THE CANCER LETTER INTERACTIVE

Vol. 25 No. 3
Jan. 22, 1999

Price $275 Per Year

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

IOM Report, NCI Clash Over Proposed Change In Tabulating Minority Research

NCI should change the system it uses for tabulation of resources devoted to projects that involve special populations, a panel convened by the Institute of Medicine said in a report released Jan. 20.

The recommendation, contained in the Congressionally mandated study, instantly triggered objections from NCI officials who said the change would create separate tracks for cancer research: one for the entire population, and another for minorities.

The accounting recommendation appears to be the central—and the most controversial—point of the report that urges NIH and its institutes

(Continued to page 2)

In Brief:

With Opening Of New 13-Story Hospital, M. D. Anderson Campus Now 4.1M Sq. Feet

UNIVERSITY OF TEXAS M.D. ANDERSON Cancer Center has opened its new Albert B. and Margaret M. Alkek Hospital, a 13-story building that increases M.D. Anderson's central campus to 4.1 million square feet. More than 120 pediatric and adult patients moved into the hospital on Jan. 9. The hospital contains 198 private rooms that replace beds in an inpatient facility dating from the 1950s, a 26-bed pediatric inpatient unit, an intensive care unit, 26 operating rooms, expanded radiation oncology services, occupational and rehabilitation facilities, and diagnostic facilities and pathology labs. "The Alkek Hospital provides quality facilities that match the expertise of our faculty, staff, and volunteers," said **John Mendelsohn**, president of M.D. Anderson. "This is a hospital that is devoted to caring, integrity, and discovery." The expansion used funds donated by more than 3,000 individuals and corporations, as well as patient revenues. No state-appropriated funds were used for construction, the center said. Vacated facilities are to be renovated over the next several years for offices and outpatient clinics. A steady increase in patients and research grants has driven the need for new facilities, the center said. The center served 65,000 patients last year, compared to about 33,000 patients 10 years ago. Federal grant support to M.D. Anderson has grown by 63 percent in the past five years. In 1998, the center ranked first in the number of grants (164) awarded by NCI. . .

UNIVERSITY OF NORTH TEXAS Health Science Center at Fort Worth announced the formation of an Institute for Cancer Research, and

(Continued to page 11)

Click Here for Photocopying Guidelines

IOM Report: Count Studies Specific To Minorities

(Continued from page 1)

to develop a strategy for studying cancer in minorities and the medically underserved.

Under the current accounting system, funds spent in connection with including minority members in studies are counted as special populations research. Using this system of accounting, NCI spending on special populations research totaled $124 million in fiscal 1997.

Under the system suggested by the committee, only studies that address cancer in minorities would fit under the classification. If this accounting method is applied, the NCI special populations research portfolio in cancer would drop to $24 million, about 1 percent of the Institute's 1997 budget.

"The approach suggested by the report is radically different from ours," said Otis Brawley, director of the NCI Office of Special Populations Research. "We at NCI have been trying to integrate special populations research into every program at the Institute.

"In contrast, this report calls for what amounts to segregation of special populations programs. I, for one, do not believe in 'separate but equal,'" Brawley said to **The Cancer Letter**.

Since the report was mandated by Congress, it could result in legislative mandates and could affect funding. Political interest in the report was immediate. After discussing the 272-page document with the press, several members of the IOM panel were driven to Capitol Hill to meet with the staff of the Labor, HHS and Education Subcommittee of the House Appropriations Committee.

Sen. Arlen Specter (R-PA), who included the mandate for the study in the fiscal 1997 appropriations bill, scheduled a Jan. 21 hearing of the Labor, HHS and Education Subcommittee of the Senate Appropriations Committee to discuss the report.

In other highlights, the report said:

—NIH should formulate a uniform definition of "special populations" with cancer. The definition should not be based on the concept of "race," which is used to imply the existence of biological differences between people of different origins and appearance, and instead rely on the concept of ethnic groups.

—NCI should continue to work with other entities that collect cancer statistics in order to improve data collection capable of yielding better information on cancer in specific ethnic groups and geographic regions.

—NIH should enhance the authority of the Office of Research on Minority Health, while NCI should give greater authority to the Office of Special Populations Research by allowing it to take part in setting priorities for the Institute and by giving it resources to fund programs targeted to special populations.

—NIH should establish a formal system for reporting to Congress on issues related to cancer research in minorities.

The report commended NCI for launching a number of programs, particularly those of the NCI Division of Cancer Control and Population Sciences. "The committee was impressed by the momentum around these issues at NCI," the report said. "In fact, some of the recommendation were already in the process of being implemented before the report was completed."

Controversial Change In Accounting System

The accounting recommendation states:

"NIH should improve the accuracy of its assessment of research that is relevant to ethnic minority and underserved groups by replacing the current `percent relevancy' accounting method with one that identifies studies whose purpose is to address

THE CANCER LETTER

Member, Newsletter Publishers Association

World Wide Web: http://www.cancerletter.com

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg

Editorial: 202-362-1809 Fax: 202-362-1681
PO Box 9905, Washington DC 20016
E-mail: kirsten@cancerletter.com or paul@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724

Subscription $275 per year US, $295 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc.

Founded Dec. 21, 1973 by Jerry D. Boyd

a priori research questions uniquely affecting ethnic minority and medically underserved groups."

At an IOM press conference Jan. 20, Alfred Haynes, chairman of the 15-member committee, said the change in the accounting system is needed to enable NCI to track cancer research and cancer data in the ethnically diverse U.S. population.

"We were asked to study the allocation of resources directed towards minorities and the medically underserved. We were answering that question," said Haynes, former president and dean of Drew Postgraduate Medical School and former director of Drew-Meharry-Morehouse Consortium Cancer Center in Los Angeles.

