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SEATTLE PANEL MEETING GENERATES MORE SUPPORT FOR INCREASED OUTREACH FUNDING, CONSORTIUM APPROACH

The meeting of the President's Cancer Panel at the Fred Hutchinson Cancer Research Center in Seattle generated further support for a major increase in cancer control outreach funds, along with remarks by NCI Director Vincent DeVita indicating that if more money for that purpose is made available, it probably will be through regional consortium grants. Support for the consortium concept was not as evident as it was at the Panel's San Francisco meeting, where the

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In Brief

MASNYK NAMED DCBD DEPUTY DIRECTOR; MAIZEL TO HEAD NCI'S "SUPERCOMPUTER" DEVELOPMENT

IHOR MASNYK, who has been associate director and head of the Intramural Research Program in NCI's Div. of Cancer Biology & Diagnosis, has been appointed deputy director of the division. Masnyk's nomination by DCBD Director Alan Rabson has been approved by HHS Secretary Margaret Heckler. Masnyk also has been serving as acting director of the Office of International Affairs and will continue in that role for the time being. The DCBD deputy director's position has been vacant since Irving Plough retired several years ago. . . . **JACOB MAIZEL,** head of the section of molecular structure in the Laboratory of Molecular Genetics of the National Institute of Child Health & Human Development, has been appointed chief of the Laboratory of Mathematical Biology in DCBD. Maizel will head NCI's "supercomputer" program which will offer time on a computer dedicated to biomedical research to NIH and extramural investigators. Maizel has made major discoveries in molecular biology involving application of computer technology to biological sciences. . . . **DIV. OF CANCER** Treatment has nearly completed recruiting for a new director of the Biological Response Modifiers Program and may announce the appointment later this month. Recruiting for a new director of the Radiation Research Program is still dragging. A third competition will be under way soon. DCT Director Bruce Chabner said he has met with representatives of the radiation therapy and diagnostic radiation communities to ask their help. "They are aware of the importance of this position and of the problems we have," Chabner told his Board of Scientific Counselors. "They agreed to help." The first two rounds did not bring in anyone who "really had the background needed to handle" the demands of the job, Chabner said. . . . **DEL WEBB** Foundation gift of $500,000 to the Univ. of Southern California Comprehensive Cancer Center will be used to establish an oncogene laboratory. To be located in USC's Norris Cancer Hospital & Research Institute, the lab will serve as a core resource for as many as 15 scientists. lab will serve as a

CONSORTIUM GRANT MORE EFFECTIVE FOR OUTREACH EFFORTS, DEVITA SAYS

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Northern California Oncology Group consortium deeply impressed DeVita, but the Seattle participants did express interest in the suggestion.

DeVita brought up the outreach consortium issue in Seattle by commenting, "We found in San Francisco, a little bit to our surprise, that the consortium grant... is probably the more effective instrument for the kind of outreach programs that we are talking about for harnessing all of the resources of the community... We were persuaded by Dr. (Saul) Rosenberg's elegant presentation that the core grant for the consortium is reviewed in a way that is really not effective. . . A review is in place for a revision of the consortium grant guidelines, which will eventually reach the National Cancer Advisory Board. The revised guidelines will try to judge them on their ability to do control research and serve as an outreach instrument."

One of the topics of discussion at the Seattle meeting was if Oregon, which is included in the Hutchinson center's "catchment area," should have a center of its own. In a question addressed to Maureen Henderson, director of the Cancer Prevention Research Unit at the Univ. of Washington who recently completed a term on the NCAB, DeVita said, "It sounds to me like what you describe, in reference to Oregon particularly, is the ideal situation for a consortium grant on top of the existing core grant here. It would be a consortium grant that would include not only all of the elements in Washington, but also pull in Oregon in such a way that you don't lose the power of the population required. Does that make sense to you?"

