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NCI, IOM Called To Congress To Explain Divergent Positions On Minority Research

Congress had a clear goal when it mandated an Institute of Medicine study on cancer in minorities and the underserved: To separate the science from politics, and to develop a plan that would inform the research agenda and public policy.

A week after the academy presented its report, "The Unequal Burden of Cancer," to NIH officials, Congress, and the press, consensus is nowhere in sight. The authors of the report and NCI officials are locked in a debate over the numbers presented in the report and ethical issues posed by the accounting system the report recommended.

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C. Gordon Zubrod, 84, Dies; Led Chemotherapy Research, Built Cooperative Group System

The origin of the mechanisms of clinical cancer research can be traced to the spring of 1954, when Charles Gordon Zubrod, then an associate professor of medicine at St. Louis University, confronted the worst crisis of his medical career.

Zubrod was on the losing side of a conflict between the Jesuits who ran the university hospital and a contingent of physicians who had been brought in to reorganize the hospital. After the brothers fired his friend, the chairman of the department of medicine, Zubrod left, too.

In the fall, Zubrod came to a basic research institution called the National Cancer Institute. Over the next two decades at NCI, Zubrod, who died Jan. 19 at age 84 at Sibley Memorial Hospital in Washington, DC, shaped the development of cancer chemotherapy. He led a team of young clinician-scientists who demonstrated the efficacy of chemotherapy in the treatment of childhood acute leukemia, resulting in the first long-term remissions of this disease. Their success led to wider development and testing of chemotherapy for other cancers, and increased public excitement about cancer research, resulting in substantial increases in federal funding for cancer research and, indirectly, all biomedical research.

Zubrod's achievements included:

—Establishing the cancer clinical trials cooperative group system, beginning with the Acute Leukemia Group B, started with James Holland.

—Starting a program to recruit clinical associates to NCI.

—Establishing the NCI Leukemia Service and hiring two physicians with similar names, Emil (Tom) Frei III and Emil J Freireich, to run it

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NCI, IOM Committee Spar Over Minority Research Funds

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The report was financed through a transfer of $662,000 from NIH to IOM.

In a nutshell, the report said NCI should refine its estimates of spending on research and training programs addressing cancer in minorities and the underserved. NCI estimates its total investment as $124 million in fiscal 1997, which includes support for programs that are uniquely addressing the problems of minorities, as well as research that seeks to answer broader questions, and is only partially relevant to minorities (**The Cancer Letter**, Jan. 22).

The principal piece of hard data presented in the report is a recalculation of the NIH research portfolio that determines that only $24 million is spent on projects that involve minorities exclusively. The committee recommended that only projects targeted to minority projects should be counted as projects involving special populations.

NCI is advancing a three-pronged challenge to the report:

—First, NCI has never made a secret of its portfolio of targeted research in special populations, Institute officials said. For the past eight years, the Institute has routinely reported such projects to the NIH Office of Research on Minority Health .

—Second, targeted projects add up to $43.9 million, not $24 million, as stated in the report, officials said. Documents obtained by **The Cancer Letter** confirm that a list of projects targeted to special populations was submitted by NCI officials to the IOM committee last January.

—Third, NCI officials said the committee's recommendation that only targeted projects should be counted as special populations research amounts to a call for segregation.

"The critical issue of different burdens of cancer and different experiences of cancer in minorities and the underserved must be pervasive through all of our areas of research," said NCI Director Richard Klausner in Jan. 21 testimony before Sen. Arlen Specter (R-PA). "We want as many studies as possible to include addressing issues of the impact of social, cultural, linguistic, economic and genetic factors in cancer.

"When a large, multifaceted study directly addresses the unequal burden of cancer, we code a fraction of the total research budget costs directed toward minority and underserved research. If, on the other hand, we only counted dollars from projects that solely address questions of unequal burden, we would get a parallel research structure segregated from researchers, projects and programs we support for all cancer.

