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Program Project Scores Have Compressed, Review Should Return To Rank Order: Broder

NCI's peer review system for program project grants (P01s) should be changed from ad hoc review of separate grant applications to one that compares and prioritizes all applications, NCI Director Samuel Broder said to the National Cancer Advisory Board last week.

Broder asked the Board for its advice on how NCI should evaluate and fund P01s given budget restrictions that tend to emphasize funding of

(Continued to page 2)

In Brief

Former ICCCR Staff Form International Marketing Firm; M.D. Anderson Names New Professorships

TWO FORMER STAFF members of the International Council for Coordinating Cancer Research have formed a marketing communications firm serving international non-profits in the fields of health, environment, and education. Founding partners of EuroAmerican Communication Inc. are **Sallie Slate**, former communication director for ICCCR, and **Corinne Servily**, former ICCCR director. The firm, based in New York City, combines the experience of Slate, a public relations professional who previously worked on health care for Burson-Marsteller Public Relations Agency, and Servily, who worked for six years for Europe's largest private cancer research organization, the French Assn. for Research on Cancer. EuroAmerican Communication will offer information and research services, publications and graphic design, fund raising, and public, press, and government relations. . . . **M.D. ANDERSON** Cancer Center named receipients of two newly created professorships. **Walter Hittelman**, professor of cell biology, was appointed to the Sophie Caroline Steves Professorship in Cancer Research, and **Raphael Pollock**, deputy chairman of research in the general surgery department, was named to the R. Lee Clark Professorship, funded by the Rogers Bros. Foundation. . . . **ROSWELL PARK** Cancer Institute appointed two new physicians to its staff: **Peter Aplan** and **James Spellman**. . . . **CLIFFORD SCHOLD** has been named chairman of neurology at Univ. of Texas Southwestern Medical Center at Dallas. Schold was professor of neurology at Duke Univ. Medical Center. . . . **JOHN MINNA**, director of the Harold Simmons Comprehensive Cancer Center at UT Southwestern Medical Center, received the C. Chester Stock Award at the Memorial Sloan-Kettering Cancer Center's academic convocation. . . . **ELLEN VITETTA**, director of the Cancer Immunobiology Center at UT Southwestern, received the first Abbott Laboratories Award in clinical and diagnositic immunology.

Broder Seeks Prioritization Of P01s; NCI Gives P01s 'Special Attention'

(Continued from page 1)
smaller grants such as the traditional research project grant (R01).

Vowing to "lay out the facts" about P01s, Broder presented data collected over several months by a special working group of NCI staff. The group compiled an extensive review of P01 funding.

"You can look at these facts and people of good will can come to totally opposite conclusions," Broder said.

"You can conclude from the facts that the program project is doing fine, and in comparison to the difficulties of other mechanisms such as traditional R01s, is getting special consideration," he continued. "Or you can look at the same set of facts and conclude that we are destroying the most important mechanism known to Western civilization."

Later, he said, "By no definition do the facts support the view that we are destroying the P01 program."

Score Compression Phenomenon

Prior to 1987, P01s were reviewed by two chartered review committees, similar to the review of R01s, except that NCI rather than the NIH Div. of Research Grants controlled the P01 study sections.

In 1987, the NCAB approved an NCI working group's recommendation to discontinue the chartered committees and use instead a "single tiered" system in which the site visit team would conduct the entire review. NCI staff said this would eliminate "poor information transfer" from the site visitors to the chartered committee, a problem that was attributed mainly to the workload on NCI staff. The only dissenting vote on the NCAB was cast by then-board member Louis Sullivan, now HHS secretary (**The Cancer Letter,** Feb. 13, 1987).

Later that year, the NCAB approved the new P01 review guidelines in which special committees would be convened to review one or a few closely related applications. Sullivan suggested that the new system be approved on a trial basis (**The Cancer Letter,** May 29, 1987).

