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NCAB SEEKS EXEMPTION FROM NEW REIMBURSEMENT PLAN FOR CLINICAL TRIALS, MODIFICATION OF HOSPICE REGS

The National Cancer Advisory Board has agreed to ask the Health Care Financing Administration to consider an exemption for patients in clinical trials from proposed reimbursement limits under the new "Disease Related Groups" system.

The Board also agreed to ask HCFA to take another look at proposed regulations for hospice care which Gale Katterhagen, chairman of the Board's Committee on Cancer Control & the Community, said could

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In Brief

HAWKINS GETS SEAT BACK ON LABOR & HUMAN RESOURCES, LOSES SUBCOMMITTEE; FOUNDATION OFFERS FELLOWSHIPS

PAULA HAWKINS regained her seat on the Senate Labor & Human Resources Committee, which has responsibility for most health authorization bills, after giving it up to go onto the Banking Committee. The Florida Republican changed her mind, after the Labor & Human Resources slot had been given to Alfonse D'Amato of New York. John East (R.-N.C.), who also had left the committee to join the Armed Services Committee, decided he wanted to stay on Labor & Human Resources after all, creating a dilemma for the GOP leadership. It was resolved by adding two seats to the committee, one for each party, and getting D'Amato to trade his for a seat on the Joint Economic Committee. Liberal Republicans Lowell Weicker (Conn.) and Robert Stafford (Vt.) complained that Chairman Orrin Hatch (Utah) was trying to stack the committee with conservatives, which Hatch denied. Hatch commented that the committee's top ranking Democrat, Edward Kennedy (Mass.) would still have a "working majority." The Oversight & Investigations Subcommittee, which Hawkins chaired and used to lambaste NCI two years ago, was abolished. . . . **FOUNDATION FOR** Cancer Chemotherapy is inviting applications for fellowships from U.S. medical oncologists wanting to work one year or longer in the Dept. of Medicine and clinical investigations of the Institut Jules Bordet, cancer center of the Univ. of Brussels. The stipend is two million Belgian francs per year, from $35-45,000 depending on the exchange rate. Write to Prof. Henri Tagnon, President, FOCA, Institut Jules Bordet, 1, Rue Heger-Bordet, B-1000 Bruxelles, phone 02-538-27-66. . . . **LITTON BIONETICS'** new Litton Institute of Applied Biotechnology will emphasize research aimed at development of biological products for the health industries, Institute Director Michael Hanna said. Initially the focus will be on diagnostic tests for a variety of diseases, with emphasis on certain forms of cancer. The Institute also will investigate and develop biological response modifiers for application in therapy of cancer and infectious diseases, Hanna said.

DRG REIMBURSEMENT PLAN WOULD KILL CLINICAL RESEARCH, KATTERHAGEN SAYS

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lead to "less adequate, inferior level of care for terminally ill patients."

Katterhagen reported to the Board that his committee had reviewed the effects of the recently passed Tax Equity & Fiscal Responsibility Act of 1982 (TEFRA), which has mandated changes in the reimbursement mechanism from the historic retrospective cost related payment method to a prospective reimbursement system based on "disease Related Groups" (DRGs).

"While the overall impact of TEFRA may be salutory," Katterhagen said, "it is likely that the limitations placed on reimbursement will discourage clinical research efforts in university based cancer centers and in community cancer programs. Specifically, the limitations on reimbursement of cancer patient costs are likely to put a cap beyond which cancer patient costs will not be reimbursed. This limit will cause hospital and university administrators to discourage clinical research efforts as too costly. Indeed, protocols frequently require additional tests, procedures, and drugs to assure the patient is receiving the highest quality of care and to assure the cooperative research group of sufficient high quality information to judge the effectiveness of the trial.

"Obviously, this shift will cause community hospital administrators and physicians to stop clinical research efforts such as CCOPs and cooperative group cancer control efforts. And, unless specific exemptions are forthcoming for university teaching hospitals, this legislation could end university clinical research efforts as well.