"We think that they should not include those funds as directed toward minorities unless the study itself is designed to answer questions about minorities. Merely including the numbers is not an answer to the question," Haynes said.

"We are suggesting that there is a better way of answering that question."

Haynes noted that low minority enrollment in NCI-sponsored cancer prevention clinical trials is a persistent problem.

"The absence of minorities in some of these trials—for example the recently concluded tests of tamoxifen to prevent breast cancer in women at high risk for the disease—raises questions about how applicable the results are to the minority populations," Haynes said.

The Breast Cancer Prevention Trial appears to provide a telling example both of the complexity of the problem as well as of the apparent problems in the accounting system proposed by the IOM committee.

Under the accounting system proposed by the IOM committee, NCI would not have been able to count expenses related to participation of non-white women in BCPT as "special populations research" since the trial was designed to answer the question for all women.

To count as special populations research, a trial would have to enroll only members of minority groups. To get an answer about the ability of tamoxifen to prevent breast cancer in a specific ethnic group, the Institute would have to conduct another BCPT, randomize about 16,000 members of a single ethnic group, and spend about $50 million per trial.

Recruitment of minority women for BCPT was no small undertaking. Ultimately, 12,902 women who identified themselves as "white" and 485 women who identified themselves as "non-white" were randomized to receive tamoxifen or placebo.

To recruit this number of women, investigators performed nearly 100,000 risk assessments, finding that white volunteers were at a higher risk of developing breast cancer and were more likely to take part in the trial after going through the informed consent process. Altogether, 61 percent of white women and 35 percent of nonwhite women met the risk criteria. Following informed consent, 24 percent of whites and 16 percent of nonwhites agreed to be randomized.

Ironically, should the Institute ever decide to conduct a four-arm side-by-side trial to answer the question of whether tamoxifen behaves differently in any specific ethnic group than in the population in general, that study would not be asking a question uniquely relevant to a minority group.

Thus, the hypothetical $100-million trial that would be needed to produce the optimal answer to this research question would not fit under the proposed definition of "special populations research."

By law, clinical trials conducted by NIH have to provide data on women and minorities. The 1993 NIH Revitalization Act states that trials should "provide for valid analysis" of data on women and minorities, including ethnic "subpopulations."

This language can be read as a mandate for NIH to generate comparative data on hundreds of small populations. The burden of this requirement was eased when the House and Senate Labor and Human Resources committees exempted NIH from producing statistically significant data on specific populations.

Instead, the agency implementation guidelines require a "valid analysis," defined as "unbiased assessment" of minority data. "A valid analysis does not need to have a high statistical power for detecting a stated effect," the guidelines state.

Committee Members Call For Separate Trials

At the press conference announcing the IOM report, several committee members stated repeatedly that data obtained from one ethnic group does not necessarily apply to another.

"You may very well have to do a separate subset of [BCPT] to have more of the group that you want," said Haynes. "If you don't have enough people in the trial to answer a question about a particular group, you can't count it as having

contributed toward that group. In this case, if you want to get an answer, then you have to do what's required to get the answer."

Gilbert Friedell, director of cancer control at the University of Kentucky Cancer Center and a member of the IOM committee, said additional funds to support studies in special populations would have to be found.

"I guess you might want to ask how important is the question we are asking," Friedell said. "If the question is important, there ought to be funds to support the research. I don't think we ought to think about the limited pie that we are cutting. We are recommending additional support. There is no free lunch. This is not an effort to constrain NCI. We are supporting NCI. You have to ask, what's the question you are asking and how important is it? If it's important to the subgroup you are talking about, then we ought to be studying it. We do all kinds of things with our money in this country."

The Cancer Letter: "In the context of [BCPT], are you suggesting that there should be a second trial, in African American women? Where do you stop?"

Haynes: "I am suggesting that if you want to get an answer to that question, you have to do whatever is necessary to get the answer."

Friedell: "What we are talking about is that you cannot extrapolate from one population to another. It's that simple. If you have a question regarding a specific population, you have to do research on it. We are in favor of research."

Haynes: "If we have not answered your question, let me see if we can come closer to it by saying it depends upon the burden of cancer in that group."

The Cancer Letter: "Given [what the committee report said] about what is race, what is the reason for asking the question? What makes you think that there may be a difference in outcomes in terms of African Americans and overall?"

Panel member Susan Scrimshaw, dean of the School of Public Health at the University of Illinois-Chicago: "What we are saying is that we don't think race is appropriate. We think ethnicity is. What is the evidence? The evidence is the unequal burden of cancer. We have epidemiological evidence that there are differences, and in order to understand those differences, which [exist] between ethnic groups, we are going to need to make these comparisons. The question at this point is based on the evidence of the burden of disease. And if we see differences in the burden of disease between ethnic groups, I think we are morally bound to explore those differences and understand them."

NCI, Advocacy Group Respond

"What's lost in this discussion is that the way to reduce the cancer burden borne by the poor and the minorities is to get them optimal treatment," said Brawley. "Data from NCI-sponsored clinical trials demonstrate that equal treatment yields equal outcomes, regardless of race or ethnicity. Sadly, data from NCI-sponsored patterns of care studies demonstrate that optimal treatment is not available to everyone.

"By focusing so much on the role of ethnicity in cancer etiology, this IOM report contributes to the obfuscation the more pressing problems of uneven quality of care," Brawley said.

The Intercultural Cancer Council, an advocacy group that lobbied Specter to mandate the IOM study, endorsed the report's recommendations.

"This study confirms what we've known all along, that ethnic minorities and the medically underserved have not shared equally in the nation's progress against cancer," said Lovell Jones, co-chairman of ICC and a professor at M.D. Anderson Cancer Center.