"I believe this is impractical, it's inefficient, and it's counterproductive," Klausner said. "It would result in our failure to answer many new questions posed by IOM."

Areas of Agreement?

Despite several meetings between IOM committee chairman Alfred Haynes and NCI officials, at Specter's hearing the parties were unable to provide a consistent list of areas of agreement.

While Haynes said NCI was in "partial agreement" with the accounting method recommended in the report, Institute officials said they strongly disagreed with that recommendation.

"There is partial agreement on our analysis of the Institute's allocation of resources to research on minorities and the medically underserved," said Haynes, former president and dean of Drew Postgraduate Medical School and former director of Drew-Meharry-Morehouse Consortium Cancer Center.

"We disagree with the method of analysis with which the Institute accounts for [special populations research] based on the percentage of minorities

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involved in a research study," Haynes said.

"This method triggers criticism that allocation is inadequate, with which NCI disagrees," Haynes said. "But they do agree with our view that it would be better to account for minorities on the basis of whether or not a study is designed to answer questions pertinent to the problem of cancer in minorities."

SPECTER: "Where is the partial agreement? On $24 million? There is disagreement over $100 million? I don't call that partial agreement, but go ahead."

HAYNES: "NCI accounts for research in minorities in two categories. In Category I is research that is specifically directed towards minorities. In Category II there is general research in which minorities may be included. And that is allocated on the basis of a percentage of populations in those studies.

"We feel that allocational basis is not the best way to approach the problem. A better way to approach the problem would be on the research question that is involved… Somehow, when we make that statement, it gets confused with segregated research. We are not recommending that research be segregated. We are recommending that research be done across and within ethnic groups."

SPECTER: "I didn't follow all of your answer, but [let us return to] $124 million versus $24 million. Do you stand by that kind of divergence? Do you think NCI spent $24 million?"

HAYNES: "What they say is clear about the $24 million. The rest of it is not clear, because it is based on the proportion of the people on the study. We want to know, was the study designed in such a way that indeed would give you an answer about a minority population."

SPECTER: "Dr. Klausner, so what did your Institute spend $124 million for?"

KLAUSNER: "Let me give you an example of a study that we code as partial, not 100 percent: the Prostate Cancer Outcomes Study. It's a large, community-based study that is trying to understand the differences in detection, diagnosis and treatment patterns across different groups, different populations. Within that we are asking explicit questions about the difference in treatment among white, Hispanic, and African American men. We calculate that about 10 to 20 percent of the total cost of the project is aimed at directly answering questions about the different burden of cancer. That's an example of partial funding, which would not be allowed in the accounting [recommended by] IOM. The majority of the difference between $24 million and $124 million is exactly these projects, pieces of the projects aimed specifically at addressing the questions relevant to the unequal burden of cancer."

SPECTER: "How much of the balance of $124 million do you account for in that way?"

KLAUSNER: "Based upon the fractions of minorities who participate in clinical trials, the total amount would be $18 million. But even there, about half of that would come from accounting based upon looking at proportional representation in treatment trials. In clinical trials, a lot of [resources are] aimed at efforts to increase the accrual of minorities and the underserved, and efforts to ask specific questions. My understanding in looking at our portfolio and our analysis is that the majority of the difference represents direct investment aimed at the issues raised by the IOM report."

OTIS BRAWLEY, Director of the NCI Office of Special Populations Research: "We are answering two questions here. One is research relevant to minorities, which is what $124 million is. The second is research directed specifically at questions related to minorities. I have here a copy of the document that we provided to the IOM, and if you would like to send your staff over to sift through the box [of documents] provided to the IOM, you will find that in 1997 we said that we [spent] $43.9 million [to fund] 127 [targeted] projects. We provided a synopsis of 127 projects that were directed specifically at minorities. So, I think the question is, why we said $43.9 million, and they said $24 million, and not why we said $124 million, and they said $24 million?"

SPECTER: "Dr. Haynes, what's your evaluation of that explanation?"