Among the findings of NCI's most recent analysis of the P01 program was that the P01 priority scores given by review groups have been compressed closer to the highest possible score of 100 since the advent of the new review system.

In 1988, the top 25 percent of P01 applications scored better than 150; in 1992, the top quartile scored better than 130. **[See charts, pages 6-7.]**

The score compression could be due to two factors, Broder said. "One is that the peer review committees have in their minds...a priority score that they wish to give to a grant that they want funded versus not funded. They therefore chase an imaginary payline.

"Alternatively, you could argue that the P01s have become more important, are better scientifically, and therefore, it is a fair statement that priority scores have to become compressed," he said. "If this trend continued indefinitely, we would have all grants falling within 100 to 110."

"We Need Rank Orders"

Broder said the current review system "is analogous to having a search committee for a new dean and asking different ad hoc groups to review each candidate individually, with no interconnection, and forbidding, in fact, direct communication among the many search teams. We need to have peer review give us rank orders."

NCAB member Sydney Salmon, who initiated the discussion of the P01 funding issue in previous Board meetings, said NCI should return to chartered study section review of P01 applications.

"The dissolution of the study sections in NCI was not a good idea," Salmon said to **The Cancer Letter.** "The clinical P01 study section functioned very effectively. The reason the system was changed was that it was felt that there were so many differences among applications that it was too difficult for one committee to review. It's difficult, but not impossible. Unless they have a study section, they have no way to develop some form of rank order."

As far as overall attention to P01s, Salmon said he was "encouraged by the Institute's support for the mechanism, and I hope they focus on its optimal use, particularly for translational research."

In the Board meeting, Salmon noted that basic researchers could use the new interactive R01 mechanism, which provides for limited shared resources.

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Henry Pitot, new member of the President's Cancer Panel, said, "Clearly there are some reasons why some basic research has to be through P01s. You can't make a generalization."

Board members ruled out a dollar cap on P01s.

To Seek Advice From BSCs

Later, Broder told **The Cancer Letter** that NCI executives will discuss the P01 issue with the divisional Boards of Scientific Counselors to get their advice on "how to get around the issue of each review being specific for each application."

In addition, he said, "We will ask peer review to take a close look at the number of projects and number of subprojects proposed in each application for their scientific appropriateness. We don't intend to limit the number of projects, but we want to make sure they are appropriate. Sometimes we have a substantial number of subprojects [in each application]."

Broder noted that three-quarters of P01 funding is allocated to translational P01s. "We will always protect and defend P01s."

The Institute's new mechanism of interactive research project grants (interactive R01s) also needs time to become fully operational, and could take some pressure off the P01 program. The IRPGs involve three related R01s that do not require extensive core support.

The Institute expects that there will be about 25 sets of IRPGs reviewed and funded by next June, at which time NCI staff would evaluate the program.

"We also expect the SPORE program [Specialized Programs of Research Excellence] to be a relief mechanism," Broder said to **The Cancer Letter.** "There will be $17.5 million of new money in that program" which will fund centers for prostate, lung, and breast cancer. Some P01s may be incorporated into those awards, he said.

NCI recently released a Request for Applications (RFA) seeking P01 applications in gene therapy, Broder noted. "The P01 is an excellent mechanism, and the only way to get certain things done. We were able to establish a meaningful gene therapy program. It would be difficult to conceive of any gene therapy research getting off the ground using the R01 mechanism."

"The Facts About P01s"

Following are the statistics Broder presented:

Every institute is given a target of research project grants (RPG) it is expected to meet each fiscal year. However, an R01 counts as one unit, while a P01 also counts as one unit, even though it may be five times as expensive.

▶The number of NCI research project grants has increased since from 3,060 in FY 1988 to 3,346 in FY 1992. The total number of P01s was 159 in 1988, and is expected to be 177 in 1992. Competing P01s rose from 45 to 48 in the same time period.