"I don't know enough about the details of the administration of the grants at this point to talk about that aspect," Henderson said. ". . . We need to have the kind of relationships that give full recognition and, if you like, partnership as investigators to all groups that are working with us... We have established a comfortable relationship with the public schools in the state of Washington to carry out smoking prevention research and hope that that will be a collaborative relationship. So I am dodging the issue, but I am trying to say that I think any mechanism that will allow us to develop healthy and mutually supportive, long term, working relationships is very much needed for the cancer control research."

Henderson acknowledged that mutual confidence and respect among various institutions "is what we have not had in the past. The story of the relationships between either universities or research centers and public agencies has not been a good one, in part because there was not that mutual respect and confidence. If the consortium grant would do that, then I think it would be very beneficial."

Alexander Fefer, professor of medicine in the Div. of Oncology at the Univ. of Washington and a member of the Hutchinson center, commented, "I think one of the problems in the consortium grant is whether there will be enough resources to really establish the kinds of relationships that you would like and that Maureen has indicated. My recollection of the Northern California situation is that it was not a very attractive one until recently. There are a lot of factors besides NCI coming up with a smidgen of funds. If the monies are spread too thinly, and if it comes out of the core grants for the existing centers which would undermine an important effort, there will be more and more difficulty and and not necessarily a big gain."

Fefer noted that the Univ. of Washington and Univ. of Oregon and various state agencies collaborate in a NIOSH grant to the former as an educational resource center. "There are some good examples of this sort. I can only tell you that distances in the west are great and the costs of doing this in terms of travel time and calendar time are important, given the best intentions.

"Finally," Fefer continued, "I should mention from the political point of view that we are not unaware and have not failed to respond to the changing political alignment. We previously had two of the three most senior Democratic senators (Warren Magnuson, who was defeated for reelection in 1980, and the late Henry Jackson). Now we have two of the most junior Republican senators, able though they be. Oregon and Alaska are two of the most potent in the Senate. We and others in those states have worked together looking at a variety of mechanisms which really do serve the region. . . I think there is a lot going on in this region and there may be ways it could be facilitated. I think you would have to look at it quite carefully."

"I think we will be talking about the consortium grant, the guidelines modification and the issue of whether or not we can use more consortium grants at the next two National Cancer Advisory Board meetings," DeVita said.

DeVita opened his remarks at the meeting by saying that "basic research has been and always will be our first priority, and the applications (of the results of basic research) come later." Despite his repeated emphasis of that point, he said, "I have recently been criticized as a result of these Panel meetings that I am not focusing enough on the important role of the cancer centers in support of basic research.

"Quite frankly, I think this is a for motherhood and against sin argument that people mount just in

case you say something that might be controversial in reference to their cancer centers. I think that actions really speak louder than words. Since the passage of the National Cancer Act (in 1971), the Institute has spent $7 billion for the support of basic research, which I think tells you where our heart is. And of the $500 million we have spent on cancer center core grants since 1971, all of that money has almost exclusively gone to the support of basic research programs at those cancer centers.

"I think the focus on the outreach program is long overdue," DeVita continued. "In fact, if we don't pay more attention to it, the public that paid for these programs will get cranky, and when the public gets cranky Congress tends to get cranky. And when Congress gets cranky we get fewer resources. When we get fewer resources, we have less to put into basic research.

"I have also mentioned at prior meetings that the Cancer Institute cut back its funding for outreach programs in centers in 1982 when we had to take some budget cuts. But I would remind you that we did not cut back the outreach programs thinking they were our highest priority. They really were not functioning very well at most centers, with few exceptions. As a matter of fact, as we go around the country we see few residual benefits from the previous outreach programs."

