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Stories On Proscar Cause Confusion In Prostate Cancer Prevention Trial

On August 22, all across America, short, pithy news stories supplied by wire services to local newspapers reported that a study found that the drug terazosin (Hytrin) had outperformed the drug finasteride (Proscar) as a treatment for benign prostatic hyperplasia.

Most of the stories were so brief that making sense of the matter would have required turning to The New England Journal of Medicine to learn what was really being reported.

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In Brief

Berger Named Dean At Case Western; Hayes Heads Lombardi's Breast Program

NATHAN BERGER was named dean of the School of Medicine and vice president for medical affairs at Case Western Reserve University, effective Sept. 1. Berger has been serving in these positions on an interim basis for the past year, replacing **Neil Cherniack**. Prior to that, Berger was an associate dean at the medical school since 1993. Berger, a professor of medicine and biochemistry at the school, served as director of Case Western's Ireland Cancer Research Center for 10 years and was chief of the hematology and oncology division at University Hospitals of Cleveland. . . . **DANIEL HAYES** was appointed director of the Clinical Breast Cancer Program at Georgetown University's Lombardi Cancer Center. Hayes will direct all of Lombardi's breast cancer activities, including patient care, clinical research and translational projects. Hayes was medical director, Breast Evaluation Center, Dana-Farber Cancer Institute, for the past five years, and assistant professor of medicine at Harvard University Medical School. . . . **IRIS SCHNEIDER**, who retired last June as assistant director of program operations and planning at NCI, died of ovarian cancer Aug. 24 at her home in Kensington, MD. She was 57. Schneider joined NCI in 1981 as a program analyst in the Office of Administrative Management. In 1983, former NCI director **Vincent DeVita** hired her as a special assistant, and later appointed her assistant director for OPOP. As executive secretary of the NCI Executive Committee and the President's Cancer Panel, Schneider participated in major policy and operating decisions. She also represented NCI on the NIH advisory committee on women's health issues. In 1990, Schneider helped establish the Office of Research on Women's Health. Schneider was born in Chicago, graduated from Goucher College, and received a master's degree in clinical psychology from University of Michigan. Survivors include her husband, Stanley; sons Alex, of Baltimore and Josh, of Seattle; and her father, Albert Byer of Rossmoor, NJ.

Hytrin Vs. Proscar Headlines Cause Concern For PCPT

(Continued from page 1)

However, virtually no one could have predicted that the stories would cause great consternation among the participants of a completely unrelated clinical investigation, the Prostate Cancer Prevention Trial, an NCI-sponsored effort to determine whether Proscar can prevent the onset of prostate cancer.

Nevermind that BPH is very different from prostate cancer. Nevermind that the paper, published in the Aug. 22 issue of NEJM, contained findings that could be viewed as scientific justification for the trial. Newspaper headlines nationwide were declaring flatly that Proscar is a bad drug:

—PROSTATE RESEARCH: 1 DRUG USELESS.

—PROSCAR ALMOST USELESS PROSTATE DRUG, STUDY SAYS.

—COMPARISON STUDY SHOWS LEADING PROSTATE DRUG VIRTUALLY WORTHLESS.

—PROSCAR NO MORE THAN 'AN EXPENSIVE PLACEBO.'

After reading these headlines, many of the men enrolled in PCPT began to wonder whether Proscar is indeed a worthless placebo that is expensive, to boot.

Many of these men called the PCPT investigators, who, in turn, alerted the statistical center of the Southwest Oncology Group, the cooperative group that is administering the $60 million trial.

Altogether, as many as 50 sites reported trouble, SWOG official said. The question most frequently asked by PCPT participants was whether they needed to stop taking their medication, SWOG officials said.

A day after the news stories appeared, SWOG officials sent a broadcast fax to the study's 217 sites. The fax included a one-page explanation of the difference between the use of Proscar for BPH and its use as a potential preventative for prostate cancer.

However, it is unknown how many sites saw the necessity (or had the funds) to forward the SWOG materials to the participants, the trial organizers say. Another unknown is how many men simply stopped taking their medication.