Armin Weinberg, ICC co-chairman and director of the Center for Cancer Control Research at Baylor College of Medicine, said the recommendations must be acted upon immediately. Said Weinberg: "We agree with the IOM that the important immediate questions are these: Is there a strategic plan for reducing the number of deaths and suffering from cancer among poor and ethnic minority individuals? And when can results be expected?"

Weinberg was scheduled to testify at Specter's hearing.

The report, titled "The Unequal Burden of Cancer: An Assessment of NIH Research and Programs for Ethnic Minorities and the Medically Underserved," is available from the National Academy Press, phone 800-624-6242, or from the online bookstore at http://www.nap.edu

Report's Recommendations

Recommendations of the Institute of Medicine report, "The Unequal Burden of Cancer":

•The Burdened of Cancer Among Ethnic Minority and Medically Underserved Communities

—NIH should develop and implement across all

Click Here for
Photocopying Guidelines

institutes a uniform definition of "special populations" with cancer. This definitional should be flexible but should be based on disproportionate or insufficiently studied burdens of cancer, as measured by cancer incidence, morbidity, mortality, and survival statistics.

—To further enhance the excellent data provided in the SEER program database, adequate resources should be provided to expand SEER program coverage beyond the existing sites to include high-risk populations for which SEER program coverage is lacking. This expansion should address a wider range of demographic and social characteristics by using consistent nomenclature and a uniform data set and by reflecting the diverse characteristics of the current U.S. population.

—NCI should continue to work with the North American Association of Central Cancer Registries and other organizations to expand the coverage and enhance the quality of the 45 non-SEER program state cancer registries, with the intent of ultimately achieving—together with the SEER program state registries—two goals: 1) a truly national data set obtained through a system of longitudinal population-based cancer registries covering the entire country, and 2) a reliable database for each state to serve as the basis for both the development and the evaluation of cancer control efforts in that state.

—Annual reporting of cancer surveillance data and population-based research needs to be expanded to include survival data for all ethnic groups, as well as for medically underserved populations.

—The committee recommends an emphasis on ethnic groups rather than on race in NIH's cancer surveillance and other population research. This implies a conceptual shift away from the emphasis on fundamental biological differences among "racial" groups to an appreciation of the range of cultural and behavioral attitudes, beliefs, life-style patterns, diet, environmental living conditions, and other factors that may affect cancer risk.

—The committee commends the proposed NCI program of expanded behavioral and epidemiologic research examining the relationship between cancer and cancer risk factors associated with various ethnic minority and medically underserved groups and recommends that these studies be conducted both across and within ethnic groups.

•Overview of Programs of Research on Ethnic Minority and Medically Underserved Populations

—The Office of Research on Minority Health should more actively serve a coordinating, planning, and facilitative function regarding research relevant to cancer among ethnic minority and medically underserved populations across relevant institutes and centers of NIH. To further this goal, the Office of Research on Minority Health should: make criteria for Minority Health Initiative project support explicit; coordinate with other specialty offices (e.g., the Office of Research on Women's Health) by participating in NIH-wide coordination efforts such as the Research Enhancement Awards Program; and ensure that Minority Health Initiative funding does not supplant funding from institutes and centers for research and programs relevant to ethnic minority and medically underserved populations.

—Research and training relevant to cancer among ethnic minority and medically underserved populations should be more adequately assessed and should be increased.

—NIH should improve the accuracy of its assessment of research that is relevant to ethnic minority and medically underserved groups by replacing the current "percent relevancy" accounting method with one that identifies studies whose purpose is to address a priori research questions uniquely affecting ethnic minority and medical underserved groups.

—The newly established program of behavioral and social science research at NCI addresses an area of research that has been neglected in the past. The committee urges that this program of research identify as one of its highest priorities a focus on the cancer prevention, control, and treatment needs of ethnic minority and medically underserved groups.

—Collaborations between NIH and research and medical institutions that serve ethnic minority and medically underserved populations should be increased to improve the study of cancers that affect these groups and to increase the involvement of such entities and populations in scientific research.

—NIH should increase its efforts to expand the number of ethnic minority investigators in the broad spectrum of cancer research to improve minority health research. These efforts should: 1) assess relevant areas of research needs and ensure that trainees are representative of these disciplines and areas of inquiry; 2) determine guidelines for the quality and expected outcomes of training experiences; and 3) maintain funding for a sufficient period of time to assess the impact of training programs on the goal of increasing minority representation in cancer research fields.

•Evaluation of Priority Setting and Programs of Research on Ethnic Minority and Medically Underserved Populations at NIH

—NCI should develop a process to increase the representation of ethnically diverse researchers and public representatives serving on all advisory and program review committees so that the makeup of these committees reflects the changing diversity of the U.S. population. NCI should develop an evaluation plan to assess the effect of increased and more diversified ethnic minority community and researcher input on changes in NCI policies and priorities toward ethnic minority cancer issues.

—The research needs of ethnic minority and medically underserved groups should be identified on the basis of the burden of cancer in these populations, with

an assessment of the most appropriate areas of research (i.e., behavioral and social sciences, biology, epidemiology and genetics, prevention and control, treatment, etc.).

—For NCI to address the needs of ethnically diverse and medically underserved populations effectively, the Office of Special Populations Research (or some other designated entity or entities) must possess the authority to coordinate and leverage programs and resources across the divisions and branches of NCI to stimulate research on ethnic minority and medically underserved populations. This authority can be established by providing such an office with: a leadership role in major NCI-wide priority-setting bodies and special resources to fund programs specifically targeted to these populations, or accountability for the institution-wide allocation of program resources.

—Investigator-initiated research must be supplemented to ensure that the cancer research needs of ethnic minority and medically underserved populations are addressed.