The Panel has conducted its review of cancer centers with meetings in Birmingham and Los Angeles, in addition to the San Francisco meeting, and will go next to Hawaii, DeVita said. "We have found a few things that are kind of interesting. We found, everywhere, elegant research and very little outreach. We found many gaps in what can be done and what should be done and what is being done, particularly in underserved populations. This was particularly evident in Southern California where we found that much of the minority population there has a lower survival, increased mortality, and higher incidence of cancer with not too much of an attempt to address those issues specifically. We had a lot of confusion about who particularly is responsible for addressing those issues. I think this is all very good because one can't solve problems that you don't address." (See the letter from Richard Steckel, director of the UCLA Jonsson Comprehensive Cancer Center which follows).

This is how NCI sees the Pacific Northwest, "from the vantage or disadvantage depending on your point of view, of Bethesda and Washington," DeVita said. "We see you as an outstanding center with excellent basic research. Certainly the strongest transplant unit in the country. We see you with a lesser clinical trials presence than, perhaps, you would like or we would like. We see you as a very healthy area... You have an incidence and mortality in this region that is less than the average of the U.S., which is the first area that we have come to that has an incidence and mortality lower than the U.S. average.

"You have fewer doctors and fewer hospital beds per 100,000. I don't know what that means, but it is an interesting observation. You have a much more homogeneous population which probably accounts for some of these good statistics, much less than the national average for Black and Hispanic populations and only slightly higher, surprisingly, in Asians. You have 24 times the population of American Indians, Aleuts and Eskimos than any other area of the country."

Questions being posed to the Northwest cancer community, DeVita said, include:

—"Is this center serving the Oregon area as well as it should or should there be an additional center in Oregon?

—"Are the clinical trials programs as effective as they can be and, if not, is there something that can be done vis a vis the relationship between practicing physicians and center physicians?

—"Should you have a consortium grant instead of a regular grant if you are going to address the issue of tying together other geographic areas? Or, as was suggested after we left California, should we begin to establish the practice of having a consortium grant in addition to the regular grant?"

DeVita continued, "If you look at Southern California, they have $7 million in core grants scattered around some seven centers. The connecting capacity is limited because the core grants do not have that written in as part of their responsibility. In Northern California they have $700,000 in a core grant but its connecting ability is very good. It is connecting institutions that do not have core grants to support basic research but do have very good basic research. Should we overlay existing core grants with the consortium apparatus so they can support both the research at the individual institution that has worked so well in the past decade, and the outreach program? If so, will all of you and all of the people we visited help us get the kind of support we need for the bypass budget so that we can, in fact, provide the resources for these overlays?"

Excerpts from remarks by invited participants at the meeting:

William Hutchinson, founding director of the center and president of its Board of Trustees—"Regional comprehensive cancer centers were not designed, nor ever intended to be, treatment centers for all the cancer in a geographic area. However, it was most definitely intended that they be a resource for hospitals, physicians and patients of the center's area... We must address ourselves in the

future to the research and contribute to the better understanding and care of the common solid tumors utilizing the input of the surgeon who is treating most of these cancer problems...(the center is) dependent on current public opinion for support. This support comes for the most part from friendly legislators whose constituents, the taxpayers, think they are getting their money's worth when a family member or their physician seeks advice for the treatment of his cancer at the regional comprehensive cancer center. This center has had such a service where patients and their physicians can seek a second opinion about their cancers. This gives the patient great confidence that his care at home is or will be in line with the best available to anyone.

". . . The serious issue of a new accepted surgical subspecialty, with all of its ramifications, must be considered at high levels and a decision reached soon. What has happened in oversupplying the country with medical oncologists would be a disaster if it were allowed to occur in surgery for a barrier of resentment toward the universities and the comprehensive cancer centers throughout the country would result. Chaos in general surgery would follow, which is really not necessary if quality and numbers are given prime attention. The surgical oncologist can and must be a welcomed regional resource to any area, not a competitor."