HAYNES: "It is our understanding that NIH does this all the time. It's an easy way to give an answer to the question. And I am not sure what is the question you want to answer. But it's an easy way of addressing the question."

SPECTER: "This is a fundamental question. Congress has been very generous with NIH, and we will follow up with the staff as to what resources are being allocated. We want to be sure that minorities and the underserved are fairly treated, and there is a big gap between $124 million and $24 million. What Dr. Klausner is contending, essentially, is that the money is under a different umbrella. I'd like to examine that. You've made a very detailed study,

and let's really find out what the facts are."

NCI, IOM Stand By Their Numbers

The Cancer Letter obtained a document submitted by NCI officials to the IOM committee last year.

The document states that the Institute has been tracking targeted research since 1990. According to the memorandum, dated Jan. 22, 1998, NCI funded 127 grants worth $43,903,168 in fiscal 1997. By comparison, in 1990, NCI spent $12,751,438 to fund 43 projects targeted to special populations.

"I stand by the number we reported to the IOM committee," Brawley said to **The Cancer Letter.** "I have gone over every project targeted to special populations. I was prepared to justify every one of these projects to the committee, and I simply wasn't asked to do so. I am troubled to find no reference to the $43.9 million figure in the report."

IOM officials said they, too, stand by their calculations. "If there is a difference in our calculations and those of NCI, it is a difference in analysis and not of fact," said IOM spokesman Dan Quinn. "We are certainly not backing down from the committee's estimate in any way."

Ironically, the dispute threatens to overshadow the more important point: the majority of the recommendations in the report are not controversial.

"All of us—people on the committee, and people at NCI—agree on the importance of increasing our commitment to special populations research," Brawley said in an interview. "We must move forward, recognizing that special populations research is an integral part of what we are doing and what we should be doing."

Specter: "How much is enough?"

After pledging to get to the bottom of the disagreement between the IOM committee and NCI, Specter moved on to establishing a target for appropriations.

"Whether it is $24 million or $124 million, it's not enough," said Louis Sullivan, former HHS Secretary, president of the Morehouse School of Medicine, and principal investigator with the NCI National Black Leadership Initiative on Cancer.

Following up on Sullivan's statement, Specter turned to another witness, Armin Weinberg, director of the Baylor College of Medicine Center for Cancer Control Research and co-chair of the Intercultural Cancer Council, an advocacy group that successfully lobbied Specter to mandate the IOM study.

SPECTER: "Dr. Weinberg, how much is enough?"

WEINBERG: "We believe there is room in the budget. It's an allocation issue… I am sorry, I frankly was not prepared to comment on the actual number, because I don't think we have the data to describe the answers to that question."

SPECTER: "If you don't know, how am I supposed to know?"

WEINBERG: "You are supposed to know, I guess, by helping us direct the agency to take this question and work with the community to answer the questions: How do we define special populations and the issues? What is relevant research?"

The National Cancer Advisory Board is expected to discuss the IOM report at a meeting Feb. 9-10.

Colleagues Recall Zubrod As Quiet But Strong Strategist

(Continued from page 1)

and develop effective treatments for the disease.

—Developing quantitative methods that remain in use today in clinical trials and cancer treatment, including the phase I, II, and III system, endpoint measurements, the Zubrod scale, and flow sheets.

—Establishing NCI's virus research program.

—Organizing and defending NCI's drug development program.

According to friends, Zubrod preferred to work behind the scenes, quietly shaping the foundations of clinical cancer research. "He would give me credit or others credit that he deserved," said Frei, physician-in-chief emeritus, Dana-Farber Cancer Institute, and the Richard and Susan Smith Distinguished Professor of Medicine, Harvard Medical School. "He rarely put his name on papers."

"He was self-effacing," said Nathaniel Berlin, former deputy director, Sylvester Comprehensive Cancer Center, University of Miami, who succeeded Zubrod as NCI clinical director. "He let many colleagues take credit for what he did. He was a generous man."