"Your committee recommends fa[illegible] of x-ray, pharmacy, blood bank, laboratory, radiation

their families. Since 85-90 percent of hospice patients are cancer patients, potential deficiencies in care are a major concern of this Institute and the physicians, other health care professionals, administrators, laypersons and scientists associated with the National Cancer Program.

"The committee and staff feel that the final regulations must be revised to reflect and guarantee the highest quality of scientifically valid care for these patients and their families. The draft of the current regulations encourages a separate system of care for the terminally ill which could decrease, rather than increase, the quality of hospice patient care. While we agree that the hospice patient will greatly benefit from a new form of reimbursement via Medicare, the best interests of patients and their families will not be met by denying terminally ill patients the benefits of modern pain and symptom control or by lowering standards of quality control and quality assurance.

"Your committee strongly recommends that the final regulations contain specific language concerning the involvement of appropriate physician specialties, and nurses with adequate credentials to assure the patient and family of the quality of care this legislation was passed in order to promote. This means that the hospice must have the involvement of the referring physician, meet accreditation standards such as those proposed by the Joint Commission on Accreditation of Hospitals for hospices, meet peer review standards for quality of care, and have a quality assurance program that assures that a hospice will have no lower standards than those imposed upon a community hospital. Moreover, the hospice patient will require access to pain and symptom control measures, without the requirement for transportation of the patient. Thus, the hospice must assure the availability

don't want to sound like we're recommending a high degree of technological care for hospice patients. . . . We do not want to prevent the opportunity for development of care that is not part of hospital care."

Katterhagen responded that JCAH has written certain quality guarantees. "I think we should offer the same thing for patients wherever they are in their journey through life."

Jerome Yates, director of NCI's Centers & Community Oncology Program, said the regulations "were written to take hospice patients out of the mainstream of the practice of medicine. Unless the regulations are broadened, they seem to preclude good palliative patient management. They also allow any physician, regardless of training or background, to sign off for the hospice. I'm afraid that patients can get the short end of the stick in order to do what is expedient for the hospice."

The regulations would not require a registered nurse on duty around the clock but requires only vocational nurses for two of three shifts, Katterhagen said. "It's an illusion that dying patients do not need technology. They do, to make their last days or months comfortable."

NCI Director Vincent DeVita said that Yates would contact HCFA about the Board's concerns, after Katterhagen's request was approved.

AACI ASKS NCI TO FUND CANCER CONTROL DIRECTORS FROM CONTROL LINE ITEM

The Assn. of American Cancer Institutes has gone on record urging NCI and its Div. of Resources, Centers & Community Activities to permit funding of cancer control "scientific leadership" from cancer control funds rather than from money allocated for center core grants.

With the phasing out of cancer control core grants for centers, funds are no longer available from NCI to fund control core activities, including directors of cancer control. The DRCCA Board of Scientific Counselors had recommended that guidelines for cancer center core grants be modified to permit such funding but split over the issue of where the money would come from. DRCCA Director Peter Greenwald and BSC Chairman Lester Breslow took the position that it should not come from the line item cancer control money in the division's budget but rather from funds allocated for centers.

Other DRCCA BSC members disagreed. Final resolution of the issue is in the hands of the National Cancer Advisory Board.

AACI also recommended in its resolution, passed unanimously at the assocation's recent meeting in Memphis, that the present caps on core grants be lifted to permit additional funding for cancer control directors. DRCCA staff and the BSC had offered no objections to that change.

The AACI resolution, offered by Paul Engstrom, said:

"AACI recognizes the important role that cancer centers play in the new directions in cancer control research as delineated by DRCCA and cancer center directors recognize the importance of monitoring and coordinating community linkages and of fostering the community relationships necessary to bring together the resources of the community and the center for implementation of innovative cancer control research. Therefore, AACI recommends to DRCCA: (1) that cancer center support (core) grant guidelines be modified or amended to allow support, in the scientific leadership category, for cancer control research disciplines; (2) that the support should be made available by the National Cancer Institute from funds allocated to cancer control, and (3) that the cap on core grants be raised to allow funding this effort in addition to the existing funding for fundamental or clinical research."