Robert Day, director of the Hutchinson center—"Our budget is 40-50 per cent over what it was last year. We have had a very, very major growth recently. The question is, will the core grant guidelines accommodate this expansion? Will those guidelines be responsive to an ever increasing competitively secured grant and contract income for this center? I would hope very much that the Panel will address itself to this question which I will restate as, do those centers that are successful in attracting peer reviewed support, in concert with the evolution of the National Cancer Plan, have assurances that their new initiatives will be responded to through enhanced core grant underwriting?

"For example, were we to build a new building, which I believe we will need in the next few years, will the NCI grant mechanism support this development and the programs for which this space is needed? Will construction funds be available to help in the development of expanded facilities? Will there be an enhancement in the continuing support through the core grant for the basic underpinning of our research efforts: These are vital questions to which we need answers as we develop our long range plans.

". . . We still have in this region excess incidence and mortality as a result of inadequate intervention programs in the communities the cancer center serves. This highlights a very important aspect of the National Cancer Program which needs to be addressed. This aspect is the elimination of funds to effect cancer control within communities. As one of the centers extensively engaged in cancer control research, we are nonetheless very much aware of our lack of support in the area of applications of cancer control science knowledge.

"...NCI has made a major investment in the building of centers such as this. The results of this investment should be maximized. To do so requires that as our centers age, we will need help in remodeling, reequipping and reorienting some of our facilities and programs to maintain currency with thrust in cancer research.

"We anticipate in this state a very major increase in the numbers of cases of cancer over the coming several decades. In fact, these increases are staggering. . . While new methods of earlier diagnosis and treatment are vitally important, the goals of preventing cancer from occurring at all, of eradicating the disease, must be pursued with all due vigor."

David Thomas, head of the Epidemiology Program at Hutchinson—"Our population is largely white and most neoplasms in our area accordingly occur in whites. There are few if any that occur in our white population in excess and the pattern of cancer occurrence in whites in this area closely approximates that for the country. We thus have few special cancer problems peculiar to our region and little opportunity to study locally the reasons for variations in incidence or mortality rates among various racial and ethnic groups. I want to emphasize that I am not in any way implying that nonwhite groups should not receive special attention for etiologic and cancer control research and cancer control activities... However, such studies and activities in such groups can, for the most part, be conducted better elsewhere. On the other hand, we have excellent opportunities to study and attempt to control cancer in the large homogeneous, largely white population in which cancer develops at rates similar to those for the general white population of the U.S....Primary prevention should be our ultimate goal. With adequate support for etiologic research I am confident that those of us engaged in epidemiologic investigations, along with our colleagues in the more basic sciences, will eventually provide the means to achieve this end."

DeVita—NCI is being criticized for "recommending certain modifications of diet which at least do not seem to do any harm and, from epidemiologic studies all over the world, seem to be very likely beneficial, that is, increase fiber and reduce fat." The critics contend that not enough is known about those factors to make recommendations.

"We need your support and I think we are getting it. I heard Dr. Day, on numerous occasions, get and support the fact that we need to be less timid in this area. I am getting a lot of angry mail. Nutritionists have been writing Secretary (Margaret) Heckler and a few other people suggesting that we should not be making such outrageous statements about fiber and fat.

"My first question to them is, when would you make them? They don't tell you. My next question is, what are you doing? In most cases, they are taking more fiber and eating less fat, but they don't feel that they should tell the American public the same thing."

DeVita asked Day, "Do you view that a consortium grant might be more effective here in establishing something that would last regardless of the fluctuations in federal funds and, if so, would that be so traumatic for this center, or should we do it in addition to this core grant?"

Day—"You have asked two questions. Let me answer the first one first, which I would rephrase. That has to do with applications of cancer control in the community setting and how best to go about it, or what the effect would be. If you look at other activities that attempt to contrtol diseases in the population, such as infectious disease control which has been very successful. . . there is a focus of responsibility, there is an authority to do this to see that it gets done.

