THE CANCER LETTER

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GROWING NUMBER OF NEW RESEARCH IDEAS CREATE NCI DILEMMA: HOW TO FUND THEM WITH A FLAT BUDGET

The President's Cancer Panel, having succeeded in eliciting suggestions from the scientific community on how NCI could improve methods for supporting research—some of which NCI has agreed to implement—brought in another group to talk on "new scientific directions for the National Cancer Program" when the Panel met during the 13th International Cancer Congress in Seattle.

Their suggestions led NCI Director Vincent DeVita to say, "This is the essence of the problem we are facing at a time when we have a flat budget—the great diversity of good ideas," ideas which might be funded adequately only at the expense of other good ideas.

Those invited to make presentations were Anthony Miller of the

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In Brief

NCAB TO HEAR NCI STAFF PLANS FOR IMPLEMENTING RECOMMENDATION ON NUTRITION & CANCER TASK FORCE

NATIONAL CANCER Advisory Board will hear how NCI intends to implement the Board's recommendation to establish a Nutrition & Cancer Task Force, with a specific amount of money to be earmarked to support new grants in that field, at the Board's meeting next week. Peter Greenwald, director of the Div. of Resources, Centers & Community Activities, and Maureen Henderson, chairman of the Board subcommittee which developed the recommendations, are scheduled to discuss the program at 11 a.m. Monday, Oct. 4. The Board's Subcommittee on National Organ Site Programs will meet Oct. 3, 7:30 p.m., to ponder the status of the Board's recommendation for major changes in the programs. That recommendation may be overturned by Congress. . . . **JAMES HOLLAND**, director of the Mount Sinai School of Medicine Cancer Center, and the Sony Corp. of America Foundation have announced establishment of the Iwama Memorial Sony International Fellowship for oncology. The fellowship is named for Kazuo Iwama, Sony president who died of cancer in August. The $300,000 grant will support two researchers a year for the next five years. . . . **FOOD & DRUG** Administration has announced that the charter of the Oncologic Drugs Advisory Committee has been renewed through Sept. 1, 1984. . . . **CORRECTION**: The list of potential research bases for CCOPs published in ***The Cancer Letter*** Sept. 10 contained an incorrect phone number for the Illinois Cancer Council Comprehensive Cancer Center. The correct number is 312-346-9813. . . . **LEE CLARK**, president emeritus of the Univ. of Texas System Cancer Center, commending Edwin Mirand for his work as secretary general of the 13th International Cancer Congress: "I don't know of anyone who worked so hard to make a congress successful. It was a heroic effort."

NCAB Subcommittee Works On Drafting Quantitative Risk Assessment Policy

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CANCER PROGRAM HAS SHATTERED MYTH THAT MONEY CAN'T BUY IDEAS: DEVITA

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National Cancer Institute of Canada; Robert Pollack, Columbia Univ. Dept. of Biology; Margaret Kripke, head of the Cancer Biology Program at the Frederick Cancer Research Facility; Robert Gallo, chief of the Laboratory of Tumor Cell Biology in NCI's Div. of Cancer Treatment; Walter Bodmer, Imperial Cancer Research, London; Norbert Fusenig, German Cancer Research Center, Heidelberg; James Holland, chairman of the Dept. of Neoplastic Diseases at Mount Sinai School of Medicine; and Leo Sachs, Weizman Institute of Science, Israel.

Panel member Harold Amos chaired the session, after an opening statement by Panel Chairman Armand Hammer. Panel member William Longmire also was present.

Pollack made three recommendations for basic research which he said should be supported in the next decade, then added a few words on the "politics of cancer research" which Amos later said was not supposed to have been on the agenda for the scientific presentations.