Since participants are examined every six months, the full extent of the damage will remain a mystery until next February.

"That's the frustration of it: It's totally out of our control, and all we can do is react by trying to get the truth out," said Otis Brawley, director of the NCI Office of Special Populations and a member of the PCPT steering committee. "You literally have to pray that these men listen to us, believe us, and stay with the trial."

An argument can be made that the rampant misunderstanding of the BPH study and the effect of this misunderstanding on an unrelated clinical trial would make a fine case study of what can go wrong in medical journalism.

To physicians, particularly urologists, the findings reported in NEJM were of great importance. "The study has taught us a lot," said Patrick Walsh, director of Brady Urological Institute at Johns Hopkins Medical Institutions and author of an editorial that accompanied the paper on BPH

"I don't think anybody has previously vocalized the concept that a simple rectal examination and estimated prostate size could direct therapy. And it's a fact: if you have a small prostate you should not get Proscar [for BPH]. If you have a large prostate, Proscar may work. I think it's pretty simple," said Walsh, whose editorial used previous studies of treatment of BPH to put the latest result in perspective.

"There is a major direction in this article, and if the news media had wanted to be constructive, they would have said that," Walsh said to **The Cancer Letter**.

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Hytrin and Proscar have different mechanisms of action. Hytrin works by relaxing the smooth muscle in the prostate. Proscar blocks the formation of dihydrotes-testosterone, thereby shrinking the prostate.

However, since most Americans are not practicing urologists, news stories about the NEJM paper had to have another angle: a comparison of two drugs finds one drug effective while another appears to be no better than placebo. Hytrin is marketed by Abbott Laboratories, and Proscar is marketed by Merck & Co.

The news story that received nationwide play was written by the Associated Press. As the story was picked up across the US, copy editors supplied the headlines. Hence, the words "expensive," "placebo" and "useless" made their way into the headlines.

"It depended on what the local newspapers did in their headlines more than anything else," said Lynda Emel, lead data coordinator at the SWOG Statistical Center, describing the confusion that ensued.

In some newspapers, the stories were cut to as little as three paragraphs. In at least one case, the words "prostate trouble" were substituted for BPH.

"Very often the references were to `prostate trouble,'" Emel said. "What kind of trouble?"

While headline writers were lambasting Proscar, careful readers of the NEJM paper would have found it to contain an argument for testing the drug as a preventative for prostate cancer.

The NEJM paper reported that the prostates in patients who received Proscar were reported to have decreased by 17 percent.

Since prostate cancer is a disease of the prostatic epithelium, a decrease in the volume of the prostate gland can be seen as evidence of prevention or delay of carcinogenesis, said Michael Brawer, one of the authors of the BPH study, which was conducted by the Department of Veterans' Affairs.

"In PCPT, the intent for [Proscar] is totally different than in BPH," Brawer, chief of the urology section at the VA Medical Center in Seattle and a member of the PCPT steering committee, said to **The Cancer Letter**. "[Proscar's] mechanism of action is such that it may offer a benefit as a preventive agent in prostate cancer."

Having accrued 17,163 men, PCPT is months away from reaching its enrollment target of 18,000.

"We may end up having to extend accrual if we have a rash of men dropping off," said Charles Coltman, chairman of SWOG and a member of the PCPT steering committee. "We are talking about a $60 million, 10-year study. If it gets screwed up, that's bad."

Breast Cancer Prevention Trial To Require Fewer Participants

The Breast Cancer Prevention Trial will require fewer participants than originally estimated and is on the threshold of meeting its recruitment targets, **The Cancer Letter** has learned.

An official announcement of the change in the trial's recruitment targets is expected next week, sources said.

Originally, the recruitment target was 16,000 women at high risk of developing breast cancer. Now, NCI officials concluded that 13,000 women will be needed to determine whether the drug tamoxifen delays the onset of breast cancer in women at high risk of developing the disease.