"Your second question is how to go about doing that. . . I think there are actors here in the Northwest who would be delighted to enter into such a consortium. We would certainly do whatever we could to help such an activity. But I think it needs to be very carefully considered as to what the output of a consortium is to be. If it is to be cancer control research in the community, that is one thing. If it is to be the application of cancer control consistently throughout the population, then that is something else. I think my former suggestions would apply more there. Perhaps the mobilizing of support would apply more in the latter case."

DeVita—"Dr. Hutchinson, do you have any comment about whether or not we would be better having a center that devoted its attention to the state of Oregon or is this region served by one comprehensive cancer center sufficiently?"

Hutchinson—"I think that we could serve Oregon as it wished to be served. In other words, they have a medical school down there and I think that rather than go in and tell Oregon how to do it, I think we should get their input and coordinate with them as to the best methods to accomplish this. But I think that we could run it very well out of the center here."

DeVita—"It seems to me that with a regular core grant being devoted to centerness at a single institution. . . you cannot expect to do that for the Univ. of Oregon because it is not a center grant for that particular area. Yet, the catchment area implies a certain capacity to do something that impacts on the population around you. It would seem to me that one center in one state is about the best or widest distribution you can possibly get."

Gilbert Omenn, dean of the School of Public Health & Community Medicine at the Univ. of Washington and former deputy science advisor in the White House Office of Science & Technology Policy—"I want to make three points. First, I strongly support the initiative which you have launched and the goals for the Year 2000. I think this is an activist and appropriate posture for the Cancer Institute. It draws public attention in a productive and desirable way and it complements the general approach under the Surgeon General and Public Health Service for healthy people, the emphasis on health promotion and disease prevention.

"Secondly, I have struggled as you have with this question about centers. I think the term itself has come to carry more weight than is warranted. There is a lot of prestige, a tremendous amount of politics about the designation of centers. We have struggled with this term 'program,' another term 'institute,' another term 'center,' and what we are really saying is that there are diseases or problems which cut across and require the bringing together of multiple disciplines. . . I think that different ways of funding and possibly even naming the initiatives you want to mount with minority schools, with outreach and with the comprehensive and clinical and basid science centers would be a productive semantic effort.

"Third, I want to focus on public health sciences. . . The science base for public heralth is being advanced substantially and especially at our place here. The mechanisms that we use, outreach to the community in trying to find meaningful denominators and population based, community based parameters, these are crucial to what you want to accomplish in the Year 2000 goals and many goals along the way, and possibly doing even better than that Year 2000 goal."

Fefer—(After describing the organization and affiliations of clinical oncologists at the center, Univ. of Washington and university affiliated hospitals commented, "Although the centerpiece of clinical research at this center, if you will excuse the pun, remains bone marrow transplantation, Hutchinson investigators wherever they are located are increasingly involved in clinical trials of chemotherapy, multimodality therapy and biological response modifier trials for hematologic and non-hematologic malignancies." The university is a

member of the Puget Sound Oncology Consortium and the Southwest Oncology Group.

"Thus the scope of clinical research of Hutchinson investigators is significantly enhanced by the strong affiliation of the center with the university whose program in clinical care, teaching and research in oncology benefits greatly from the same affiliation," Fefer said. "The relationship between Hutchinson and the university has been very close and very productive and we look forward to its continuation."

Henderson—"The most dramatic fall in cancer death rates is going to come from the prevention of new cases in the future. And I believe that when this happens it is going to be due to an across the board small effect in the majority of people in addition to the effects, the larger effects, we are now hoping to get in targeted groups at particularly high risk.

"...The primary prevention research has to be carried out in the general public in healthy people and in either representative or random samples of the population at large. That is going to take a working relationship, a close working relationship, with the public, representatives of the public, be they public agencies or private agencies. We need to be working in the long term with those agencies and with the public and to maintain their respect and confidence even though the individuals who are in our assessment trials will not probably get recognizable personal rewards from their participation in the studies.