AACI members also approved a resolution objecting to NCI funding plans which will pay competing core grants amounts less than levels recommended by peer review. The current plan is that most new and competing renewals will be funded at approximately 15 percent less than recommended levels. Program directors may make exceptions up to 10 percent either way. The resolution stated:

"AACI strongly urges that competing renewals for core grants and new core grants be funded at levels that more nearly approximate those levels recommended by peer review. If necessary, any administrative reductions should be guided by the peer review priority score, as previously recommended by AACI."

AACI pointed out that since core grant applications are already subjected to a cap which is not applied to any other type of grant, an additional reduction "constitutes double jeopardy for cancer center core grants."

In other actions, AACI:

—Called on NCI, in changing DRCCA's name, to "take into account and name specifically 'centers' as a major component." (Too late—the new name—Div. of Cancer Prevention & Control—has already been submitted to NIH along with the new alignment of the division).

—Commended Director Vincent DeVita and his staff for the favorable findings by the General Accounting Office in its review of the intramural program.

—Recommended renewal of the National Cancer Act.

—Recommended that "the proportionality in center core grants with R01 and P01 support be maintained at a reasonable level."

NCAB ACCEPTS NEW OUTLINE FOR ORGAN SYSTEMS PROGRAM, WITH SOME CHANGES

The full National Cancer Advisory Board accepted the report and recommendations of its Committee for Organ Systems Program, with some modifications, but the discussion left little doubt the Board is still split over some aspects of how the program will be administered once the revisions have been implemented.

Committee Chairman William Powers presented the recommendations drawn up at the conclusion of the weekend meeting which was attended by 11 members of the Board plus William Longmire, member of the President's Cancer Panel, and Virgil Loeb and Charles Moertel, members of the Board of Scientific Counselors of the Div. of Resources, Centers & Community Activities, where the staff that will administer the program is housed.

The Board made a number of changes in the wording of the committee's recommendations as presented by Powers, but the general thrust remained the same. Debate over the recommendations was rambling, and the precise language was left unclear. NCI staff went to the transcript of the meeting later in the week in an attempt to produce a document that complied with the consensus of the Board. This is the Board's recommendation, subject to further refinements by NCI staff and Board members:

- That NCI maintain and operate a strong, multidisciplinary Organ Systems Program.
- That the NCAB Committee for Organ Systems Program (NCAB/OSP) be continued and that this committee will report to the NCAB on the progress of the program. The NCAB/OSP Committee will pay particular attention to the merit review of all OSP activities and to the OSP budget.
- That a single Organ Systems Coordinating Center (OSCC), external to but coordinated with NCI, be established through open competition in response to an NCI RFP for the administration of an Organ Systems Program. The Organ Systems Program will consist of Organ Systems Working Groups targeted to the prostate, bladder, large bowel, pancreas, breast, and any future sites or systems that may be selected.
- That the OSCC shall develop guidelines to initiate, operate, and—when necessary—to terminate individual working groups, with NCAB review.
- That planning for the Organ Systems Program should take place with consideration for the possibility of establishing other working groups as feasible, e.g., upper respiratory tract and central nervous system.
- That the working groups carry out program planning, and develop and stimulate research initiatives. The groups will also hold workshops, seminars, etc. in order to have extensive communication with the scientific community.
- That NCI maintain the Organ Systems Branch to continue to provide support to these working groups.
- That the NCAB reaffirm separation of review from program in the Organ Systems Program.
- That an appropriate mechanism for review of Organ Systems Program grant applications be established, taking note of the multidisciplinary and programmatic nature of these grants. This may necessitate the creation, within the Div. of Extramural Activities of NCI, of a special review group or groups to handle grant applications to the Organ Systems Program.
- That the working groups be informed of all research in their respective areas, including progress of all relevant current and future grants and contracts.
- That the OSCC and the Organ Systems Branch will assist the working groups in this informational overview of all organ system related research supported by the various divisions of NCI, including research in clinical trials.
- That NCI continue to provide funds, through the above mechanisms, for continuing the Organ Systems Program at a level approximately equal to that of the previous funding for the Organ Systems Programs and the Breast Cancer Task Force. NCI will adjust funding, as available, to provide for additional working groups that may be established in the future.
- That the OSCC's funding will be adequate to provide all working groups with the necessary staff and support to carry out their designated missions.
- That the NCAB/OSP Committee will advise the NCAB Planning & Budget Committee regarding budget recommendations.