"NCI should be proud of the many scientists in-house and extramural who have put in their time to read and review grant applications, as well as the ones who have carried out the research," Pollack said. "National and local politics ought to have no place in this process. Recently I have begun to hear fairly reproducible horror stories of peer review bent beyond recognition by the severe cutting of funds available for competitive grants. At the same time I have received calls from many of my favorite scientists, both inside and out of NCI, who describe in graphic detail a decline in morale as people leave academic jobs for industrial ones, government ones for academic ones under conditions where replacement is difficult or forbidden.

"Peer review works best when it fosters creativity in science," Pollack continued. "It degrades into farce, in my opinion, when money is so abruptly cut back that priority scores fall below grade at the slightest hesitation from even one panel member. This is now commonplace on some study sections . . . . I believe the most immediate political obligation you have is to assure the continued availability of money for the initiation and continuation of grants for basic research."

DeVita, in his summary of the presentations, said, "I think Dr. Pollack started it out on the right trend by pointing out that you can't separate science from the support of science and from the instruments that are used to support science if you want to continue to be able to do all of the things that we have to do now in the face of short supplies.

"There is one great myth about science, and the Cancer Program has proven it was a myth—that money can't buy ideas," DeVita continued. "The answer is that money does indeed buy ideas. Money puts good scientists to work and good scientists come up with ideas. It is true that you can't go out with a million dollars in your hand and buy ideas in the hallway."

DeVita pointed out that since the advent of the National Cancer Program (which started in the 1972 fiscal year), NCI support of cancer research has only a little more than doubled in constant dollars. However, the number of new grantees supported each year has been four and a half times the number in 1971. "We are supporting many more investigators on less dollars than we were back in the beginning, but money does, in fact, buy good ideas.

"What do we do then? It isn't a matter of supporting the areas that are mentioned by the investigators here tonight. We are supporting them. As a matter of fact, Dr. Amos has picked some very excellent investigators, obviously, and in many of the areas described the normal peer review process does support a great deal of the grant supported research in here. . . .

"The problem we are having now in the Cancer Program is getting some of the older programs that had their day and phasing them out in this time of a flat budget, because I am a staunch believer that the biggest mistake we can make now is to stand still because our budget is standing still. . . .

"We all agree, I think, that the peer review system may be the best system ever invented in the sense that we can't find something to replace it, but it is inadequate under certain circumstances. One of the things that it fails to do, especially in times when resources are tight, is to support very risky research and to support collaborative research. The people who said here tonight that when there is a risk that you will not be supported, and that young investigators are very likely to take the short term experiment that will get them the publication so that they will be in a good position to apply for a grant, are absolutely correct. I think those are the kinds of distortions that we are seeing in the peer review system. What we have to do is come up with a different instrument."

DeVita said that NCI's new Outstanding Investigator Award, developed following suggestions coming out of a previous Panel meeting (***The Cancer Letter,*** June 18), is one instrument aimed at addressing the problem. They will be five year renewable awards based on the track records of investigators.

Miller, an epidemiologist whose main interest is in prevention, said antismoking efforts remain as a major objective, with smoking causing 30 percent of cancers. "However, we do not really know where our efforts should be concentrated in smoking control. De we concentrate on young people, seeking to

prevent them taking up smoking? Do we concentrate on older people, seeking to stop smoking, if they still are? Or do we concentrate on less harmful cigarettes?

"I would submit that we need to encourage research into smoking control in the population, moving from less sophisticated endeavors in education to approaches in defined populations to find out what best will reduce mortality from smoking associated diseases. I believe this is a role for the new Cancer Control Research Units which are likely to be developed over the next few years.

"The second major role for prevention concerns diet and nutrition. Many have estimated that something like 35 to 50 percent of cancers are associated in some way with diet. The evidence from epidemiologic studies at both the group and individual level is increasingly congruent with the evidence from laboratory studies."

Miller noted that the National Academy of Sciences' recommendations on diet, "relatively simple measures," have not convinced many people and that those changes "may not be enough to produce a major impact on diet associated cancer. We thus need to encourage research in this area. We need to do studies to improve dietary methodology and epidemiology. We need to find the mechanism of action of dietary risk factors, the interrelationships of such risk factors. For example, if coffee is associated with pancreatic cancer, is it primarily because fat intake is associated with coffee intake?