"I would like to make one comment in relation to Dr. DeVita's question about Oregon. That is, as far as primary prevention research goes, the size of the population is very important. We are counting incidence cases and they are relatively rare. Our population that is under surveillance by the cancer registry is probably at the lower limit of what is necessary to carry out the primary prevention research. I therefore, from the point of view of primary prevention, would vote very strongly for a regional rather than an individual state approach."

Paul Nieman, associate director of basic research at Hutchinson—"Investigator initiated peer reviewed RO1 grants are overwhelmingly the principal support for our research efforts. We are grateful and strongly support NCI's continued commitment to this bedrock of foundation for progress in biology and medicine. My perception from the field is that such support has become progressively more competitive. That is despite all of the funds that have been spent. I believe there is some degree of career discouragement among young scientists particularly and I think that is rather paradoxical in view of the progress and promise that exists in our field. My colleagues and I would encourage the continued efforts to stabilize and even expand the basic research grant mechanism. The core grant and construction support from NCI have also played an obvious and essential role in the development of the basic science program... Without this support there simply would not be a basic sciences division here."

Albert Einstein, medical oncologist at the Virginia Mason Clinic in Seattle—"We have a very strong active talented group of people in private practice. I think it is a major resource that the Fred Hutchinson Cancer Center should be able to take advantage of in terms of extending its activities out into the area. Unfortunately, in the past, I think that this relationship has not been all that smooth. The professional relationship between physicians and community at the center have been, in general, excellent. I think there is excellent interpersonal relationships and I think each has been supportive of other activities and respectful of other activities. However, I think at the administrative level in the past, there have been problems. What I would like to see is the center do those things that are unique in basic research, epidemiological research in providing unique clinical research programs, such as bone marrow transplantation to the community. What I would not like to see is the center entering into those areas that are directly competitive with the talents and expertise that is available in the community. I look upon the area of surgical oncology as a potential problem in that area... I think the Community Clinical Oncology Program will provide a new approach for NCI in conducting some particular kinds of trials, perhaps in trying to have some innovative changes occur rapidly within communities." (Einstein is principal investigator for the Virginia Mason CCOP).

Saul Rivkin, medical oncologist and chairman of the Puget Sound Oncology Consortium—The PSOC is a regional group engaged in clinical trials with protocols selected from SWOG, RTOG, Gynecologic Oncology Group, and the prostate and bladder cancer study groups. The Tacoma CCOP is a member. "There is a spirit as well as active cooperation within the oncology community in the Northwest that allows for all of the strengths of our region to be available and to be used throughout the entire region and to work together on improving cancer treatment. The oncology community, however, is not currently supported well by the current funding mechanism. I strongly urge consideration of funding for innovative and productive programs such as we have developed here in Seattle."

The next meeting of the President's Cancer Panel will be held Nov. 9 at the Univ. of Hawaii at Manoa, 1236 Lauhala St., Rm. 401, from 9 a.m.-4 p.m.

STECKEL OBJECTS TO KORN'S COMMENTS ON NORTH VS. SOUTH IN CALIFORNIA

Richard Steckel, director of the UCLA Jonsson Comprehensive Cancer Center, took exception to remarks by National Cancer Advisory Board Chairman David Korn at the last NCAB meeting, as well as to comments by NCI Director Vincent DeVita and other staff members which unfavorably compared Southern California cancer centers to the Northern California Oncology Program. Portions of the letter follow:

"Through my own colleague Helene Brown and through The Cancer Letter, I noted some of your comments at the Board concerning the President's Cancer Panel meetings in Los Angeles and San Francisco. I was concerned that you were quoted as feeling that the discussion in Los Angeles indicated 'a lack of effective interaction among centers in an area of great diversification. It was emphasized that these centers were not quite getting through to underserved groups.' According to The Cancer Letter, you contrasted the Los Angeles meeting sharply with the subsequent Panel meeting in San Francisco, where the Panel allegedly found the Northern California Cancer Program (a consortium) 'a very unusual program. There is a tremendous amount of outreach, community action and interaction. It serves a host of diverse groups.'