"Representatives of the NCAB/OSP Committee will work with the director of NCI, OSB staff, and the Board of Scientific Counselors of DRCCA to bring about this transition and will report regularly to the full committee and to the NCAB," the recommendations concluded.

Board member Janet Rowley objected to the implication that the NCAB would continue to have oversight responsibility for the program. "In line with what has been done with our centers committee, I would assume that in a year or so, the DRCCA Board of Scientific Counselors might take over the Organ Systems Program."

"The Organ Systems Program cuts across all divisions," Powers answered. "It's been my experience that each board of scientific counselors has rather narrower purview than the NCAB."

"The boards of scientific counselors have responsibility for budgeting of programs in their divisions," Maureen Henderson commented. "The way this is described, it seems to be an opportunity for continued confounding of the boards of scientific counselors."

Powers referred to the last paragraph of the state-

ment. "I recognize the problem. Our Board's committee will work with the director and staff to prepare for the transition."

Director Vincent DeVita expressed concern about the recommendation's intention regarding the make-up of the working groups. "You don't mean that you insist that the OSCC contract with the same people who are now members of the working groups, do you? The people who win the competition (for the OSCC) should not be restricted in subcontracting for working groups."

Powers responded that that was not the committee's intention.

"I hope that when the program becomes integrated with the other division programs, the decision to change to one or the other organ systems will be the prerogative of the Board of Scientific Counselors and not that of the NCAB," Henderson said.

"That is the meaning we meant to convey," Powers said. "But if it is a change of emphasis, we're (NCAB) concerned."

DeVita agreed that any such decision should be reviewed by the NCAB before it becomes final.

Harold Amos, member of the President's Cancer Panel, supported retention by the NCAB of its oversight function. "I would point out that so far the boards of scientific counselors have not distinguished themselves in moving programs across divisions," Amos said, suggesting that markers research is one such area. "We see things differently than the other boards."

DeVita argued that "there is no better coordinating anywhere than in markers. We put the controlling emphasis in the Div. of Cancer Biology & Diagnosis, and it is very well coordinated."

"We should not confuse the function of the boards of scientific counselors and ours," Sheldon Samuels said. "I don't think we can relegate any responsibility we have to those boards."

Rowley objected to including by name the five organ systems. "We're getting into managerial function," she said. "To define the RFA too narrowly to what our ideas are can be stifling."

Victor Breren answered that description of the new program written by NCI staff following the NCAB's recommendation of last May "makes it a discipline program. I want it to be an organ systems approach."

"But by being too specific, we limit the creativity of the scientific community," Rowley said.

"DeVita suggested that the budget of the program "will wax and wane—hopefully wax—with the fortunes of the Cancer Institute. I wonder if we don't have concurrence here that will allow us to get the RFA out."

Answering Rowley's question about the recommendation which may lead to creation of special review groups in DEA, DeVita said that could happen in some cases, "when we see the need."