"We need to identify low risk foods and hence a low risk diet. There is encouraging evidence that many foods contain inhibitors of cancer and we need to find out how to best use this knowledge and we need to evaluate some specific potentially cancer reducing factors such as beta carotene, vitamin C, or other reducing agents in intervention studies.

"The third approach to prevention which I believe must concern us is the need for environmental monitoring. It is our responsibility to assess the effect of occupationally associated and general population associated exposures to existing and new chemicals."

Pollack said that it is "my believe that the National Cancer Institute should structure its policies for research, for technology, and for political strategy so as to understand the underlying causes of the disease as well as to treat its victims. . . . First, research. The mechanisms of growth control of cells of the body is not yet well understood. This remains the second half of the great war against cancer in which NCI has enlisted the commitment of so many physicians and scientists. The first half of the war, the discovery of the genetic elements necessary and sufficicient to derange a cell and the demonstration that some of these are encapsulated in viruses is well under way and deserves continued support. However, the second part of the war is where the victory will be most quickly felt on the home front when it comes.

"Novel pharmacologic intervention will require knowledge of the cellular molecules with which these cancer genes and their products interact. So, specifically, I recommend that the following three points be taken into consideration for policy in the next decade on basic research. . . .

"The technology of DNA transfection is a rapidly growing one and deficiencies of DNA transfer approach unity. This technology should provide selective systems for studying and for isolating genetic elements capable of regulating normal mammalian cell growth.

"Second, some cellular molecules must interact in solution with the molecules encoded by the set of onc genes defined by transfection. The study of these cellular molecules and the genes that encode and regulate their expression is the best step outward from what is known to what must be learned about cancer at the cellular level.

"Third, DNA moves. This. . . has now been confirmed and extended to the resolution of single base pairs. . . . The role of such movement in the rapidity of evolutionary change is one of the most exciting new problems in biology, joining molecular, macroscopic and behavioral biologists for the first time in a common body of answerable questions. But for our purposes, the elucidation of DNA movement in somatic cells is central insofar as it offers one easy resolution of the two problems I have mentioned. That is, the position of a given stretch of DNA in the genome can, in some cases, be responsible for its capacity to express its information so that DNA movement itself has potential to be a regulatory element in normal and cancerous cell growth."

Kripke said that promising areas of research include DNA transfection "which gives us the ability to move cancer related genes from one cell to another; the study of onc genes and their products; human tumor viruses and their epidemiology; tumor cell heterogeneity and implications of this heterogeneity for cancer treatment; the growth factors that regulate cellular interactions and cellular differentiation; and the experiments of nature, if I may steal a term from Robert Good, such as the genetic diseases that are associated with a high cancer incidence. . . .

"I think the most important theoretical question concerning tumor antigens is how these antigens are related to the process of neoplastic transformation. I think that the most important practical question about tumor antigens is how can we make use of these for the benefit of cancer patients. The key to answering both of these questions lies in being able to determine the chemical structure of these antigens. Over the past 10 to 15 years there has been an enormous effort expended in trying to accomplish this task using primarily conventional biochemical approaches.

"These have been relatively unsuccessful in that

we still do not have the answers to these questions. However, I think that the availability of systems for transferring genes, using the technique of DNA transfection, gives us a genetic approach to this problem that may be much more successful than the purely biochemical approach that has been used so far. For example, this technique permits us to ask the questions posed recently by Hopkins and Lawe. Are tumore specific transplantation antigens genetically associated with the process of neoplastic transformation? This approach also brings within reach the possibility of gene cloning for tumor antigens which would provide sufficient material to finally permit appropriate biochemical characterization of these gene products.