A smaller number of participants will be needed since women who enrolled in the trial were at over twice the originally estimated risk of developing the disease, sources said.

Currently, enrollment in the trial is over 12,000. The new, lower enrollment target can be expected to be reached by the end of the year, sources said.

Sources said the women who enrolled in the study had about a 5.5 percent risk of developing breast cancer in any year during the trial. That was more than double the original estimate of relative risk of 2.5 percent, sources said.

The trial is open to women over age 35. The participants' risk is evaluated on the basis of the number of first degree relatives who have been diagnosed with the disease, age at chidbirth, frequency of breast biopsies, age of first menstrual period and the presence of lobular carcinoma in situ.

The trial, conducted by the National Surgical Adjuvant Breast & Bowel Project, has been criticized by several women's groups for subjecting asymptomatic women to tamoxifen's side effects which include endometrial cancer.

Three years ago, in the midst of the controversy surrounding NSABP, the trial received negative publicity nationwide, which resulted in a drop in enrollment. Also at that time, the trial's requirements and informed consent documents were altered to reflect the previously unknown risks.

Cancer Patient Advocacy

Prostate Cancer Activists Form National Coalition

A group of prostate cancer activists formed the National Prostate Cancer Coalition, a group that in name, structure and strategy seeks to duplicate the National Breast Cancer Coalition.

At a meeting of patient activists Aug. 18, Robert Samuels, a 58-year-old retired banker residing in Tampa, was named president of NPCC (**The Cancer Letter**, Aug. 16). The group also named a 20-member board of directors.

Samuels said his No. 1 goal will be to organize the many prostate cancer groups into a single coalition.

"The toughest task I see is keeping everybody focused on our vision," Samuels said to **The Cancer Letter**. "We have to hit the ground running, but we can't have people running all over the place."

To Hold Conference Oct. 12

NPCC's next move will be to hold a conference of scientists and cancer survivors to determine how much money can be usefully spent on prostate cancer research.

The conference has been scheduled to take place at the University of Texas M.D. Anderson Cancer Center Oct. 12.

Five years ago, a similar conference by NBCC led to that coalition's "$300 Million More" campaign. That lobbying effort culminated in the creation of the breast cancer research program at the Department of Defense.

In the upcoming weeks, NPCC is likely to be involved in last-minute lobbying for a $100 million appropriation for prostate cancer research at DOD (**The Cancer Letter**, July 12).

The House and Senate appropriations bills, now nearing the final conference, contain proposals to beef up the DOD prostate cancer program as well as to continue the $150 million breast cancer research program.

Several observers said the conference could turn into a war between the sexes if the new funds for prostate cancer are perceived to come from the breast cancer program.

Others said they feared that if both programs are launched, the DOD breast cancer program would lose both its rigor and its focus.

NCI, NABCO In Partnership On Clinical Trials Web Site

In an effort to disseminate information on clinical trials, NCI has formed a partnership with a patient advocacy group to display summaries of clinical trials on its World Wide Web site.

Under the arrangement, the summaries of trials listed in the NCI Physician Data Quiery database will be available through the home page of the National Allinace of Breast Cancer Organizations.

NCI officials described the collaboration as a "pilot project" that will serve as a prototype for similar arrangements with other patient groups.

A demonstration version of PDQ summaries is currently available on NABCO's home page (http://www.nabco.org), under the Trial News section. The complete listing of about 150 summaries of breast cancer trials contained in PDQ is expected to be available in October, NCI officials said.

"An increasing number of breast cancer patients and high-risk women are using the Web," Amy Langer, NABCO executive director, said in a statement. "By marketing PDQ and other trial information through our site, we hope to make clinical trials an automatic option to be considered by each women, her family, and her medical team."

Langer recently took a leave as NABCO's executive director, following a car accident in which she was seriously injured. Betsy Gardella, the group's associate executive director, was named acting executive director.

While NABCO and NCI are working to distribute information contained in PDQ, the National Breast Cancer Coalition is considering a broader effort called a "Clinical Trials Project."