The Board's action, following more than a year of controversy over the fate of the four off campus national organ site projects and the Breast Cancer Task Force, makes these significant changes:

1. The headquarters grants to the four national projects will be phased out.
2. Review of all organ systems related grants will be at NIH, either by Div. of Research Grants study sections or review groups at NCI's Div. of Extramural Activities, removing the review function of the external working groups.
3. An external advisory body (the OSCC) will oversee the entire program.
4. A mechanism will be in place for initiation of new groups and termination of existing ones.
5. There no longer will be a specific line item in NCI's budget for organ site related research, except possibly for the OSCC grant (or cooperative agreement, which probably will be the funding mechanism).
6. The working groups will monitor all NCI grants and contracts in their respective areas, not just those they initiate themselves.
7. Recommendations for RFAs, RFPs, and program announcements will come from an external source, initiated by the working groups, with concurrence of the OSCC advisory committee, and directed to one of the NCI boards of scientific counselors.
8. The Breast Cancer Task Force will be administered exactly like the other organ systems programs, with NCI staff integrated into the Organ Systems Branch and the BCTF committee designated as one of the Organ Systems Working Groups.

A few issues may remain in dispute: Whether the NCAB or DRCCA Board of Scientific Counselors will have primary oversight responsibility; and where the review of OSP grants will be done.

The first round of grants initiated by the four national projects to be reviewed by DRG study sections met disaster. Of 34, only three scored high enough to be funded, if the payline is 172, four if it goes to 180. Those grants came before the NCAB last week, and the Board did not make any funding exceptions.

"I agree that program should be separate from review," Powers said in closing the discussion. "But I believe those grants we saw yesterday would have fared better if they had been reviewed by a group which cut across disciplines. Some organ systems grants will require special study sections."

NCAB COMMITTEE CLOSE TO DEFINITION OF QUANTITATIVE RISK ASSESSMENT

The National Cancer Advisory Board's Committee on Environmental Carcinogenesis is at least "one meeting away" from completing its assigned task of writing a definition of quantitative risk assessment, Chairman Sheldon Samuels told the Board last week.

Samuels presented an interim report and noted that the additional meeting will be necessary to "take account of comments received after the last meeting from Dr. (Paul) Deisler (of Shell Oil Co.) and Roy Albert (professor of environmental medicine at New York Univ. and a member of the board of scientific counselors of the Environmental Protection Agency). Both raise the issue of how to use animal as well as human data in the same estimation of human risk. While the use of such data necessarily increases the level of uncertainty in the assessment, the heuristic value of the work may also increase. We are engaged, after all, not in the determination of truth, but in its approximation," Samuels said.

Samuels' report:

The reactivation of the Committee on Environmental Carcinogenesis, and my appointment as its chair by Dr. Pitot and later by Dr. Carter, has come at a particularly turbulent period in the war against cancer. The turbulence rises from the rediscovery that a significant portion of cancer is a cultural artifact, i.e., not genetically based or inherent in natural occurrences but produced by society itself. That portion, therefore, is controllable only by painful social and personal change. Consensus on the magnitude of that portion does not exist and the range of estimates reflects a political polarization. Given our policy function and the synonymity of policy and politics, we are the appropriate body to deal with the cluster of issues of which quantitative risk assessment is only one.

The meetings we have had were, predictably, reflective of trenchant yet broad socio-economic and philosophic issues at the very base of public health policy. There is something especially significant in this regard about quantitative risk assessment. The questions raised in its consideration are answered only by making presumptions about the nature of operative science, the possibility of uncontaminated objectivity, social decision-making based on technical uncertainty, and the choice of methods in the face of the impossibility of satisfactory empirical verification.

Quantitative risk assessment, while it sounds "scientific," is a method understood only by the realization that it is a process of rough approximation regardless of the impression of axiomatic precision lent by its mathematic expression.

The Limitations

In a paper submitted to the Committee by Dr. (Irving) Selikoff, we have outlined for us some of the limitations:

- (Quantitative risk assessment is) expressed in static terms even though a dynamic situation is expressed.
- Current estimates generally are restricted to those few agents for which reliable epidemiological data exists.
- Identification of agents and effects is obscured by latency factors.
- The spectrum of neoplasms is frequently unstudied since we focus on unique associations: angiosarcoma of the liver and vinyl chloride are examples.
- Fragmentary information on the number of people exposed and the general absence of dose measurement.
- The multiple sequential or concomitant exposure to interacting agents are not considered.
- Diagnostic uncertainties leading to underdiagnosis.
- Little is known about intrauterine exposures.