"If you just looked at this, you could not conclude that the P01 program is being savaged," Broder said.

The following data only focus on R01s that go through standing study sections, the traditional R01s; it does not include FIRST awards or other RPGs.

▶NCI funded 2,300 traditional R01s in 1988, compared to 2,073 in 1992. Competing R01s fell from 698 to 594 during that time.

▶Funding commitments: P01 funding rose slightly, from $170 million in 1988 to $202 million in 1992. In comparison, funding for all research project grants rose from $665 million in 1988 to $876 million in 1992.

"Clearly, P01 growth has not kept pace with RPGs as a whole," Broder said. In the competing P01s, NCI spent $52 million in 1988 and $53 million in 1992. "That is roughly flat. I view this as bad news. There was not appropriate growth in the P01 program."

▶R01 funding: In 1988, NCI spent $368 million on R01s; of that, $115 million was for competing R01s. The 1992 estimate is $424 million, of which $122 million is for competing R01s.

▶Average cost of an R01 grew from $158,000 in 1988 to $205,000 in 1992. For RPGs as a whole, average cost rose from $218,000 to $262,000 during that time.

"This in part reflects that it is more expensive to do research," Broder said. "The costs really do exceed inflation."

▶Growth in average cost of a P01 has been kept down, from $1 million in 1988 to $1.1 million in 1992. "This is some bad news," Broder said.

▶Percentage change: R01s have grown by about 30 percent since 1988, RPGs as a whole grew 20 percent, and P01s only grew 7 percent.

▶For every percentage increase of growth in the P01 program, there are 10 R01s that will go unfunded, Broder noted.

▶Success rate, defined as number of funded applications versus the number received, is consistently higher for P01s than for R01s. In 1992, the success rate for P01s is expected to be 57 percent, while the success rate for R01s will be 31 percent.

"You could either conclude that we are giving special attention to P01s or you could conclude that P01s, because of their synergistic, collaborative, and translational value, and because of the inherent excellence of people who are in P01s deserve a

success rate of 57 percent," Broder said.

▶In 1988, P01s were funded through a priority score of 150, in priority order. "If you got a score of 150 or better, you got your P01 funded," Broder said. "And even if your score was below 150, you had a good chance of being funded, even down to a priority score of 190."

In 1991, there was a shift. Twenty-five awards were made in the upper quartile, which fell at the priority score of 130. However, NCI funded 19 awards that were below the score of 130. This funding by exception picked up 15 awards that fell in the second quartile and four awards that fell in the third quartile.

▶Percentage of recommended dollars funded. In 1991, the upper quartile of R01s received 90 percent of the funding recommended by peer review. A few R01s were funded by exception that fell in the second quartile, and these received 83 percent of recommended funding.

P01s in the upper quartile, got 90 percent of recommended funding. The P01s funded by exception in the second quartile received slightly less than 75 percent of recommended funding, and the four awards that were funded from the third quartile got about 45 percent of recommended funding.

▶NCI will fund 48 competing P01s in FY92. If they were taken in rank order and fully funded, the Institute would be able to fund only 32 P01s, Broder said.

Broder concluded: "One interpretation is the P01s are in trouble. Another interpretation is, having said that, the Institute has made a special effort to keep P01s going, makes a special effort to reach P01s that are in a lower quartile that would not normally be fundable, and we will do the very best we can to keep P01s functioning."

Translational Vs. Basic P01s

Marvin Kalt, deputy director of NCI's Div. of Extramural Activities, presented additional data at the NCAB's Planning & Budget Committee meeting:

▶Translational vs. basic research P01s. As of June 1, 72 percent of P01s awarded (95 grants), were for "translational" research, which NCI defines as research that moves from the lab to the clinic. The rest, 28 percent (57 grants), were for basic research.

▶Funding order. Three-quarters of all P01s, or 73 percent (111 grants) were funded by rank order. The other 27 percent (41 grants) were funded by exception.