"So one promising area for future research, I believe, is the genetic approach to the structure and function of tumor antigens. The second area has to do with how the immune response to these tumor antigens is actually regulated. This speculation, and it is mainly speculating, is based partly although not exclusively on the system of ultraviolet carcinogenesis in the mouse.

"It appears that these tumors may have two types of antigens. One type is the ordinary, individually specific tumor specific transplantation antigen, against which the immunologic effector cells are directed. The second type of antigen shared by all tumors induced by this particular carcinogen and it appears that the common antigen is what is recognized by the immunological regulatory cells.

"So, we have a situation in which the regulatory cells recognize one antigen and through this antigen control the immune response that is directed against a set of different antigens.

"What is the significance of this situation? Until now, the only tumor antigens that we have been able to study are those detectable by antibodies or by immunologic effector cells.

"If there really is a separate class of antigens that is recognized by the immunological regulatory cells, this gives us a new possible approach for controlling the immune response against the individually specific antigens on tumor cells.

"In addition, if these regulatory antigens are indeed common on tumors of a given etiology as they are in the case of ultraviolet radiation, this would give us a new antigenic marker that could tell us which carcinogen was responsible for inducing a particular cancer.

"This brings me to my very last point which is that it is very easy to predict the direction and advances in research up to a certain point. The things that I have mentioned as promising directions are based on principles and techniques that have already been discovered. What we are really discussing this evening is the application and the logical extension of these principles that have already been discovered.

"What I do not think is possible to do is to predict where the new principles will come from that will change the directions of our current thinking and the current directions of research.

"Historically, these major scientific advances have come from the most unexpected quarters, and I do not think that the ones that will arise in the next decade will be any more predictable than the ones that we have seen in the past."

Bodmer said that new technology would permit a "major contribution" in studies of inherited susceptibility to cancer, studies which may require more collaboration and "perhaps the sort of more directed support than is usual. . . . New approaches have been made possible in doing this through the use of DNA markers, the restriction enzyme polymorphisms that we can now use to study genetic differences between people with recombinant DNA techniques. . . .

"The DNA polymorphisms which are detected because of variations between individuals in the sites that restriction enzymes see which can then be detected in now very standard ways. The application of these variations. . . could revolutionize our approach to finding genetic factors in susceptibility. We can take any DNA clone and find out what part of the genome it comes from, either by using somatic cell genetic techniques in situ or even conventional family studies. . . . I think this will be a very powerful approach to finding susceptibilities to cancer. . . .

"These sorts of studies don't easily fit into the framework of the usual grant system. They need collaboration between many different groups because no one laboratory is going to find the total range of DNA markers which can answer these questions of DNA susceptibility."

Gallo said he wanted to talk about, not something new, but something old—the Virus Cancer Program, although he was not formally part of it. "Perhaps it was an overinflated program, and perhaps it wasn't administratively tight as it should have been at the time, but I think today in the 1980s there is a lot of evidence that this past significant effort has paid off in a lot of different ways, some of it in basic science and some of it in I guess what we would call applied, at least identification of viruses in man associated with human cancers. . . . Viral oncology was out when I first came to the National Cancer Institute. Then it became very in. Then it went out when we were told that all human cancer was due to environmental carcinogens. I think the big bulk of human cancers we don't know the cause, but there are an increasing number of examples that viruses are primarily etiological factors in a significant number of human cancers. The list is going to grow."

Gallo cited Epstein-Barr virus in Burkitt's lymphoma, and nasopharyngeal cancer and cervical cancer as those where the evidence of a viral etiology is strong. Herpes simplex had been suspected in cervical cancer,

"but there is new evidence that looks extremely interesting, that papilloma viruses may be involved in human cervical cancer. This is new data. It is not something that we can talk about widely yet, but there are a lot of interesting new developments." The evidence that hepatitis, a viral induced disease, initiates hepatoma also is strong, Gallo pointed out.