To the Selikoff list, I would add two others: the arbitrariness of the conceptual and mathematic models used in the actual calculation of risks and the unexamined value judgments made in the selection of a model to be used.

The statistical and stochastic biological models, summarized in the work done by Lester Lave for the American Petroleum Institute and submitted by them to the committee, makes very clear the arbitrary nature of estimating the dose/-response function in the current state of the science.

Lave's discussion reminds me of an observation by Bertrand Russell that "...all deliberations and choice, all decisions as to policies demand the validity of causal series whose terms do not and will not exist. For the rational choice depends upon the construction of two causal series, only one of which can be made to exist. Unless both were valid, the choice would have no foundation. The rejected series consists of equally valid causal connections, but the events connected are not to be found among existents. Thus, all statesmanship and all rational conduct of life is based upon the method of the frivolous historical game in which we discuss what the world would be like if Cleopatra's nose had been half an inch longer."

That "the events connected are not to be found among existents" may explain why Charles Brown, in advising the committee, repeatedly made clear (with no contradiction by David Hoel or William Nicholson) that the models cannot be verified. How, then, are they chosen? A series of value judgments are made reflecting the outlook and moral condition of the maker.

Utility

In the past, quantitative risk assessment has been used in various legitimate economic endeavors, e.g., for the insurance industry, but also in attempted cost/benefit analysis by regulators. Thus, many of its uses are in processes, like cost/benefit analysis, which many of us question methodologically and ethically as appropriate decision making tools for environmental or health regulation.

Nevertheless, I would contend that it is a tool worth developing because its application is not limited necessarily to regulation. It could become an essential part of nonregulatory policies for the management of populations at high risk of cancer because of environmental exposure. As the submission from Deisler points out, it can be used by a company in the setting of priorities in the absence of regulation. I have suggested its use as part of a trigger mechanism to select populations for special programs of intervention, including notification, medical screening and educational programs.

Following is Deisler's submission, with minor editing:

In the material I sent you I addressed the question of the assessment and abatement of carcinogenic risk from two different perspectives, that of an organization such as a company acting to abate risk in the absence of regulation (or in the face of inadequate regulation) and that of a regulatory agency seeking to determine what regulation is needed, if any. The

principal difference between the two cases is the capability each has of determining whether a given level of risk is acceptable or not.

A company or other similar individual organization is not in a position to judge the question of acceptability, however good a grasp it may have of the scientific information and analyses relating to a given case. The qeustion of acceptability of any level of risk is a societal one, and regulatory agencies, as an instrument of society, are in a better position (however imperfect it may be) and have at least some mandate to make this judgment. Thus, while companies need and can construct for themselves systematic ways for estimating the level of risk and even of making statements about them and setting priorities for action with a pre-chosen goal for risk reduction in mind, they cannot decide whether a given level of risk is or should be called societally acceptable. My reponse to you is related solely to the perspective of a regulatory agency and its efforts to use quantitative risk assessment in its regulatory work.

First of all, it is my view that a risk assessment must be made at a given point in time, using all the information then available. While such an assessment may lead to conclusions as to what further research is needed in the future, the assessment is needed as part of the regulatory effort then under way and that effort frequently cannot await the outcome of research which may take years to conduct. The results of such research may cause regulations to be modified later, as a result of new regulatory actions.

Assembling and assessing the quality and applicability of available scientific data, the analysis of such data to determine whether a hazard (that is, the potential to do harm) is identified as being likely to exist, the development of the necessary extrapolations of the data (high to low dose and, for observations made with nonhuman species, from animal to Man) or "hazard evaluation" are both scientific activities. Whether conducted by scientists in a research institute, by scientists serving on one of several types of panels, or otherwise, their activities are purely scientific in character. The results should be capable of withstanding review by scientific peers.