•Advancing State-of-the-Art Treatment and Prevention

—NIH and other federal agencies (particularly the Health Care Financing Administration) should coordinate to address funding for clinical trials, particularly to address the additional diagnostic and therapeutic costs associated with prevention trials and third-party payment barriers associated with clinical treatment trials.

—NCI should continue to work with other appropriate federal agencies and institutional review boards to explore creative approaches to improving patients' understanding of research and encouraging them to provide consent to participate in research. These approaches should address cultural bias, mistrust, literacy, and other issues that may pose barriers to the participation of ethnic minority and medically underserved groups.

—NCI should report on the accrual and retention of ethnic minority and medically underserved populations in clinical trials using a consistent definition for medically underserved populations, including such characteristics as rural versus urban population, insurance status, socioeconomic status, and level of literacy.

—NCI should continue to assess its dissemination practices to identify effective cancer information delivery strategies among ethnic minority and medically underserved populations, revise and implement the strategic dissemination plan on the basis of the results of that research, and institute an ongoing system of monitoring to assess its effectiveness.

•Cancer Survivorship

—NCI should establish a strategic plan to address the cancer survivorship needs of ethnic minority and medically underserved groups, including coordination of an overall research agenda on survivorship and a more structured framework for monitoring knowledge, attitudes, and behavior regarding cancer survivorship.

•Monitoring and Reporting

—The committee recommends a regular reporting mechanism to increase NIH accountability to the U.S. Congress and public constituencies. Such reports should:

—report on data on progress against cancer using the nomenclature "ethnic groups" rather than "racial" groups and include data on medically underserved populations with ethnic group data;

—provide data on the incidence of cancer at several cancer sites, including those cancers that disproportionately affect ethnic minority and medically underserved populations;

—consider as one alternative reporting of mortality data in terms of "potential reduction of deaths," a statistic that is based on the lowest mortality rate among U.S. ethnic groups and that emphasizes the need for cross-cultural studies to ascertain optimally strategies for cancer prevention, treatment, and control;

—link research findings to reductions in cancer incidence and mortality and identify any gaps that may occur in this linkage; and,

—report on developments, such as the number and type of research programs specifically targeted to ethnic minority and medically underserved groups and the contributions of ethnic minority scientists and community groups to the research priority-setting process.

Food & Drug Administration:

ODAC Supports Temodal For Treatment Of Astrocytoma

The FDA Oncologic Drugs Advisory Committee last week recommended accelerated approval of Temodal (temozolomide) Capsules for the treatment of adult patients with anaplastic astrocytoma who have relapsed following treatment with a nitrosourea and procarbazine.

Temodal, an oral cytotoxic, alkylating agent, is part of a class of compounds known as imidazotetrazines. The drug is sponsored by Schering-Plough Corp. (NYSE: SGP) of Madison, NJ.

The committee decided the data presented by the company did not support full approval of Temodal for the treatment of recurrent glioblastoma multiforme in adults.

The recommendation for accelerated approval for anaplastic astrocytoma was based on the surrogate endpoints of time to progression and tumor response rate. Accelerated approval is conditional on the sponsor's completion of clinical trials to demonstrate that these surrogate endpoints translate into tangible patient benefit, such as extended survival or quality

of life. FDA and Schering have agreed on the design of the phase 4 studies, the company said.

In other actions, ODAC:

—Recommended that Busulfex (busulfan) Injection be approved to prepare patients for bone marrow and blood stem cell transplants. The committee recommended approval for use of the treatment in chronic myeloid leukemia.

The company sought approval for a broader set of indications, including acute lymphocytic leukemia, acute non-lymphocytic leukemia, acute myeloid leukemia, non-Hodgkins lymphoma, Hodgkins disease, multiple myeloma, myelodysplastic syndrome, breast cancer, ovarian cancer, and genetic diseases.

The committee said Busulfex Injection, an orphan drug, offers a more accurate regimen than the oral formulation of busulfan, which has been available since the 1960s, the company said.

Busulfex, was developed at MD Anderson Cancer Center and is sponsored by Orphan Medical Inc. (Nasdaq: ORPH)of Minneapolis.

—Did not recommend approval for two therapies: Prograf (tacrolimus), for the profilaxis of acute graft-versus-host disease in allogenic bone marrow transplants,

The drug's sponsor, Fujisawa Healthcare Inc., presented two pivotal studies. The larger of the studies, showed lower survival with in the Prograf arm than in the control arm, which was treated with cyclosporine. The company attributed the difference to an imbalance in randomization that placed patients with more advanced stage disease into the Prograf arm.

Since the smaller study was not sufficiently powerful to exclude a survival deficit, the committee asked the company to produce additional data to explain this discrepancy in outcomes.

—Did not recommend approval for OraTest for detection of early-stage, asymptomatic oral cancer lesions and defining margins for biopsy and surgery. OraTest is sponsored by Zila Inc. (Nasdaq: ZILA).

Temodal: Discussion Of Patient Benefit

Definition of patient benefit and the value of surrogate endpoints were the central issues in ODAC discussion of the Temodal application.

The committee vote on questions related to the recurrent glioblasatoma multiforme indication reaffirmed the following standards in data interpretation:

To begin with, in an 11-1 vote ODAC rejected six-month progression-free survival and overall progression-free survival as principal endpoints for regular approval for drugs for relapsed malignant gliomas.

Then, in a 12-0 vote, the committee said a single-arm uncontrolled study as that the sponsor said demonstrated objective response to treatment as unreliable.

"I am much more reassured by survival per se as an endpoint than progression-free survival," said Jan Buckner, associate professor of oncology at Mayo Medical School. "It's not that controversial in terms of when it occurred."