"He was quiet. He didn't get enough credit, but he was a strong person behind the scenes," said Vincent DeVita, director of the Yale Cancer Center, who became the director of the Division of Cancer Treatment when Zubrod left NCI in 1974. "All of us owe him a great deal."

"His name wasn't on the papers, but those of us involved in the system afterwards recognized that he was instrumental," said Bruce Chabner, clinical director, Massachusetts General Hospital Cancer Center, who succeeded DeVita as the DCT director.

The Quiet Strategist

To his colleagues, Zubrod was a brilliant strategist who bucked conventional wisdom that held that little could be done about cancer beyond surgery and radiation.

It is difficult to imagine today the view of the medical establishment in the early 1950s toward cancer. In his book, "The Cure of Childhood Leukemia: Into the Age of Miracles" (1995, Rutgers University Press), John Laszlo quotes leukemia treatment pioneer Donald Pinkel, who interned at Children's Hospital in Buffalo in 1951:

"Back then, when we made rounds, if we found that a patient on the ward had leukemia or any other form of advanced cancer, when we got to that room someone would say 'leukemia' and there would be no further discussion. We'd pass by the door and go on to the next patient."

Interesting laboratory findings were emerging using 6-MP and methotrexate, but the drugs were considered too toxic to give patients.

"At that time there were no really good drugs and most people didn't want to do medical oncology because cancer was a surgical disease," NCI Deputy Director Alan Rabson said. "People in internal medicine at the time looked upon medical oncology as a primitive specialty. They looked upon it with disdain."

Zubrod had worked with James Shannon at Goldwater Hospital in New York on the first nationally organized drug discovery program, the search for treatments for malaria during World War II. He had learned that by bringing bright people together to work on a problem, progress could be made, he wrote in his 1997 self-published autobiography, "Stairway of Surprise."

"He came to NCI with a vision that with the proper design of clinical trials and animal models, that progress in the treatment of cancer could occur," Frei said. "That was revolutionary at the time. Most thought the development of science wasn't good enough. He had a lot of opposition."

"One of the great things that Zubrod did was to visualize NCI, including its Clinical Center, as a place where one could have a great range and depth of scientists to do things that could not be done in community hospitals," Laszlo wrote.

"Zubrod pushed chemotherapy into its important place in medicine, not by doing the experiments, but by facilitating the experiments and seeing what had to be done," said Holland, the Distinguished Professor of Neoplastic Diseases at Mt. Sinai School of Medicine.

"He was a giant," said Freireich, director of the Adult Leukemia Research Program at University of Texas M. D. Anderson Cancer Center.

Influenced By Shannon and Marshall

Zubrod, born in 1914 in Brooklyn, NY, was the son of a stockbroker. His mother died of pneumococcal pneumonia when he was eight years old. Growing up in Baldwin, NY, Zubrod's main interest was sports until illness with a bacterial pneumonia ended his athletic ambitions and left him with myopia and, after a two-week hospital stay, a fascination with hospital life. When the Depression hit, his family couldn't afford tuition and he dropped out of College of the Holy Cross. The college president ordered him to return. Years later, he received a bill for the tuition.

Zubrod received a medical degree from Columbia University College of Physicians & Surgeons in 1940, and interned at Central Islip State Hospital in New Jersey, Jersey City Hospital, and Presbyterian Hospital in New York. At Presbyterian, he worked with Michael Heidelberger, the pioneer of quantitative immunology, in research on pneumonia.

In 1943, Zubrod was recruited to military service at Goldwater Hospital to work on the malaria program. Clinical trials were conducted on patients with central nervous system syphilis, who were given malaria to induce fever, then the only successful treatment for syphilis, Zubrod wrote.

"We aimed at giving each patient a hundred hours of fever above 103 degrees Fahrenheit, but this much continuous fever was debilitating, so Shannon's strategy called for interrupting the malaria by drug administration after four days of fever," Zubrod wrote. This allowed for testing the drugs atabrine and quinine. Pharmacologic and clinical studies then produced superior drugs for malaria, chloroquine and pamaquine, he wrote.