"So I would predict that viruses are going to be important in human cancer to a significant degree, more important than they are now. Some of the other factors are going to be secondary. They are not going to be the only cause. That is obvious.

"I think we need to save some of the people interested in the natural biology of virus induced cancers. That is an area that by peer review often doesn't do so well. There are things that are needed—reagents, virus supply—it's hard to argue for that on a grant. There are laboratories that have track records of major discoveries, like Dr. Ludwig Gross, but on a peer review today, if he is not doing molecular biology, it might not go as well as it did years ago. He obviously, among others, merits continuous support for this area of research."

DeVita commented that the Virus Cancer Program had cost about $1 billion in total. "If I had the exclusive rights to all of the information we generated in the Virus Cancer Program, I think I could sell it for $8 billion today, and that would be a bargain." He quoted James Watson who said recently, "In view of the public misperception of the success of the Virus Cancer Program, it is about time you told people that the public purse has been well spent."

Sachs said, "I would like to make one statement, that although one usually hears all the rude remarks about what has gone wrong, an enormous amount has gone right with the National Cancer Program. It is a program which has been extremely valuable, not only within the United States. . . . Other countries have benefitted from it to a very large extent. The National Cancer Program is a very good thing, and we hope it will continue for many years to come."

Fusenig noted that a recent report to the German minister of research and technology recommended better support of basic research and improved coordination of basic and clinically oriented cancer research.

"Since funding is not unlimited," Fusenig said, "there is always the tendency to favor those fields which promise the quickest approach to help cancer patients, and it may not always be the best way. However, experience in science indicates that real progress in complex and difficult problems mostly comes from the coordinated efforts in different disciplines. Thus in selecting and promoting scientific programs, one should not so strictly look at the formal or apparent linkage to one or the other specific questions on work in cancer research, but more for the originality in the different approaches.

"It is my opinion that much of the work done and published under the heading and support of cancer research is linked to the problem merely by formal reasons and by following fashionable trends than by real devotion to the program itself."

Fusenig offered two suggestions for research areas requiring increased emphasis:

—Cell differentiation and its regulation in cell growth. "The well balanced regulation of cell growth and differentiation is what we call normality and disturbances in this regulation usually lead to the appearance of diseases. This regulation in growth and and differentiation, when they are genetically fixed, may eventually lead to unregulated or what we call malignant growth. This problem is still poorly understood and expresses itself under different phenotypic expressions in vivo in different organs in different tissues and is probably under different control mechanisms in each specific tissue. . . . There are no in vitro models available which at least express a large variety of the phenotypic expressions or differentiation as we know from the organism.

"We always have the possibility to compare these studies in vitro with what is happening in vivo either by retransplantation or by trying to recombine in vivo and in vitro systems."

—Genetics. "The association of an altered genotype or chromosome set and cancer cells has been obvious since the beginning of this century. The visible chromosomal changes, however, have until recently been considered more at random and mere consequences of the malignant transformation process. With more sensitive techniques and expanding studies to the careful examination of the variety of animal and human tumors, it could be shown that many of those share nonrandom chromosomal alterations. . . .

"It has been turned out during the last years that genetics has a renaissance due to new techniques. The recombination with classical cytogenetics and modern molecular biology which made it possible to dissect out genomic parts and reintroduce it into other cells makes this field one of the most promising for the future. The methods which we really need are not yet established which is, on one hand, much better and much detailed feasibility for analysis of chromosomes which are the banding techniques we have at the moment and, on the other hand, much more known on mapping of the genome."

Holland, referring to great progress made in curing some forms of cancer, said, "This is such an enormous step forward in our perception of cancer that I would like to make sure that those who caution that we not eat the seed crop be aware that there is a time to harvest the fruit. We must recognize that clinical research has a momentum of its own and it does not depend upon standing idly by waiting for the beautiful concepts advanced tonight which I support and

have much interest in. We are in position to make forward steps that are palpable for mankind today in the clinical realm and it cannot be sacrificed for laboratory studies only.

