increased support for the documentation and investigation of these aspects of the field and to assist in the liaison with other federal agencies interested in environmental cancer problems.

This office, with a staff of only three people, was removed from the Carcinogenesis Program and placed in the Office of the DCCP Director in 1974 without a thorough discussion with me of the implication of this action and against my recommendation. I still believe that this action has significantly weakened the Carcinogenesis Program in an important area. Cooperation with other agencies on scientific matter and evaluations became more difficult for me and the function of explaining new scientific methods, criteria, and findings to those other agencies that needed them as a basis for their regulatory actions became, in my view, excessively "bureaucratic", by being withdrawn from its scientific matrix. No replacement was allowed by the division director to compensate for the loss of these positions in the study and the documentation of key substances related to high research priorities in the program.

Recently, the DCCP director has decided to remove further personnel and functions from the Carcinogenesis Program. A veterinarian in charge of the animal resources was reassigned to the division director to work with the scientific coordinator for environmental cancer. In my view, his background and qualifications, excellent as they were for the previous job, seem hardly adequate for this new assignment. Adequate replacement will undoubtedly take months, during which close competent monitoring of this large animal population, a delicate and vulnerable resource on which millions of dollars worth of research are dependent, is perilously vacant. This transfer seriously undermines the already insufficient professional staff in the Carcinogen Bioassay and Program Resources Branch (a total of five doctoral level permanent positions!) and it represents a policy decision that I cannot accept.

On April 9 the NCI director informed me that on the recommendation of the DCCP director, he had decided to transfer immediately from the Carcinogenesis Program into the office of the DCCP director a "Program on In Vitro Carcinogenesis-Mutagenesis" to be put under the direction of a manager, stating this this "relocation would provide better visibility and a better focal point for coordination". This decision followed several recent discussions with Drs. Rauscher and Peters in which I expressed my strong views against it, which can be summarized as follows. The extent of the activities to be transferred was not defined but from the discussion it appeared to cover only a portion of the total effort of the Carcinogenesis Program in this area; this separation would therefore indeed create a serious operating split between various lines of research and development in this most important area, instead of providing the desired "better focal point for coordination"; the development of in vitro methods for carcinogenesis is still at a stage where a great deal of research work is needed to define, validate, and standardize short-term methods before they can be applied to the systematic short-term screening of environmental chemicals of unknown activity—with any hope to figure out what the results may mean in terms of predicting carcinogenic effects in vivo.

The Carcinogenesis Program has made extensive and outstanding contributions to this whole area of in vitro methods for carcinogenesis research and towards the development and validation of new screening methods.

Methods for chemical interactions, mutagenesis and neoplastic transformation of cells in culture were developed and interrelated with the necessary research on key mechanisms and functional requirements. Investigators in the intramural laboratories and in the collaborative projects are leading the advances in this field. These in vitro studies now represent an integral part of the total field of carcinogenesis research: I believe that an arbitrary segregation of a group of projects into a separate program under a manager without a scientific staff is likely to be detrimental to the rapid development of this still delicate research area on a solid scientific basis. Once again, the accomplishments of the Carcinogenesis Program in this area speak for themselves. I find the new policy unacceptable.

The manager of the Bioassay Operations Segment was assigned to be full-time executive secretary of the new "Clearinghouse on Environmental Carcinogenesis," thereby depriving the segment of an experienced manager at a time when personnel resources are already below the minimum necessary level. This decision was announced without even prior discussion with me or my responsible senior staff. Other members of the Carcinogenesis Program staff received offers to transfer to the division director's office without my previous knowledge of such proposals.

In summary, a pattern of erosion of staff resources from the Carcinogenesis Program with a corresponding build-up in the office of the division director was becoming apparent. I found this situation unacceptable.

After I announced my decision to resign as associate director, Drs. Rauscher and Peters indicated to me their intention to replace my position with two associate directors for two separate program areas—one for carcinogenesis research and one for carcinogenesis testing, the latter to include animal bioassays, short-term screening methods and related resources.

They offered me to stay on as associate director for the Carcinogenesis Research Program, expressing their support and trust in my scientific activity. I thanked them for this, but I indicated that since I firmly believe in the need for unified scientific leadership in the entire field of carcinogenesis, I decided to dissociate my responsibilities completely from the direction of the program under the present circumstances.