At the war's end, Shannon sent the team to medical meetings to present the research, exposing Zubrod to the wider world of clinical investigation.

He abandoned plans to enter private practice and accepted a fellowship in pharmacology and medicine at Johns Hopkins University. It was "a difficult decision to exchange the security of life in medical practice for the uncertainty of a career in clinical research," he wrote.

At Hopkins, Zubrod worked under E.K. Marshall studying penicillin. When penicillin first became available, it was administered every three hours on the assumption that it acted like the sulfonamides, Zubrod wrote. Zubrod compared dosage schedules in treating mice with induced streptococcal infections and found that a 12-hour schedule was more effective. Clinical studies proved the 12-hour schedule was effective in patients.

Around 1950, the Hopkins group organized a committee to discuss the medical, statistical, and ethical issues of proposed trials. Zubrod served as secretary.

"I became thoroughly grounded in the theoretical and practical aspects of the controlled clinical trial, at a time when this approach, although already under way in England, was virtually unused in America," Zubrod wrote. "This experience, combined with what I had learned about the key role of pharmacological disposition studies in the malaria trials, were major determinants in my later career at the NIH."

"The Hopkins Committee, to my knowledge, was the first of its kind in the nation and it was not until the 1960s that similar groups were mandated by the federal government for approval and surveillance of all clinical trials," Zubrod wrote.

"The National Mouse Cancer Institute"

It was with considerable apprehension that Zubrod reported to NCI on Oct. 1, 1954. "Could I adapt to government service after 20 years of university life?" he wrote. "How would I, without experience in cancer research, provide leadership to scientists who had spent a lifetime studying cancer?"

He had been recruited by Shannon, who was scientific director of the Heart Institute (later to become the NIH director), and G. Burroughs Mider, the NCI scientific director. A brand-new hospital, a 500-bed Clinical Center, had just been built at NIH. A clinical research program needed to be developed and staffed.

"I took comfort in Dr. Mider's conviction that the National Cancer Institute had mediocre clinical research and chemotherapy programs and that my leadership in both areas would provide what the Institute lacked," Zubrod wrote.

"My friends at Hopkins teased me about joining a non-clinical group to which they mockingly attached the sobriquet 'The National Mouse Cancer Institute.'"

Zubrod set about to change that view, first by organizing the NCI clinical branches and working with the other Institutes to make the new Clinical Center function more smoothly.

James Holland was at NCI studying acute leukemia, but he was scheduled to leave in a month for Roswell Park Cancer Institute. Methotrexate looked to be effective against leukemia in mice. Zubrod proposed a trial of methotrexate to be conducted at Buffalo and NCI. This was the beginning of the first prospective cancer chemotherapy trial in the U.S. and the first cooperative group, the Acute Leukemia Group B.

Zubrod hired Frei, then age 31, who had been a resident at St. Louis University, to manage the NCI portion of the study. A year later, he hired Freireich, a 28-year-old hematology trainee at Boston University who needed a position at NIH to avoid the doctor draft.

"Zubrod said, 'I see you have training in hematology. Do you know anything about leukemia?'" Freireich said. "I said, 'Of course,' even though I didn't know much. He said, 'I've decided we need to make progress in leukemia, and therefore, you're hired."

As the leukemia studies began, it became clear that quantitative methods were needed to assess the severity of disease, measure response, and specify dose, schedule, and duration of treatment, Laszlo wrote. Zubrod insisted on quantitative measurements in clinical trial designs.

Though positive results came relatively quickly, the NCI physicians had to convince the entire medical profession of the value of chemotherapy.

"At a conference once, a pathologist said finding a drug for cancer was like finding a drug that could dissolve off the left ear and leave the right ear intact," Frei said.

"General medicine thought we were members of the Poison-of-the-Month Club," Holland said. "There was little confidence in chemotherapy."