"Since I have had similar impressions presented to me by NCI staff since the San Francisco meeting, I felt it was important for me to outline my thoughts to you directly. It seems to me that the Southern California centers have been getting a very unfavorable press, and that this is quite unfair. To contrast the situation in Northern California with that in Southern California as you did seems to endorse the idea that the centers are not cooperating in the southern part of the state and have been ineffectual in meeting needs of 'underserved' (not defined) groups, as contrasted with the situation in the northern half of the state. I am confident that you are familiar first hand with NCCP, which is indeed excellent. I am not as confident that you have a first hand knowledge of the situation in the southern half of the state, and I would very much like to invite you to visit with us or to obtain a better impression of the situation in some other way. The two comprehensive cancer centers in Los Angeles (UCLA and USC) have a long and rich history of close cooperation, particularly in cancer control and outreach programs. We have excellent interactions in many scientific programs also with the specialized cancer centers in this part of the state. I submit to you the situation is not greatly different in the north, except for the important existence of the Northern California Oncology Group."

REMAINING CONCEPTS APPROVED BY DCT BOARD OF SCIENTIFIC COUNSELORS

Contract recompetition concepts approved by the Board of Scientific Counselors of NCI's Div. of Cancer Treatment follow below. Other concepts approved by the Board appeared in last week's issue of **The Cancer Letter.**

Title: Master agreements for preclinical pharmacology studies of antitumor agents. Recompetition of agreements with the following institutions: Arthur D. Little, Southern Research Institute, Ohio State Univ., Research Triangle Institute, Univ. of Southern California, Mayo Foundation, Univ. of Texas System Cancer Center, Bowman Gray School of Medicine, Midwest Research Institute, SRI International, Univ. of Vermont and Univ. of Tennessee. Those selected for master agreements will be eligible to compete for task order awards. Total estimated annual cost, $700,000, three years.

Preclinical pharmacology studies of antitumor agents under development by DTP are conducted under the aegis of the DCT Blood Level Working Group which was established by the DCT director and charged with the responsibility for investigating the use of pharmacologic measurements to improve the efficiency of the Phase 1 trials of new agents. Task orders are awarded competitively to master agreement holders to perform defined pharmacologic projects. In general these studies are conducted in parallel with preclinical toxicology evaluations of the experimental agents. It is the expectation that from these studies will come assays of the agent in a biological milieu of sufficient sensitivity to be used in the clinic. Further studies investigate the pharmacokinetics of the drug after bolus or infusion dosing in mice and/or dogs. A major objective of this project is the development of data which among other things will ultimately lead to a significant reduction in the number of ineffective dose levels which sometimes result in the dose escalation schemes employed in phase 1 clinical trials. The pharmacological information which is obtained through the master agreements will probably play a potentially greater role in the drug development process in the future because of the increasing emphasis on in vitro screens contemplated.

None of the current 12 month task orders, of which 10 have been awarded, has concluded work yet. Tasks have been under way for several months on pibenzimol, caracemide, phyllanthoside and retrospective study on 5-azacytidine. Six additional 12 month tasks have just started. These include aphidicolin glyciniate, L-cysteine derivative, deoxyspergualin (discreet compound), and two retrospective studies on teroxirone and melphalan. The retrospective studies are designed to shed light on differences observed between human and animal effects of the drugs. Assay methods have been successfully developed for pibenzimol, caracemide and phyllanthoside. Preliminary work has shown that phyllanthoside exhibits marked species differences in its rate of metabolism, the highest rate being observed in the mouse and the lowest in man.

Carcemide is extensively metabolized to CO_2 in the mouse and this information together with pharmacokinetic data on pibenzimol in animals has been communicated to the Cancer Therapy Evaluation Program clinicians involved in monitoring the phase 1 trial of the drugs.