5. Administrative actions and management policies — My operating management criteria have always been that scientific programs should be directed by qualified scientists supported by managers rather than by managers controlling scientists. Using the former approach, we were able to develop a well-articulated collaborative program which expanded almost eightfold in eight years and yet maintained a high degree of scientific integrity. Administrative decisions involving space, personnel actions and resources have made the operation of an efficient program in carcinogenesis extremely difficult and to me often discouraging.

After the only short period of personnel increase which allowed us to develop a small management staff in 1971-1972, the space available to the program became extremely crowded. A decision was made by the division director to transfer out of the laboratory facility all office space that could be relocated in an office building off campus. We in the Carcinogenesis Program accepted this policy and transferred our offices to the Landow building. Even so, several laboratory areas remained short of the space they would have needed to expand efficiently

in view of needed new methodologies, particularly for cell culture and analysis of carcinogen metabolites, and also to comply with new requirements for safety standards in the handling of carcinogens and for laboratory animal care. The move of the offices to the Landow building has made close interaction with the laboratory staff much more difficult. Renovations in Building 37, after the offices were moved out, took two years to be made, thus delaying the development of much urgent research. While carcinogenesis offices were moved out, the other major program area in our division, Viral Oncology, has remained to this date in the laboratory building with a large number of offices.

A major transfer of space and positions from the Carcinogenesis Program to another NCI division is planned for July 1976, as a group of immunology laboratories in the Biology Branch will become part of the Tumor Immunology Program in the Div. of Cancer Biology & Diagnosis. While these reassignments may contribute to the development of more unified efforts in other NCI program areas, the resources needed to develop a more intensive effort in carcinogenesis were not available.

Animal-housing resources in Building 37 are totally inadequate for the needs of intramural research in carcinogenesis. A supporting contract provides some resources outside NIH but the necessary in-house facilities are still lacking, even in their need was recognized seven years ago.

Other administrative delays and increasing complications are still cause of serious concern: As an example, the distinguished senior pathologist who provides invaluable leadership to the development and monitoring of pathology standards for bioassays was recruited as an expert three years ago and offered a regular position in the Civil Service. His appointment has still not been provided, and we risk losing one of the key scientists in this essential area.

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

The deadline for submission of proposals in response to the following requests for proposals, previously announced as May 14, (***The Cancer Letter,*** April 30), has been extended to May 28.

RFP-NCI-CP-VO-61041-03 – Influence of interaction between environmental factors.

RFP-NCI-CP-VO-61042-63 – In vitro transformation of mammalian cells resulting from the intracellular interaction of a nononcogenic virus and chemicals.

RFP-NCI-CP-VO-61043-63 – In vitro malignant transformation of human and subhuman primate cells by interaction between viruses and chemicals.

RFP-NCI-CP-VO-61044-63 – Effect of environmental factors on in vivo endogenous sarcogene expression in primates and rodents.

RFP-NCI-CP-VO-61045-63 – Development of mammalian cell lines, known to contain endogenous oncogenic virus sequences, which can be utilized in testing mutagenic and carcinogenic effects of environmental factors.

Contract specialist for the above RFPs is Jacque Labovitz, Cause & Prevention, 301-496-6496.

CONTRACT AWARDS

Title: Antibody-dependent cell-mediated cytotoxicity
Contractor: Sloan-Kettering Institute, $119,182.

Title: Planning for special oncologic diagnostic radiology conference
Contractor: American College of Radiology, $66,180.

Title: Assembly and distribution of committee books
Contractor: Small Business Administration, $177,676.

Title: Organization and dynamics of cell surface membrane components
Contractor: Columbia Univ., $55,182.

Title: Demographic studies of Japan-Hawaii cancer cases
Contractor: Kuakini Medical Center, Honolulu, $129,433.

Title: Program services in support of contract management system
Contractor: Sigma Data Computing Corp., $24,977.

Title: Selective stimulation or suppression of humoral or cellular immunologic responses
Contractor: New England Medical Center Hospital, $70,500.

Title: Incorporation of two additional alternation/renovation projects as necessary for the performance of the cancer research program being conducted at the Frederick Cancer Research Center
Contractor: Litton Bionetics, $377,331.

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available.

Title: Study of human milk and mammary tumors
Contractor: Institute for Medical Research, Camden, N.J.

The Cancer Letter—*Editor* JERRY D. BOYD

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