Of the 56 basic research P01s, 90 percent were funded by rank order, while 10 percent were funded by exception. Of the translational research P01s, 60 percent were funded by rank order and 35 percent were funded by exception.

▶P01s funded by rank order received 86 percent of peer review recommended dollars whether they were translational or basic P01s. Basic P01s funded by exception received 76 percent of recommended dollars, while translational P01s funded by exception received 66 percent of recommended dollars, a different Kalt said was not significant.

▶Average total cost of awards per year per grant was $753,000 for basic P01s paid in rank order, $703,000 for basic P01s paid by exception, $1.479 million for translational P01s paid in rank order, and $819,000 for translational P01s paid by exception.

▶Average number of cores and projects in funded P01s: There were an average of 5 projects in basic P01s funded in rank order, 1.6 cores in those funded in rank order, 4.3 projects in those funded by exception, and 1.5 cores in those funded by exception.

In translational P01s, there were an average of 5.8 projects and 3.6 cores in those funded in rank order, and 4.1 projects and 2.5 cores in those funded by exception.

▶Total cost per project, including prorated core costs: Basic P01s funded in rank order received $151,000, while those funded by exception received $162,000. Translational P01s funded in rank order received $260,000, while those funded by exception received $201,000.

▶Distribution of P01 dollars by NCI operating division: The Div. of Cancer Treatment received 44 percent of P01 dollars, while the Div. of Cancer Etiology received 25 percent, the Div. of Cancer Prevention & Control received 16 percent and the Div. of Cancer Biology, Diagnosis & Centers received 15 percent.

▶NCI led all other NIH institutes with 165 active P01s in FY 1991, followed by:

--National Heart, Lung & Blood Institute: 125.

--National Institute of Neurological Disorders & Stroke: 84

--National Institute on Aging: 68

--National Institute of Allergy & Infectious Diseases: 67

--National Institute of Child Health & Human Development: 65

--National Institute of Diabetes & Digestive & Kidney Diseases: 55

--National Institute of General Medical Sciences: 42

--National Institute on Deafness & Other Communication Disorders: 23

--National Institute of Environmental Health Sciences: 18

▶Accordingly, NCI led the other institutes in dollars awarded to P01s in FY 1991, with $190 million. Followed by: NHLBI: $153 million; NINDS: $72 million; NIA: $54 million; NIDDK: $48 million; NICHHD: $47 million; NIAID: $44 million; NIGMS: $28 million; NIDCD: $22 million; NIEHS: $14 million.

▶NCI was second in percent of the research project grant pool funding allocated to P01s. The National Institute on Aging devoted 28 percent of its RPG dollars to P01s in FY91, while NCI devoted 24 percent.

▶Distribution of P01s across programs, as of last June:

Div. of Cancer Treatment: 5 projects, $6.5 million in Biochemistry & Pharmacology; 8 projects, $8.7 million in Biological Response Modifiers; 32 projects, $44.3 million in Clinical Oncology; 8 projects, $7.2 million in Diagnostic Imaging; 15 projects, $18.2 million in Radiation; 1 project, $332,049 in Surgical Oncology. Total 69 projects, $85,312,090. Average P01 cost $1.236 million.

Div. of Cancer Prevention & Control: 1 project, $1.8 million, in Cancer Control; 4 projects, $5.3 million in cancer prevention; 9 projects, $20.34 million in Cancer Control Science; 3 projects, $2.18 million in Nutrition; 1 project, $1.5 million in Chemoprevention. Total 18 projects, $31,149,828. Average P01 cost $1.73 million.

Div. of Cancer Etiology: 19 projects, $20.56 million in Biological Carcinogenesis; 15 projects, $12.66 million in Chemical & Physical Carcinogenesis; 9 projects, $9.6 million in Epidemiology; 2 projects, $2.6 million in Low-level Radiation; 2 projects, $2.8 million in Nutrition. Total 47 projects, $48,187,184. Average P01 cost $1.025 million.