Similar assembly of information on the amounts, levels, distributions, routes, etc., of exposure humans may encounter is a scientific and technological activity, and the combination of this kind of information with the results of hazard evaluation is also a scientific and technological activity which should be carried out by appropriate scientific and/or technological people, working through or within appropriate organizational structures. The combination of the results of hazard evaluation with the results of the characterization of exposures leads, in a quantitative risk assessment, to statements of the ranges of risks that sets of exposed individuals may run together with statements of the uncertainties associated with such estimates of the ranges of risk. The state of the art of quantitative risk assessment today usually permits us to achieve no more than this kind of result and often not so much; even the estimate of the "most probable" risk, as a single, credible value relating to a given set of people and the exposures to which they may be subjected is usually not possible because of the uncertainty as to the extrapolation model to use. Nonetheless, this portion of the process of risk assessment must be performed by scientists and technologists who together cover the fields of expertise required, since the actions and judgments involved are purely scientific and/or technological in character.

With the results of the above efforts in hand, the regulator must now decide whether the ranges of risks are societally acceptable or not and, if not, what to do to decrease the levels of risk to the point—considering many additional factors, both technological and otherwise—of being judged acceptable. Typically, requests for public comment in writing or at hearings, together with feasibility and other analyses, provide relevant information for this judgment—and it is a judgment—to be made. In my view, a regulatory agency should be charged with and held accountable for managing the overall process (as distinct from making each and every kind of assessment or judgment) leading up to the final stage in which the acceptability of risk is judged, and, in that stage, should be charged with making the judgment after pulling together all relevant scientific, technological and other factors. It is in an agency's interest to be sure the scientists and technologists are protected from a priori policy influences and to see to it that their results are independently attained in the best atmosphere of objectivity achievable. This assurance must be a management objective of an agency.

There are many ways to organize to achieve the above independence while ensuring that necessary communications take place. Indeed, for an agency to manage the overall process it is not even necessary for all parts of that process to be administratively part of the agency and, in some respects, there are advantages in administrative separation.

The role of research institutes in quantitative risk assessment is one which I touch on only indirectly in the materials I sent to you earlier. Clearly, research institutes working in this field have ample research to do. Such work ranges from chronic testing to establish facts or test hypotheses to the development of better test methods, of better understanding of mechanisms and metabolysis, and work on interspecies translation, as well as work needed to develop better dose-response models based on pharmacokinetic models. The utilization and interpretation of in vitro and in vivo tests and work in related fields such as genetics and immunology, to name only two, are all fit meat for research institutes, as is work on epidemiological methods, biostatistical techniques, etc. Not only is such work needed to advance the art of quantitative risk assessment beyond its current primitive and highly uncertain state, but such work also can produce information of direct utility, either directly or as a byproduct, in renewed risk assessments for regulatory needs. I don't see a research institute having the conducting of risk assessments for specific regulatory purposes as a primary objective, though some of the scientists in such an institute might well become involved in the scientific stages of risk assessment described above.

In summary, I answer the questions you pose in the last paragraph of your letter as follows:

1. . . . "who should do such analyses"—Scientists chosen on the basis of their qualifications and from the fields needed and who work in an atmosphere promoting objectivity and sound scientific independence, yet who can communicate as needed with scientists within the agencies to be sure the questions the agency has are fully posed and responded to.

2. "Is it possible to be general enough in such analyses so as to conceptually and institutionally separate the analytic process from its specific applications?"—Yes, but not to the extent of having a kind of handbook of formulas available to accomplish this purpose. The "separation" can readily be made conceptually, it can be institutionalized, and the institutionalization will help to maintain the correct kind of separation-with-communication.

UNIV. OF SOUTHERN CALIFORNIA SETS COMMEMORATION FOR HEIDELBERGER

A commemoration of Charles Heidelberger will be held Saturday, Feb. 19, at 2 p.m. in the Louis B. Mayer Auditorium on the Univ. of Southern California's Health Sciences campus. The public is invited to attend.