Buckner, who served as a voting consultant to ODAC, said progression-free survival is an unreliable indicator of benefit in the Temodal studies as well as in brain tumor studies in general.

To begin with, evaluation of patients is complicated by delayed treatment effects from radiation and artifacts from steroids, Buckner said. "There will be a certain percentage of patients who do not have true tumor progression," he said. "We don't know what that percentage is."

Assessment of neurologic worsening—which also considered progression—is complicated because of side effects of concurrent medications, particularly anticonvulsants, delayed adverse effects of radiation, Buckner said. The picture is further complicated by the risk of tumor heterogeneity, which occurs when pioneer differs from secondary glioblastoma.

Investigator bias could cause problems as well, Buckner said. This can materialize two ways. "All of us at some point—perhaps as a benefit of the doubt—decided that this is not necessarily tumor progression," Buckner said. Another sort of bias could occur when physicians have the incentives to put patients on trials.

"When physicians are paid on case by case basis, this provides opportunity for bias," Buckner said. "Endpoints which rely on human judgment are likely to be influenced by human nature, and you cannot completely ignore that aspect of this trial."

In an 11:0 vote with one abstention, the committee said the drug was not approvable for glioblastoma multiforme.

Accelerated approval for anaplastic astrocytoma was another issue entirely. By law, surrogate endpoints that could be reasonably believed to predict patient benefit are regarded as acceptable for accelerated approval, provided that the sponsor

agrees to continue to study the drug.

Here, ODAC was less conservative. The committee voted unanimously for accelerated approval of the drug.

The sponsor sought accelerated approval based on progression-free survival in a single-arm trial, an endpoint FDA generally doesn't recognize. However, the study also demonstrated objective responses that appeared to show improvement over other therapies, agency reviewers pointed out in questions to ODAC.

According to FDA calculations, 6% of astrocytoma patients treated with Temodal had complete responses, and 27% had partial responses. Median progression free survival in that group was 6.64 months.

FDA officials said that before the trial was initiated, the company argued that a phase III study in relapsed anaplastic astrocytoma would not be possible because all patients would have been pretreated with all effective drugs, particularly nitrosoureas and procarbazine.

However, the data presented by the company indicated that 57 of the 143 patirnts in the study had received no prior chemotherapy. Thus, FDA officials concluded that a phase III study would have been feasible after all.

Though the committee voted unanimously for accelerated approval of Temodal, it did not answer the broader question of whether objective response constitutes an adequate surrogate for clinical benefit as a basis for accelerated approval.

Schering has worldwide rights to market temozolomide through a licensing agreement with Cancer Research Campaign Technology Ltd., of the United Kingdom.

Literature Review Key To Busulfex

The Busulfex application by Orphan Medical was based partly on a literature search which confirmed that the amount of drug actually delivered to patients for transplant preparation is variable when delivered via the oral route, the company said.

Data presented to the FDA committee showed that 100 percent of patients received their entire Busulfex Injection regimen. All evaluable patients met the clinical endpoints of profound myelosuppression and clinical engraftment.

No patient with chimeric evidence of allogeneic engraftment suffered a later loss of the allogeneic graft, the company said. The pivotal clinical trials were conducted in a group of high-risk patients with advanced hematologic malignancies, many of whom were transplanted in active disease state.

Data from pharmacokinetic trials of Busulfex also showed that patients received a reliable and consistent dose of the drug, the company said. The pharmacokinetic data also confirmed the dosage of 0.8 mg/kg, infused every six hours for four days beginning seven days before transplant.

The company said no unexpected adverse effects occurred with Busulfex in the clinical trials. All adverse effects reported were consistent with those in patients receiving oral busulfan, and occurred as a consequence of myelosuppression and progenitor cell transplantation.

Veno-occlusive disease, an adverse effect that is often fatal and considered to be dose-limiting with oral busulfan administration, was also decreased in these trials, when compared to the rates associated with oral busulfan reported in the literature, the company said.

The White House:

Justice Department May Sue Tobacco Firms, Clinton Says

The Justice Department is planning to sue tobacco companies to recover the costs to the federal government of smoking-related illnesses, President Clinton said this week.

"Taxpayers shouldn't pay for the cost of lung cancer, emphysema and other smoking-related illnesses. The tobacco companies should," Clinton said in his State of the Union speech Jan. 19.

Clinton said smoking had cost taxpayers "hundreds of millions of dollars" through Medicare and other programs. He said funds recovered would be used to "strengthen Medicare."

The Justice Department said the federal litigation would not seek funds that are to be collected by 46 states in their recent $206 billion settlement with tobacco companies.

The Administration is also said to be planning a proposal for federal tax increase on cigarettes of 55-cents a pack. The proposal would be included in the President's budget request for fiscal year 2000, scheduled to be submitted to Congress on Feb. 1.

"I ask this Congress to resist the tobacco lobby, to reaffirm the FDA's authority to protect our children from tobacco and to hold tobacco companies accountable, while protecting tobacco farmers," Clinton said.

In his State of the Union remarks, Clinton said his budget proposal would include funding to help public hospitals and community and university health centers provide basic care for people who do not have insurance.

Clinton urged Congress to pass a Patient's Bill of Rights that would ensure that all managed care plans provide access to specialists, emergency care, and information on all medical treatment options. He also called for privacy protections on medical records.

Science Policy:

HHS Concludes NIH May Fund Human Stem Cell Research

The Department of Health and Human Services has concluded that a Congressional ban on human embryo research does not apply to research using human pluripotent stem cells, paving the way for NIH to fund research using the cells, which are capable of developing into most of the body's cell types.

In a legal opinion announced Jan. 19, HHS said its Office of General Counsel concluded that the law prohibiting human embryo research does not apply to stem cells because "such cells are not an embryo as defined by statute," according to an NIH statement.