As the master agreements become more established as a means of acquiring pharmacological data it is anticipated that at a minimum, assay methodology and bolus infusion pharmacokinetics will be determined in animals concurrently with the entry of the drug into preclinical toxicological evaluation, currently about seven to eight drugs a year. Additionally, pertinent retrospective studies may be undertaken and special studies will be conducted to investigate problems which arise either in preclinical or clinical evaluation of the drugs. The master agreement holders will be required to maintain capabilities in all aspects of pharmacology ranging from analytical chemistry through pharmacokinetics to metabolite identification.

Title: Animal disease diagnostic labs. Recompetition of contracts held by Univ. of Missouri and Papanicolau Cancer Research Institute. Estimated total cost, $375,000 a year, five years.

A program decision was made several years ago to upgrade the health quality of the laboratory animals produced under the Animal Genetics and Production Branch contracts. Several diagnostic contracts were negotiated in order to monitor the progress of animal production suppliers in this area. The diagnostic contracts described herein provide a complete workup on animal health including histological, serological, and microbiological information.

The documented animal health profiles provided by the contracts have been utilized to upgrade production procedures at supplier facilities and to select suppliers capable of meeting program needs for quality animals.

A recent decision was made by DTP to upgrade contract screening laboratory facilities and procedures to permit them to receive and maintain laboraltory animals free of pathogenic organisms. Other users within DCT (intramural and extramural) and NCI are also attempting to upgrade laboratory capabilities. Diagnostic data from these laboratory facilities will be essential for evaluating the success of individual efforts.

Title: Supportive services in cell biology, virology and immunology. Recompetition of a support contract for Robert Gallo's laboratory now held by SBA-Biotech. Estimated annual cost, $280,000, four years.

This contract was established to obtain routine services needed by the Laboratory of Tumor Cell Biology on a regular schedule. These services include the examination of tissue culture cells for mycoplasma contamination, karyotypic analysis of the cultured cell lines, immunological testing of tissues and serum specimens for HTLV antigens and antibodies, and the supply of small quantities of tissue cultured cells.

The contractor has provided excellent service in carrying out mycoplasma testing, cytogenetic analysis, immunofluorescence and ELISA assays for detection of HTLV antigens and antibodies in tissues and sera from patients with adult T cell leukemia and acquired immune deficiency syndrome, and in supplying small quantities of fresh tissue cultured cells.

Title: Support services for extramural clinical trials. Recompetition of a contract held by EMMES Corp. Estimated annual cost, $390,000, five years.

The Cancer Therapy Evaluation Program requires a facility within 45 minutes of NIH which will provide support services for its management of the extramural clinical trials program. Specific requirements include the following:

1. Data managment personnel and facilities in support of extramural clinical trials in adult T-lymphocyte malignancies, including those being organized by NCI in Okinawa and Jamaica.

2. Data management personnel and facilities in support of CTEP supported intergroup activities, including (a) the intergroup testicular cancer studies; (b) intergroup trials in rare malignancies, including carcinoid tumors, thyroid cancer, and pheochromocytoma; (c) intergroup studies of hepatoma; and (d) coordinated intergroup trials of autologous bone marrow transplantation.

3. Program analysis in support of the development of priorities for future initiatives and clinical research directions.

This contract will continue to provide the kind of analytical support which assists CTEP staff in organizing and prioritizing ongoing clinical research efforts in specific disease areas.

CTEP Director Robert Wittes told the Board that "we are seriously thinking of starting autologous bone marrow transplant intergroup studies." They would focus on lymphoma and neuroblastoma, he said. Also, the program collaborates with the Pan American Health Organization "which may be ready for multinational clinical trials."

The Board also approved adding $350,000 to the $500,000 a year it had previously approved for support services CTEP needs to meet FDA requirements for IND drug studies. The contract, with Social and Scientific Systems Inc., also was expanded to provide support for biological response modifiers, with more than 25 NCI IND filings on biologics in the last two years.

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