Div. of Cancer Biology & Diagnosis: 3 projects, $3.75 million in Diagnostic Research; 9 projects, $6.7 million in Immunology; 20 projects, $18 million in Tumor Biology. Total 32 projects, $28,629,519. Average P01 cost $895,000.

Definitions. The NCI working group defined a basic P01 as "one in which the intent is to focus on discovery of new phenomena or to elucidate fundamental mechanisms (for example, at the cellular, subcellular genetic or molecular level) that do not have immediate linkage within that specific project to application in humans within the projected full-term award period." Preclinical translational projects were defined as "a mixture of basic and preclinical science where the basic science projects are related to one or more preclinical projects in the same grant and to an overall intent clearly leading to testing and/or application in humans, in areas such as prevention, control, diagnosis, intervention, treatment, or cure of cancer."

Clinical translational projects were defined as "a mixture of clinical, preclinical and perhaps basic research projects where overall there is a direct focus and intention towards applications of clinical relevance, either within a given project or within other directly related clinical projects in the program; to prevention, control, diagnosis, intervention, treatment or cure of cancer in humans."

Since the analysis demonstrated that only 17 percent of translational program project dollars were in preclinical grants, the translational data was aggregated into a single category.

Broder Urges Slow-Accruing Trials Be Pulled From High Priority List

Three clinical trials designated "high priority" by NCI and its cooperative groups are accruing patients so slowly that they should be removed from the special program, NCI Director Samuel Broder said to the National Cancer Advisory Board last week.

Southwest Oncology Group Chairman Charles Coltman presented data to the Board on the three trials, which are:

--Bladder intergroup study INT-0080, accruing patients at less than half the anticipated rate and will require accrual until 1995.

--National Surgical Adjuvant Breast & Bowel Project breast study B-21 (occult stage 1 disease), expected to complete accrual by 1999.