"Moreover, because pluripotent stem cells do not have the capacity to develop into a human being, they cannot be considered human embryos consistent with the commonly accepted or scientific understanding of that term," NIH said. Full text of the statement is available at http://www.nih.gov/news

NIH Director Harold Varmus had sought the legal opinion from HHS after scientists at the University of Wisconsin and Johns Hopkins University isolated and successfully cultured human pluripotent stem cells. Neither project was supported by federal research funds, NIH said.

The Wisconsin scientists derived the stem cells from early-stage embryos donated by people undergoing fertility treatment. The Hopkins scientists isolated the stem cells from non-living fetuses from terminated pregnancies.

The legal opinion said stem cells derived from non-living fetuses fall within the legal definition of human tissue and therefore are subject to federal restrictions on the use of such tissue.

"In view of the tremendous scientific and medical benefits that may result from research using pluripotent stem cells, the NIH plans to fund research using these cells," the Institutes said. "It is essential that the federal government play a role in funding and overseeing the conduct of this research so that all scientists—both privately and federally funded—have the opportunity to pursue this important line of research. Federal funding will provide oversight and direction that would be lacking if this research were the sole province of industry and academe."

The statement said NIH would not fund such research until the Institutes have developed guidelines and an oversight process. NIH plans to convene a special oversight group to review all research grant applications using stem cells, in addition to the existing peer review process.

NIH also has asked the National Bioethics Advisory Board for additional guidance.

Funding Opportunities:

Society To Fund Grants In Women's Health Research

The Society for the Advancement of Women's Health Research plans to award nearly $600,000 in grants to medical school faculty for the next three years, supporting the study of three areas of women's health: cardiovascular disease, mental health and reproductive physiology.

The grants are made possible through a program sponsored by Pfizer Women's Health. Each of three MD, MD/PHD or DO scholars will receive $65,000 per year for three years.

Eligible applicants must have completed clinical training, demonstrate strong motivation, be able to conduct original research involving women's health, and have a university appointment when the grant begins. New faculty members and those working to advance their academic ranking are welcome. Applicants must also have a primary sponsor at their respective institution and may work with an off-site mentor.

Interested applicants may call 800-210-1214 and request the Pfizer/Society Scholars Application Form.

NCI RFP Available

RFP N01-CM-97019-58: Preclinical Pharmacological Studies of Antitumor and Anti-HIV Agents

The NCI Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, is soliciting

organizations having the necessary experience, scientific and technical personnel and facilities to conduct a series of preclinical pharmacokinetic and other pharmacology studies in animals on agents having demonstrated antitumor or anti-HIV activity and considered by DCTD to merit further development. The studies to be performed will include: the development of methodology for the quantitative measurement of test agents and/or metabolites in body fluids and tissues; stability studies of test agents in biological fluids; plasma protein binding determinations; characterization of *in vivo* plasma concentration-time profiles and calculation of relevant pharmacokinetic parameters; determination of test agent levels in samples provided by other DTP contractors; determination of the most effective mode of agent administration to achieve and maintain effective concentrations in body fluids and tissues; bioavailability studies following administration of an agent by various routes; tissue distribution and urinary excretion studies; structural determination of metabolites and/or degradation products of parent agents produced in animals and in model *in vitro* systems (e.g., animal and/or human liver slices, hepatocytes, S9 fractions, and microsomal preparations). Where appropriate, this information will be related to mechanisms of antitumor or antiviral action. The government will supply all animals (mice, rats, dogs, non-human primates), test agents, and radiolabeled test agents. Contractors will be expected to provide all equipment, solvents, reagents and animal facilities needed to conduct this type of work. AAALAC accreditation is highly desirable. It is anticipated that five or six awards will be made, each for a five-year, incrementally-funded completion type contract. Offerors have the opportunity to propose studies at two levels: one compound per year or equivalent or two compounds per year or equivalent. Only one award will be made to an institution. The following Mandatory Qualification Criteria will apply: (1) the Contractor may not be a pharmaceutical or chemical firm since agents of a commercially confidential nature (discreet) may be evaluated; (2) the Contractor must possess a valid NRC license permitting the purchase, storage and use of typical quantities of radioisotopes (e.g., ^{3}H, ^{14}C, ^{35}S) likely to be used in the proposed pharmacological research. SIC for this acquisition is 8731. The RFP may be accessed through NCI's Research Contracts and Acquisition Branch homepage at http://amb.nci.nih.gov/RFP.htm

Contact: Michael Veesart, Contract Specialist, (301) 435-3815, mv64b@nih.gov

RFAs Available

RFA HS-99-001: Measures Of Quality Of Care For Vulnerable Populations

Letter of Intent Receipt Date: Jan. 29

Application Receipt Date: March 15

The Agency for Health Care Policy and Research invites applications to stimulate and support research to develop measures of quality of care for vulnerable populations, including those whose vulnerability is due to demographic characteristics (such as age or race/ethnicity), economic status, illness, disability, or place of residence. Vulnerable populations may be less able than others to safeguard their own needs and interests adequately during rapid health system change, and may incur different health outcomes traceable to unwarranted disparities in their care or stemming from special needs or barriers for care.

AHCPR expects to award up to $3 million in fiscal year 1999 to support the first year of up to 10 projects under this RFA. AHCPR will set aside approximately $1 million of that $3 million to support projects that address quality measures for racial and ethnic minority population groups regarding the six clinical areas identified in the President's Race and Health Disparities Initiative.