"Now, having said that, I would like to present some information which represents continued support of a multidisciplinary program. I think that it is important to recognize the great importance of having scientists and physicians interact at the bedside and at the bench. Everything doesn't get into brain cells by diffusion. Some of it gets there by active transport.

"My colleagues, Jay George Bacasi and Peter Sange are most responsible for the work that I am going to present. Millions of dollars, probably hundreds of millions of dollars, are spent each year in this country on cancer diagnosis. We have a new development in cancer diagnosis which I believe merits substantial work in the next decade and we are in the process of doing so. . . .

"Twenty-seven women on the way to the operating room for a breast mass, unrecognized at the time of the test as to its histologic nature, were studied. By a technique that Bacasi and Sange have elaborated, separating the different peripheral blood cells by an entirely new technique that depends upon multiple centrifugations and differential densities on fical hypake using amino ethylthiuronium bromide-treated red cells for rosetting and using and here isolating B cells and O cells and monocytes after T cells are out, one can separate the several types of peripheral mononuclear cells to 90-odd percent purity of each type.

"Then, when one takes these same women on the way to the operating room with a breast mass, you can see that the T cells or the memory cells can recognize the antigens of an alogeneic breast tumor. The test as of the present is 100 percent accurate for positives and 100 percent accurate for negatives among 27 patients with breast cancer, 14 patients with colon cancer and seven patients with mesothelioma.

"Monocytes which have been thought by previous workers to represent the active cell are, in fact, nonspecifically active and do not help and it is the removal of these monocytes that makes a specific diagnosis with these T lymphocytes possible. . . .

"This is a very useful diagnostic technique. Within 10 minutes the surgeon was to biopsy the breast and thus it was not critical that we do this test, but we are in the process of a field trial with coded specimens at the time of mammography and at the time of colonoscopy so that one can determine whether we can, in fact, use this for a more discriminating test.

"It has several potential importances, though, besides its immediate diagnostic significance. One, the reason that this happens is that the T lymphocytes secrete a lymphokine and, if this lymphokine is placed upon normal lymphocytes, one can reproduce the effect.

"In fact, if you take healthy control T cells and incubate them with either breast cancer or colon cancer, there is no leukocyte adhere inhibition. If one incubates the leukocytes of breast cancer with breast cancer antigen, there is a lymphokine in the supernatant medium which inhibits the adherence of normal lymphocytes, but it does not inhibit when breast cancer patient lymphocytes are incubated with colon cancer. It does not inhibit the adherence of lymphocytes, indicating that the memory cell and conversely for colon cancer, the memory cell is specific for the tumor type of the membranes that have been isolated.

"Thus, the technique offers some expectation of being able to identify specific tumor cell antigens, although we haven't done so. It constitutes a new tool.

"It also has not escaped our attention, of course, that these lymphocytes might themselves be of considerable importance in therapeutic considerations."

NCAB SUBCOMMITTEE WORKS ON WRITING QUANTITATIVE RISK ASSESSMENT POLICY

The National Cancer Advisory Board's Subcommittee on Environmental Carcinogenesis has met twice to develop a policy position, for consideration by the full Board, on the adequacy, limitations and use of quantitative risk assessment methodologies.

That issue has been a source of sometimes bitter controversy pitting regulatory agencies against the courts, consumer advocates against industry, and agencies involved in testing and evaluating potentially carcinogenic substances somewhere in the middle. The controversy flared anew earlier this year when Congressman David Obey charged that NCI executives pressured the International Agency for Research on Cancer to soften its assessment on the risk of benzene. NCI denied the charge.

The subcommittee is chaired by Sheldon Samuels, who submitted questions to be considered:

1. What is the definition of quantitative risk assessment (QRA) as distinct from qualitative risk assessment?

2. Which models or paradigms of QRA have been, are, or are likely to be heuristic in terms of data fit, testability, and predictive experience?