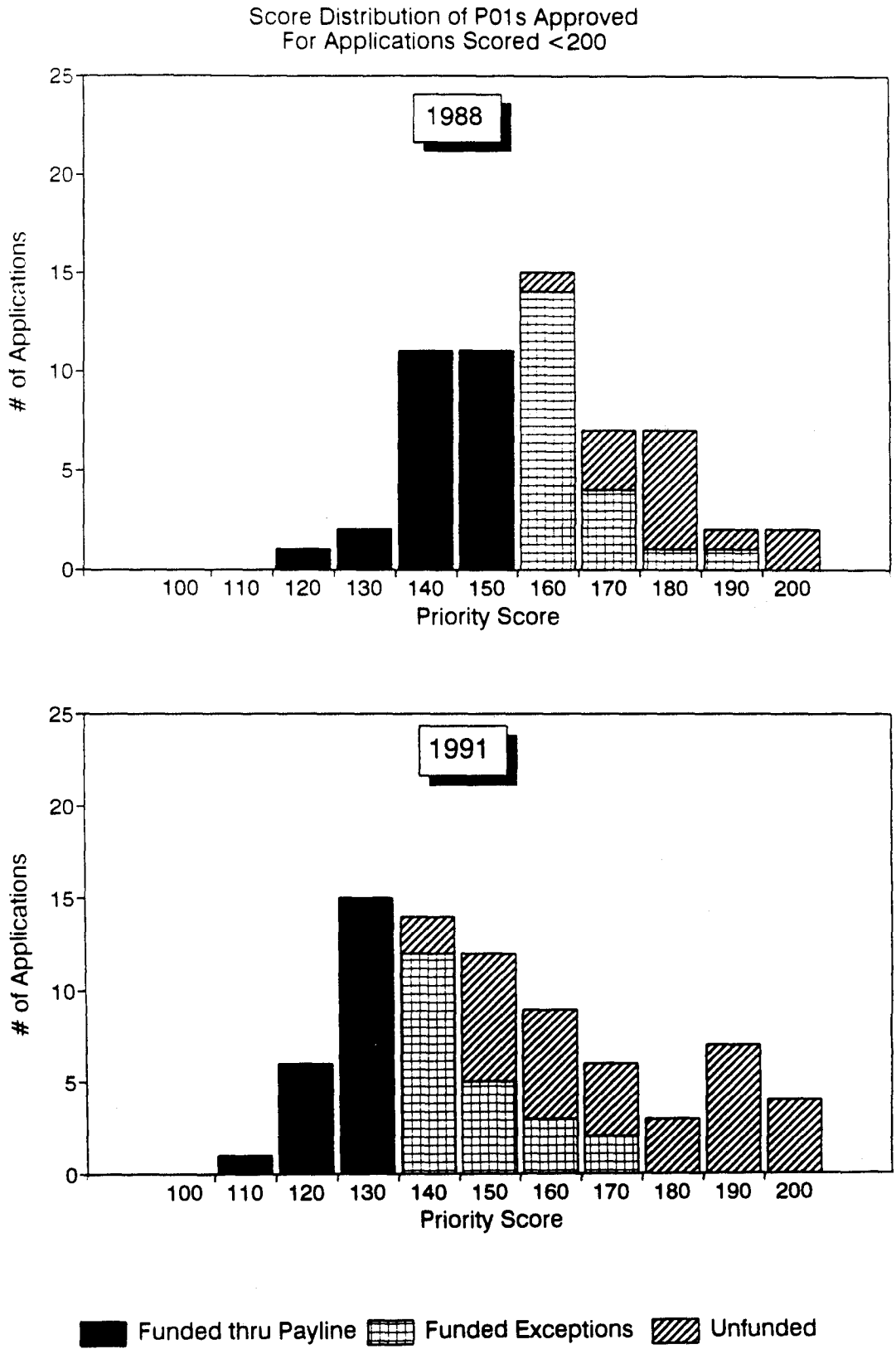
--Eastern Cooperative Oncology Group study 3886, assessing hormonal therapy in prostate cancer, has been accruing patients since Feb. 1988, and at the current rate will require another 16 years of accrual.

"I urge any study that requires seven to eight years to accrue patients to be pulled," Broder said. "I have a self-interest. I will be dragged to a Congressional committee to explain why it's taking so long. We have to do triage for clinical trials like we do everything else."

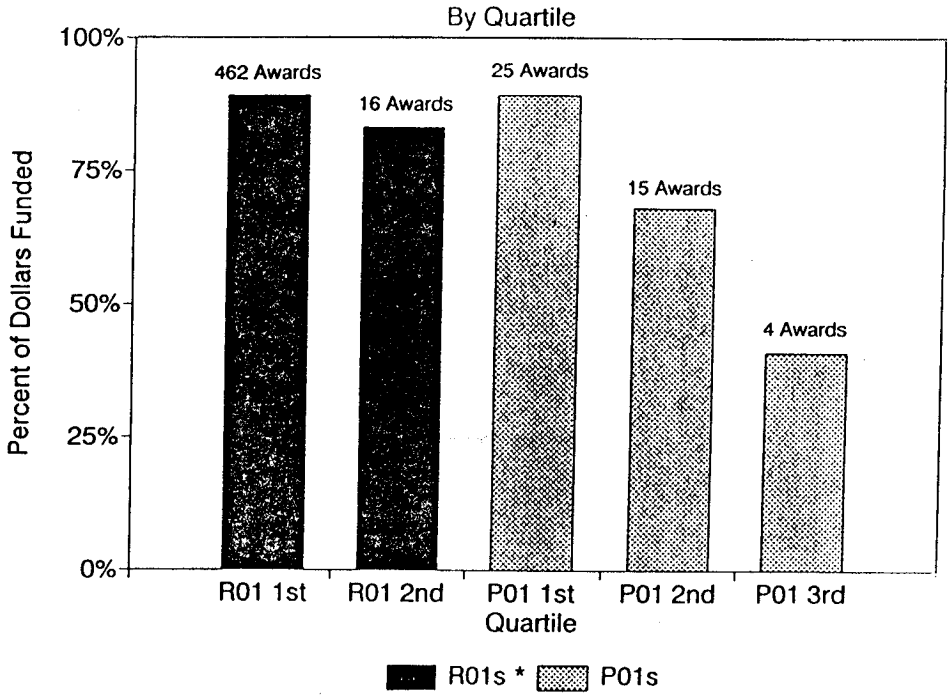
Broder said his comments were not intended as criticism of the investigators. "This is just a reality assessment. [The problems] have to do with issues we can't address at the NCI level....When we have a high priority mechanism, we ought to live by it."