AHCPR wishes to assure that new applications build on existing research, as appropriate, and are not unnecessarily redundant with currently supported research. Applicants are encouraged to use AHCPR's Web site at http://www.ahcpr.gov

Inquiries: Al Deal, Grants Management Specialist, Agency for Health Care Policy and Research, 2101 East Jefferson Street, Suite 601, Rockville, MD 20852-4908, phone 301-594-1843, fax: 301-594-3210, email: adeal@ahcpr.gov

RFA RR-99-002: National Stem Cell Resource

Letter of Intent Receipt Date: Feb. 11

Application Receipt Date: March 11

The purpose of this RFA is to solicit applications to establish a National Stem Cell Resource. The resource will be for deposit, maintenance, preservation and distribution of nonhuman-derived embryonic and other stem cells from a variety of species, as well as for deposit and distribution of related reagents and information in order to make these critical research tools available for biomedical research.

Approximately $700,000 (including direct and indirect costs) will be available for this initiative in FY 2000 and for each subsequent year. It is anticipated that one award will be made.

Inquiries: Jill Carrington, Ph.D. Comparative Medicine, National Center for Research Resources, 6705 Rockledge Drive, Room 6164, Bethesda, MD 20892, phone 301-435-0744, fax: 301-480-3819, email: jillc@ncrr.nih.gov

RFA RR-99-003: Integrated Genomics Technologies

Application Receipt Date: Feb. 23

This RFA targets new, innovative, multidisciplinary efforts to develop integrated genomics technologies,

which will lead to the biologists' tools of five or more years hence. The resulting highly integrated technologies will be capable of high-speed serial or highly parallel analyses at a sensitivity level capable of single-cell genomics analysis. Such technologies will enable new levels of understanding of cellular processes and will, for example, permit development of highly specific drugs through screening against in vivo cellular processes. Development of new ex vivo analytical capabilities will permit high throughput analysis of cellular/organelle constituents; single-cell protein and nucleic acid sequencing, including characterization of phosphorylation and methylation states; and single-cell genome expression analysis. Similarly, new in vivo analytical and methodological capabilities will permit: characterization of protein interactions, including protein-protein, protein-nucleic acid, protein-ligand interactions in single cells; in vivo protein and nucleic acid sequencing; the biosynthetic production and self-assembly of intracellular sensors and probes; and single-molecule detection in single cells.

Contemporary genome sequencing and expression studies have suggested the feasibility of our understanding the information encoded in the genome in the context of the cell's protein world. These studies also indicated large gaps in our understanding of the protein constituents of the cell, their local environment, and the quantitative details of the intracellular protein-protein, protein-macromolecule, and protein-small molecule interactions—which together define the material, energetic, and informational flows of the living cell.

It is expected that four to eight awards will be made in FY99, and $4 million will be designated for this purpose.

Inquiries: Karl Koehler, Ph.D., Biomedical Technology, National Center for Research Resources, 6705 Rockledge Drive Room 6160 MSC 7965, Bethesda, MD 20892-7965, phone 301-435-0755, fax 301-480-3659, email: Karlk@ep.ncrr.nih.gov or BTAdir@ep.ncrr.nih.gov

Jeffery Schloss, Ph.D., Technology Development Coordination, National Human Genome Research Institute, Building 38A, Room 614, Bethesda, MD 20892-6050. Phone 301-496-7531, fax 301-480-2770, email: jeff_schloss@nih.gov

James Cassatt, Ph.D., CCB Division, National Institute of General Medical Sciences, 45 Center Drive, Bethesda, MD 20892-6200, phone 301-594-0533, fax 301-480-2004, email: Jc12b@nih.gov

RFA RR-99-004: Advanced NMR Spectroscopy Instrumentation

Letter of Intent Receipt Date: Feb. 17

Application Receipt Date: March 17

The purpose of this RFA is to stimulate advanced TNMR instrumentation development, particularly for liquid phase protein and solid state membrane protein applications, and their effective integration into high-field NMR spectrometer systems. The Small Business Innovation Research program has supported such development efforts; however, the extent of such support has been limited. Recently, the NIH has announced that applicants may request a larger budget and period of support if necessary for completion of the project (See NIH Guide for Grants and Contracts, Feb. 13, 1998, http://www.nih.gov/grants/guide/notice-files/not98-014.html). This RFA provides a means within the SBIR program to more fully accommodate the high expenses involved in such technology development, particularly multidisciplinary staffing, custom-fabrication, and long-term project support through the prototype development stage. A recent report (High Field NMR: A New Millennium Resource; http://www.magnet.fsu.edu/NMRcoll) points out the virtual revolution in biological NMR which would occur if an order of magnitude gain in sensitivity could be achieved, bringing many experiments within the feasible envelope and increasing the throughput of current studies. To accomplish this, it is essential to stimulate innovative new research and development efforts in the following areas: design of 1GHz+ superconducting magnets for NMR spectroscopy, development of flexible probes for such high-field spectrometers, and related preamplifier design.

It is expected that two to six awards will be made in FY99, and approximately $2 million from the SBIR set-aside will be designated for this purpose.

Inquiries: Dr. Abraham Levy, Biomedical Technology National Center for Research Resources, 6705 Rockledge Drive, Room 6160, MSC 7965, Bethesda, MD 20892-7965, phone 301-435-0755, fax 301-480-3659, email: BTAdir@ep.ncrr.nih.gov

In Brief:

James Cancer Hospital Receives $20M Donation

(Continued from page 1)

the addition of cancer to its research priorities, which include aging, heart disease, harmful substances, and human vision. **David Richards** is the center's president. **Ronald Goldfarb**, formerly with University of Pittsburgh Cancer Research Institute, was named director of the new cancer institute. . . . **ARTHUR G. JAMES** Cancer Hospital and Research Institute at Ohio State University received a $20 million donation from **Richard Solove**, a founding board member of the hospital, to support cancer genetics research. . . . **DONALD PODOLOFF**, chairman of the Department of Nuclear Medicine at University of Texas M.D. Anderson Cancer Center,

was named president-elect of the American College of Nuclear Physicians. Podoloff will become president of the organization in February 2000. . . . **SUSAN G. KOMEN** Breast Cancer Foundation presented its 1998 Brinker International Awards for Breast Cancer Research recently in San Antonio. The Basic Research Award honors **Lee Hartwell**, president and director of the Fred Hutchinson Cancer Research Center in Seattle. The Clinical Research Award was presented to **Henry Lynch**, president of the Hereditary Cancer Institute and director of the Cancer Center at Creighton University School of Medicine in Omaha, NE. Each award recipient receives a $10,000 honorarium and citation. . . . **RECORDED CANCER INFORMATION** is now available 24 hours a day, seven days a week, from NCI's Cancer Information Service. Previously, callers to 800-4-CANCER could order publications, learn about FDA-certified mammography facilities, or speak to an information specialist. The new, fourth option is to listen to brief recorded messages about cancer issues. . . . **NEW JOBS AT NCI:** The NCI Division of Cancer Control and Population Sciences, Epidemiology and Genetics Program, is recruiting for chiefs of two new branches, the Analytic Epidemiology Branch and the Clinical and Genetic Epidemiology Research Branch. The positions are at the GS-15 level, with salary range of $77,798 to $101,142, not including physician's allowance of up to $30,000. Closing date for applications is Feb. 26. For application information, contact 301-402-2789. . . . **ROSWELL PARK** Cancer Institute received a $746,964 grant from NIH to renovate laboratory space its Molecular Genetics Program. The grant will be matched by funds from RPCI, and renovations on the 10,000 square feet of space should be finished by the end of 1999. . . . **EDWIN MIRAND**, emeritus vice president for educational affairs and emeritus dean, Roswell Park Graduate Division of the University of Buffalo, will head a new Office of Alumni Relations. The office plans to strengthen communications with alumni and establish the Roswell Park Alumni Association. . . . **NEW JERSEY** Governor **Christine Todd Whitman** and **William Hait**, director of The Cancer Institute of New Jersey and professor of medicine and pharmacology at UMDNJ-Robert Wood Johnson Medical School, are co-recipients of the Medical Society of New Jersey's Person of the Year award. The Cancer Institute of New Jersey achieved NCI cancer center designation in 1996. . . . **GIORGIO TRINCHIERI** was appointed the first Hilary Koprowski Endowed Professor at the Wistar Institute. Trinchieri has been at Wistar 23 years, serving as head of the Immunology Program for the past seven years. . . . **RESEARCH!AMERICA'S** Third Annual Advocacy Award winners for distinguished contributions to medical research include former **Sen. Mark Hatfield** and Today Show anchor **Katie Couric**. Hatfield was honored for Lifetime Achievement as an Advocate for Medical Research. Couric was honored for Impact on Public Opinion Through the Media for colon cancer research advocacy. **Tenley Albright**, with the American Cancer Society, the Whitehead Institute and the National Library of Medicine, was recognized for "exceptional contributions as a volunteer advocate for medical research." **Margaret Mahoney**, for her work on behalf of the Carnegie Corporation and Robert Wood Johnson Foundation, was honored for "sustained leadership at the national level." . . . **NIH OFFICE** of Dietary Supplements has opened the International Bibliographic Information on Dietary Supplements database containing published scientific literature on dietary supplements. The database is available at http://dietary-supplements.info.nih.gov . . . . **DORIS DUKE** Charitable Foundation has established a Distinguished Clinical Scientist Award Program, a $12 million initiative to fund the research teams of four leading scientists studying cancer and other diseases. A Scientific Advisory Council chaired by **James Wyngaarden**, former director of NIH, will oversee the program. The foundation will invite the submission of applications from senior clinical scientists at the 25 medical schools that receive the greatest amount of support from NIH in each of four disease areas. Award recipients are expected to be named in late 1999. . . . **JOSEPH WOELKERS** has joined the H. Lee Moffitt Cancer Center and Research Institute in Tampa, FL, as vice president for Clinical Outreach Programs. Woelkers formerly was president and CEO of Cancer Center from Healthcare Operations International in Atlanta. . . . **NATIONAL GUIDELINE** Clearinghouse, an Internet-based service at http://www.guideline.gov has been opened by the Department of Health and Human Services to serve as a repository for evidence-based clinical practice guidelines. The clearinghouse was developed by the Agency for Health Care Policy and Research in partnership with the American Medical Association and the American Association of Health Plans.

Click Here for
Photocopying Guidelines

Copying Policy for The Cancer Letter Interactive

The software that comes with your issue allows you to make a printout, intended for your own personal use. Because we cannot control what you do with the printout, we would like to remind you that routine cover-to-cover photocopying of The Cancer Letter Interactive is theft of intellectual property and is a crime under U.S. and international law.

Here are guidelines we advise our subscribers to follow regarding photocopying or distribution of the copyrighted material in The Cancer Letter Inc. publications in compliance with the U.S. Copyright Act:

What you can do:

--Route the printout of the newsletter to anyone in your office.

--Copy, on an occasional basis, a single story or article and send it to colleagues.

--Consider purchasing multiple subscriptions. Contact us for information on multiple subscription discounts.

What you can't do without prior permission:

--Make copies of an entire issue of the newsletter. The law forbids cover-to-cover photocopying.

--Routinely copy and distribute portions of the newsletter.

--Republish or repackage the contents of the newsletter.

We can provide reprints for nominal fees. If you have any questions or comments regarding photocopying, please contact Publisher Kirsten Boyd Goldberg, phone: 202-362-1809, email: kirsten@cancerletter.com

We welcome the opportunity to speak to you regarding your information needs.

Click Here for
Photocopying Guidelines