DeVita recalled attending a seminar Zubrod gave at Mt. Desert Island Biological Laboratory in Bar Harbor, ME, in the summer of 1959. Zubrod spoke about the NCI drug development program. "I

remember being stunned at how hostile the crowd was that there would be any success at random screening," he said. "He deserves a lot of credit for that program, which I would submit has been a great success."

The ALGB conducted 10 trials between 1955 and 1968 which demonstrated the efficacy of combined chemotherapy for acute leukemia, of fresh platelets to control bleeding, and led to multi-agent chemotherapy using the VAMP regimen (vincristine, aminopterin, 6-MP, and prednisone) and other agents.

In 1955, virtually all children with acute leukemia died of the disease. Today about 80 percent of children with acute leukemia are cured.

Freireich gives Zubrod credit for launching him on the work that led to the use of platelets to stop hemorrhage in leukemia patients.

"Zubrod would occasionally come on rounds, and in those days, it could be really an ugly place with blood splattered over the entire room, all over the linens, and the staff," Freireich said. "Zubrod said to me, 'You're a hematologist, why don't you do something about this bleeding.' I took that as an order."

Freireich's work began to show that fresh platelets were effective, but the NIH blood bank would not give him the fresh blood needed, because at the time everyone thought that platelets wouldn't work and might even be harmful.

A grand rounds meeting on blood transfusion was called. "We presented our data, but during the discussion, the director of the blood bank said platelet transfusions were not effective and the bank would not issue fresh blood," Freireich said.

Recalled Frei: "Zubrod got up and said something like, 'Speaking for NCI and patients with cancer currently and in the future, we truly don't know whether we can cure cancer in the near future or if ever, but we are here to try. Progress is going to come incrementally and not all at once, and one hurdle is to control bleeding, and platelets offer the best chance to do that. I plan to support platelet research to get it done.'"

"It took a lot of courage to do that," Frei said.

"Within five years, we had eliminated hemorrhage as a cause of death in 90 percent of the patients," Freireich said. "I always give Zubrod credit for that. He never obstructed research."

"He kept Frei and Freireich out of trouble," said DeVita, who arrived at NCI in 1963. "They were doing what was considered very wild stuff. They needed a distinguished guy like Zubrod over them."

In 1972, the Lasker Foundation recognized Zubrod for his work with a special recognition award for his leadership of chemotherapy research.

Results Begat Research Dollars

Had Zubrod selected any other cancer than acute leukemia in which to test the first chemotherapeutic drugs, progress would have been slow and perhaps even discouraging, holding back the field for years, Berlin said.

"Zubrod's selection of acute leukemia as a target disease turned out to be extraordinarily prophetic on his part," said Berlin. "If you had taken anything else, it would have failed."

The disease had a known marker that could be detected in the blood and bone marrow. "In other tumors, you can only follow whether the tumor shrank or not, and we didn't have good ways of measuring tumors," Berlin said. Also, there were data on the activity of a few drugs.

Cancer research advocates, led by Mary Lasker, persuaded Congress to appropriate $25 million to NCI to expand chemotherapy research in the mid-1950s. NCI formed the Cancer Chemotherapy National Service Center to supply drugs and services to university scientists. The clinical panel of the center decided to provide support for the Acute Leukemia Group B, and form another group to study chemotherapy for Hodgkin's disease, melanoma, and breast cancer. This was the Eastern Solid Tumor Group, and Zubrod was the chairman. Proposals began to pour in from universities for other cooperative groups, Zubrod wrote.

Zubrod also served as chairman of an Experimental Design Committee to review and approve each study protocol. "This enabled us to insist on adherence to the principles of the controlled clinical trial, including ethical standards, for cancer studies throughout the United States and I believe later similarly influenced clinical research generally," Zubrod wrote.

When Ken Endicott became the NCI director, Zubrod succeeded Mider as the NCI scientific director, and Berlin became the clinical director. Zubrod now controlled the Institute's intramural program budget.