The high priority designation provides increased publicity for trials and financial incentives that allow cooperative groups to accrue patients outside their usual network.

Cooperative group chairmen will discuss the situation at their next meeting Dec. 11. NCI is soliciting nominations for another series of five or six high priority trials to replace those that have closed.

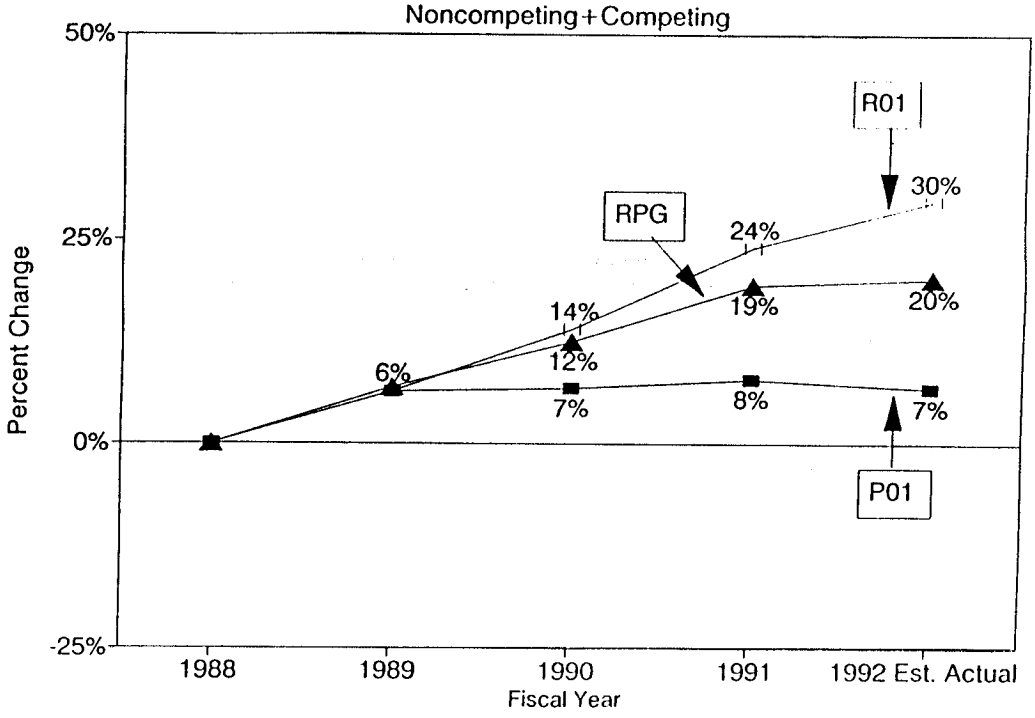

Score Distribution of P01s Approved
For Applications Scored <200
1988
# of Applications
25
20
15
10
5
0
100 110 120 130 140 150 160 170 180 190 200
Priority Score
1991
# of Applications
25
20
15
10
5
0
100 110 120 130 140 150 160 170 180 190 200
Priority Score
Funded thru Payline
Funded Exceptions
Unfunded

1991 Competing P01 & R01 Awards
Percent of Recommended Dollars Funded



There were no R01s funded beyond the 2nd quartile and no P01s funded beyond the 3rd quartile.
* R01s from standing study sections.