3. Is QRA practical in terms of data adequacy of both dose and effects?

4. Are the regulatory issues which involve QRA separable from the scientific problems of QRA? For example: Should economic implications be used in the selection of specific QRA method? Should QRA be used regardless of the level of certainty relative to the availability of data? Can QRA be used by itself or in combination with other factors in determining a "significant risk"?

5. Who should do QRA: Scientific organizations or regulatory agencies?

Other members of the subcommittee are Board members William Powers, Janet Rowley, and Irving Selikoff. Gerald Wogan had been listed as a member, but he has resigned from the Board. Also, ex-officio Board members on the subcommittee are Elliott Harris, National Institute for Occupational Safety & Health; Allen Heim, Food & Drug Administration; Peter Preuss, Consumer Product Safety Commission; David Rall, director of the National Instituteof Environmental Health Sciences; and John Todhunter, Environmental Protection Agency.

Ad hoc consultants to the subcommittee, retained for the QRA task, include former NCAB members Arnold Brown, dean of the Univ. of Wisconsin Medical School, and Philippe Shubik, now senior research fellow at Oxford. Others are Donald Barnes, EPA; Patricia Breslin, Dept. of Labor; Charles Brown, NCI Biometry Branch; David Hoel, NIEHS director of biometry and risk assessment; Kenneth Crump, president of Science Research Systems Inc.; and William Nicholson, Mount Sinai School of Medicine Environmental Sciences Laboratory. Richard Adamson, director of NCI's Div. of Cancer Cause & Prevention, is executive secretary.

Shubik was chairman of the subcommittee and Brown a member when, about seven years ago, it was charged with a similar controversial task of writing a definition of a chemical carcinogen. That job required a series of meetings over nearly two years, and countless rewrites, before a consensus was reached. The definition developed then has stood the test of time and has frequently been cited in regulatory proceedings.

The subcommittee hopes to submit a draft statement to the NCAB at its meeting in November.

Three definitions the subcommittee is using in its deliberations:

Hazard identification or characterization (qualitative risk assessment)—The determination of the toxicity of a test substance in experimental systems and the prediction of such effects in man.

Quantitative risk estimation—The process by which the risk of disease or death in a population exposed to a toxic agent is related quantitatively to the intensity and duration of exposure.

Quantitative risk assessment—The scientific assessment of both hazard and exposure information for purposes of estimating the likelihood that hazards associated with the substance will be realized in exposed populations or individuals.

NCI CONTRACT AWARDS

Title: Surveillance of the health effects of less hazardous cigarettes, continuation
Contractor: Kaiser Foundation Research Institute, Oakland, Calif., $86,050.

Title: Technical writing, public distribution and telephone answering services in response to cancer related inquiries
Contractor: Biospherics Inc., Rockville, Md., $615,667.

Title: Cancer Communications Program support services, additional effort
Contractor: Porter, Novelli & Associates, Washington D.C., $425,523.

Title: Lung cancer--early detection, localization and therapy, continuation
Contractor: Memorial Hospital, New York, $3,587,390.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair Building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP NCI-CP-31007-78

Title: *Collection and evaluation of human tissues and cells from donors with an epidemiological profile*
Deadline: *Approximately Nov. 23*

NCI has a requirement for an intramural resource contract for the collection of both biopsy and noncancerous surgical specimens from humans with and without cancer. The place of performance for this requirement must be within a 40 mile radius of the NIH campus in Bethesda, Md.

The services required include:

1. Collection of surgical, biopsy, lavage and pleural effusion specimens from nontumorous and neoplastic human tissues, e.g., bronchus, and cell, e.g., lung macrophages, white blood cells and mesothelial cells.
2. Assessment of tissue and cellular viability.
3. Transport of viable tissue and cell specimens to Bldg. 37, Rm 2C27 or 2C16 on the NIH reservation within three hours of collection.
4. Collection of an epidemiological data base from the tissue donors, using a questionnaire provided by NCI.