"In 1961, I decided to take a major initiative in using NCI's resources to attempt cure of acute leukemia in children, because I reasoned that with

five highly active drugs, this goal was within reach," Zubrod wrote. "My experience with the rapid success of the malaria program, when the top scientists in the country worked together intensively, led me to choose this approach as a model."

Zubrod formed a Leukemia Task Force and served as chairman. Among its many contributions, the task force followed up leads from the NCI drug screening program and developed the method of translating drug dosage from animals to humans using body surface area measurement. Later, task forces for other cancers were formed.

Zubrod also worked with pharmaceutical companies to develop cancer drugs, first by issuing contracts to the firms. "Ours is the only responsibility in the country for drug development [in cancer]," he said at a public meeting in 1974. "The pharmaceutical houses are not seriously involved in developing new anticancer drugs" (**The Cancer Letter**, May 10, 1974).

The results in acute leukemia were picked up by Lasker and other advocates and used to persuade Congress to pass the National Cancer Act of 1971.

After a reorganization of NCI, Zubrod became director of the Division of Chemotherapy, which in 1972 was renamed the Division of Cancer Treatment.

Zubrod's view of the clinical trials cooperative groups 20 years after the first group began is reminiscent of more recent statements about the system. At a meeting of the NCI Cancer Treatment Advisory Committee in 1974, Zubrod said:

"A plurality of efforts is not necessarily wrong, since no single group has a monopoly on good ideas regarding therapy. What is unfortunate is the existence of overlaps, the absence of standard protocols for identical disease situations, the dispersion of already limited clinical resources, the lack of uniform definitions and data reporting techniques, poor coordination and inadequate exchange of information, all leading to...decreased operational efficiency" (**The Cancer Letter**, May 3, 1974).

Move To Miami

By 1974, with four of his five children in college at the same time, Zubrod began to worry about his finances, he wrote. Also, Frei said, Zubrod began to tire of the administrative duties.

He accepted an offer as director of the cancer center at the University of Miami. When he arrived, however, he found that despite an NCI grant, "a cancer center did not exist," he wrote. "The existing faculty parceled out the funds to continue their usual activities without a coordinated strategy aimed at increasing research potential."

Said Berlin: "I don't think it was a happy period of his life scientifically or administratively. They weren't prepared for him, they didn't give him what he needed."

Zubrod wrote that by the time he retired, the center's laboratory research had "improved markedly," resulting in increased funding. "Clinical research, so close to my heart, to my disappointment, never prospered."

However, Zubrod was instrumental in describing the need for a unified clinical facility to a potential donor, Court Sylvester, who donated $30 million to the center, which was renamed the Sylvester Comprehensive Cancer Center. The new facility opened shortly after Zubrod retired in 1988.

Zubrod moved back to Chevy Case, MD, in 1990, due to his wife's advancing Alzheimer's disease. He was an active member of the Church of the Little Flower and visited his wife every week at a nursing home.

"He was a deeply religious man who was concerned about people, ethics, and morality," Rabson said. "He was a good person. He was very kind."

"He was a very gentle man," Frei said. "He was soft spoken. He did not like confrontation, but if he had to, he could confront.

"He had the major influence on my career," said Frei. "He was a friend."

Zubrod's wife of 58 years, the former Christina Catherine Mullins, died in 1998.

Zubrod is survived by two daughters, Christine Craun and Margaret Mary Fleury, both of Bethesda, MD; three sons, Gordon, of Camp Hill, PA, Justin, of Chicago, and Stephen, of Omaha; 18 grandchildren, and three great-grandchildren.

A Mass was held Jan. 22 at the Church of the Little Flower. Memorial contributions in his name may be made to the Brooke Grove Foundation Sharon Nursing Home, 18100 Slade School Rd., Sandy Spring, MD 20860.

Editor's note: Zubrod's self-published autobiography is out of print, but another printing is being planned. To be placed on a list of those interested in ordering a copy, contact Kirsten Goldberg at The Cancer Letter, tel: 202-362-1809, fax: 202-362-1681, email: kirsten@cancerletter.com

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