P01 & R01 Average Cost
Cumulative Change Over 1988



In Congress

Senate Approves Harkin Amendment To Add $185 Mil. For Breast Cancer

Senate and House conferees last week were expected to reconcile the differences between the NCI appropriations bills proposed by the two chambers. The stakes were high:

Not only did the Senate allowance for NCI exceed the House recommendation by $11.8 million, but a separate measure introduced by Sen. Tom Harkin (D-IA) aimed to put an additional $185 million of the Dept. of Defense funding into breast cancer research.

The viability of Harkin's amendment, approved Sept. 22 in an 89-to-4 vote, hinged on the arrangement that the money would remain in the defense budget, but would in effect be turned over to NCI. By keeping the money in defense, the Senate was attempting to get around the mandated cap on domestic spending.

However, last Monday, the day before the conference committee was to debate defense appropriations, the Administration said it intended to score the DoD funds Harkin proposed to appropriate to breast cancer as domestic spending, a move that would put domestic spending over the mandated cap.

Under the Harkin amendment, funds would be cut from the proposed $3.8 billion appropriation for the Strategic Defense Initiative and would be added to the $25 million DOD was mandated to spend on breast cancer under the Senate Appropriation bill. Altogether, Defense spending on breast cancer would add up to $210 million.

Defense and NCI would make an interagency agreement that would utilize the Institute's peer review system and distribute the funds through the NCI network.

"I am offering an amendment that does not violate the budget agreement," Harkin, chairman of Labor, HHS, Education Appropriations Subcommittee said on the Senate floor. "It does not break the firewalls. It just opens the door that is already there."

Previous attempts by Harkin and Sen. Alfonse D'Amato (R-NY) to break through the so called "firewall" separating defense from domestic appropriations were unsuccessful.

Capitol Hill sources said much of the language in Harkin's amendment was drafted with the help of the National Coalition for Cancer Research. At the same time, Harkin and other key Senate members were lobbied by the Breast Cancer Coalition, a patient advocacy group seeking a $300 million increase in breast cancer research.

Whatever happens to the bill, NCCR and BCC appeared to have reached an uneasy understanding over the Harkin amendment and the two groups have met several times recently.

"The Breast Cancer Coalition has helped create the climate where additional appropriations for breast cancer are viewed favorably," Terry Lierman, president of Capitol Associates Inc., the lobbying group for NCCR, said to **The Cancer Letter.**

"The important thing is that as the ocean rises for cancer research, all ships rise with it. It doesn't make any difference who gets the credit for Harkin's amendment. What's important is that it passed," he said.

Joanne Howes, of Bass and Howes, the lobbying group that represents the Breast Cancer Coalition, confirmed that her group has been working closer with NCCR.

"I've always thought that we could work together," she said to **The Cancer Letter.**

While the two groups are in agreement over the best uses for DoD funds, they remain at odds over NCI appropriations.

Both House and Senate responded to BCC demands by earmarking a greater share of NCI funds for breast cancer. NCCR opposes these provisions since they will take money from other programs.

"We are working with [NCCR] to keep the DoD money," Fran Visco, BCC president, said to **The Cancer Letter.** "We are not talking about NIH. We don't see eye-to-eye about that."

NCI Contract Awards

Title: Large scale production of bulgula neritina in a controlled culture system to produce bryostatin
Contractor: CalBio Marine Technologies Inc., Leucadia, CA; $500,000.

Title: Nutrition intervention trials in Linxian, China
Contractor: Chinese Academy of Medical Sciences, $75,823.

Title: Reculture of selected phototrophic microorganisms for anti-AIDS drugs
Contractor: Martek Corp., Columbia, MD; $6,830.