The procurement will require approximately 1,400 hours of technician time and 400 hours of professional effort per year.

Contracting Officer: Elizabeth Osinski
RCB, Blair Bldg. Rm. 117
301-427-8888

RFP NCI-CM-37562

Title: *Development of parenteral dosage forms for clinical investigation*

Deadline: *Approximately Dec. 3*

The Developmental Therapeutics Program, Div. of Cancer Treatment, NCI is seeking contractors to 1) develop parenteral dosage forms of potential antitumor agents that exhibit inadequate solubility and/-or stability in vehicles commonly used for intravenous administration and 2) for innovative studies leading to more effective approaches to the intravenous delivery of compounds that possess limited solubility and/or stability.

Compounds to be studied are selected by NCI. The goal of the contract effort is a pharmaceutical dosage form suitable for intravenous administration. The government will provide certain target solubility and stability goals. The contractor will prepare a pilot batch (30-100 units) of the finished dosage form as a product of the research effort. Resolution of these problems requires approaches more complex than simple solvent approaches or pH adjustment. Frequently the difference between inherent and desired solubility is 10^3 to 10^4.

These projects will also require considerable analytical work, particularly, the development of a suitable stability indicating assay. As a minimum requirement, the contractor must be equipped with the following: ultraviolet, infrared, and proton magnetic resonance spectroscopy; high pressure liquid chromatograph with variable wavelength ultraviolet detection, optical rotation apparatus and thermal analysis equipment.

The government anticipates multiple contract awards. Offerors must propose at the two and three staff year levels and may also propose at the four staff year level. The contracts will be awarded on an incrementally funded basis for a three year period beginning on or about June 1, 1983. Each increment will be for a one year period.

Contracting Officer: John Palmieri
RCB, Blair Bldg. Rm. 228
301-427-8737

RFP NCI-CM-37560

Title: *Development and production of pharmaceutical dosage forms*

Deadline: *Approximately Dec. 3*

The Pharmaceutical Resources Branch of the Developmental Therapeutics Program, NCI, is seeking a contractor to provide dosage form development capability in the preparation, primarily, of sterile freeze dried dosage forms plus the facilities and staff to manufacture small production size batches (about 4,000 units) of these formulations for evaluation in preclinical toxicology studies and in clinical trial.

The contractor must prepare all products in accord with FDA's current Good Manufacturing Practice Regulations and NCI's product specifications. The contractor selected for this work shall be experienced in both the development and production of sterile freeze dried products and sterile liquid fill dosage forms. The capability to develop and manufacture other pharmaceutical dosage forms (i.e. tablets, capsules, etc.) is desirable but not essential.

As a minimum requirement, the contractor must be registered as a pharmaceutical manufacturing facility with FDA for sterile products and shall be required to have in house all essential equipment at time of contract award. All compounds to be developed and produced as pharmaceutical dosage forms will be assigned by the government. Annual workload estimates for development and production are, respectively, 3,000 hours of technical staff time and 11 production assignments. The number of development assignments is estimated to be six to eight annually.

The complexity of the dosage form development will vary from simple familiarization work up on existing formulation to a thorough study on a new chemical entity. Each production assignment will not exceed solution volumes comparable to 5,000 x 20 ml vials. The contractor will be responsible for the quality control testing of all formulation components including the active ingredient, excipients, container-closure system as well as the finished product.

The contractor will not be responsible for the shelf life surveillance of the dosage forms prepared on production scale since a separate contract resource will perform this task. All products will be labeled and packaged according to specifications supplied by the government. Label preparation may be subcontracted but labeling must be performed at the contract site.

It is anticipated that the government will award a single contract on an incrementally funded basis. Each increment will be for a period of one year and the total contract will be awarded for a three year period beginning on or about June 1, 1983.

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