Heidelberger, who died Jan. 18 at the age of 62, was distinguished professor of biochemistry and pathology and director for basic research at the USC Comprehensive Cancer Center.

Speakers at the commemoration will be:

Vincent DeVita, director of the National Cancer Institute; Daniel Dexter, research associate, E.I. du Pont de Nemours' Glenolden Laboratories; and Beppino Giovanella, director of laboratories at the Stehlin Foundation for Cancer Research, Houston.

Also, Toshio Kuroki, Institute of Medical Science, Univ. of Tokyo; Richard O'Brien, dean of the School of Medicine, Creighton Univ.; and Van Rensselaer Potter, Hillsdale Professor of Oncology Emeritus, McArdle Laboratory for Cancer Research.

Following the commemoration, a reception will be held at the Kenneth Norris Jr. Cancer Hospital and Research Institute.

NOTICE REMINDER

Submission of Form HHS-596—Protection of Human Subjects: Assurance/Certification/Declaration

Under current policy, an applicant organization is responsible for certifying, on form HHS-596, that each nonexempt research activity relating to human subjects described in every application has been reviewed and approved by an Institutional Review Board, as required by 45 CFR 46. An HHS-596 form must be submitted with the application, as clearly indicated in the instructions for form 398. However, if the institutional review is unavoidably delayed beyond the submission of the application, enter "pending" on the form HHS-596 and provide an explanation. A followup certification on another form HHS-596 must then be submitted and received within 60 days after the receipt date for which the application is submitted. Any modifications of the research plan section of the application are to be submitted with the followup certification. If the certification is not received within this period, the application will be considered incomplete and will be deferred for a later review.

In the past, staff of the Div. of Research Grants tried to obtain from the principal investigator those HHS-596 forms that did not arrive within 60 days after the receipt date. However, due to limited personnel and heavy workloads, DRG can no longer carry out this practice. It is the responsibility of the principal investigator and the applicant organization to see that the HHS-596 form arrives in a timely manner.

In many instances, the forms arrive late because they are sent to the wrong office. Thus, when the HHS-596 form is not submitted with the completed application, it should be submitted to the Executive Secretary of the initial review group (IRG) to which the application has been assigned for review. Notification of IRG assignment is sent to the principal investigator, except in those instances where NIH is requested by the applicant organization to send notification to a designated official. If the assignment information is unknown at the time a separately mailed HHS-596 form is submitted, it may be obtained by contacting: Project Control Section, Referral Branch, Div. of Research Grants, NIH, Westwood Bldg. Rm 253, Bethesda, Md. 20205.

ANNOUNCEMENT

Cotton-Topped Marmoset Colony

This announcement is being issued to inform investigators of the availability of a colony of cotton-topped marmosets Saguinus oedipus oedipus and a holding facility for experimental animals where researchers can conduct cancer research.

The Biological Carcinogenesis Branch, Div. of Cancer Cause & Prevention, supports a colony of cotton-topped marmosets at Oak Ridge Associated Universities (ORAU) under NCI contract. ORAU operates a breeding colony of the animals, operates a containment holding facility for them, and provides experienced professional and technical personnel who will work with investigators to carry out their protocols.

Individual investigators may request animals and services to conduct studies on cancer research. In return the researchers will be charged a per diem cost of $1.78 per day for adults and $16.50 for experimental newborns held in the nursery. This fee includes housing the animal, collection of specimens and minor surgery. Other services available for a fee are biopsy, necropsy, bone marrow differential count, blood chemistry profile and individual blood chemistry tests.

Investigators interested in making use of this service should contact Dr. Harry Walburg, Director, Comparative Animal Research Laboratory, Oak Ridge Associated Universities, P.O. Box 117, Oak Ridge, Tenn. phone 615-576-4000.

The Cancer Letter _Editor Jerry D. Boyd

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