The project would be a continuation of the NBCC's current activities that include lobbying and educational programs as well as the formation of a partnership with industry and the creation of a clearinghouse, NBCC officials said.

The clearinghouse will be a database of clinical trials that will include the trials listed in PDQ. Also, NBCC is planning to list industry-sponsored trials and international trials, which are not always listed in the NCI database, the coalition's officials said. The coalition is raising funds for the database, sources said.

NABCO is a member of NBCC, and Langer is a member of the coalition's board of directors.

Regulatory Agencies

Clinton Signs Order Finalizing FDA Regulation Of Tobacco

President Clinton signed an executive order on Aug. 23 putting into effect the Food and Drug Administration's proposed rule to make it more difficult for young people to buy cigarettes and smokeless tobacco and reduce the appeal of tobacco products to children under 18.

The goal of the regulation, which FDA proposed one year ago, is to cut in half tobacco use by children over the next seven years.

"This is the most important public health initiative of our generation," said HHS Secretary Donna Shalala. "Our children's futures are at stake. President Clinton's action will ensure that children get their information about tobacco from their parents—and not from Joe Camel."

"Nicotine addiction is a pediatric disease that often begins at 12, 13, and 14 only to manifest itself at 16 and 17 when these children find they cannot quit," said FDA Commissioner David Kessler. "By then our children have lost their freedom and face the prospect of lives shortened by terrible diseases."

The rule is based on FDA's finding that cigarettes and smokeless tobacco products are delivery devices for nicotine, an addictive drug. FDA concluded that cigarettes and smokeless tobacco are "combination products," having both a drug component, including nicotine, and device components, namely processed tobacco.

The FDA rule will:

●Require age verification by photo ID for anyone under the age of 27 purchasing tobacco products.

●Ban vending machines and self-service displays except in "adult" facilities where children are not allowed, such as certain nightclubs totally inaccessible to anyone under 18.

●Ban free samples, the sale of single cigarettes, and packages containing fewer than 20 cigarettes.

●Prohibit billboards within 1,000 feet of schools and playgrounds. Other advertising is restricted to black-and-white text only; this includes all billboards, signs inside and outside of buses, and all advertising in stores. Advertising inside "adult only" facilities such as nightclubs can have color and imagery.

●Permit black-and-white text-only advertising in publications with significant youth readership, defined as 15 percent or more than 2 million readers under 18; there are no restrictions on print advertising below these thresholds.

●Prohibit sale or giveaways of items that carry tobacco product brand names or logos.

●Prohibit brand-name sponsorship of sporting or entertainment events (including teams and entries), but permitting it in the corporate name.

The provisions will be phased in between six months and two years from the date of publication in the Federal Register, the White House said.

In addition to the rule on access and advertising, FDA will require tobacco companies to educate children and adolescents about the health risks of tobacco use. The national mass media campaign would be monitored for its effectiveness.

In the past four years, tobacco use by persons under age 18 in the US has increased dramatically, the White House said. Between 1991 and 1995, the percentage of eighth- and tenth-graders who smoke rose 34 percent. In 1995, more than a third of 12th-graders reported smoking in the past month, and daily smoking in that group was up to 21.6 percent.

The Coalition on Smoking OR Health, comprised of the American Cancer Society, the American Heart Association and the American Lung Association, commended the President for the regulations.

"The FDA proposal is the first comprehensive, national policy dedicated to ending the epidemic of underage smoking," said Scott Ballin, American Heart Association. "These regulations come at a time when smoking among teens has risen to its highest level in 16 years. When more than 1 million children begin smoking each year, we have to say enough is enough."

The tobacco industry spends an estimated $6 billion a year on product advertising. "Each year more than 2 million tobacco customers either quit smoking or die from their addictions," said Susan Polan, American Cancer Society. "With a net loss of 2 million customers, common sense tells us that the industry must attract children to stay in business. Studies have shown that 90 percent of adult smokers begin before the age of 18."

NCI, in a statement, said tobacco causes one-third of all cancer deaths in the US. "NCI views the President's actions as a major opportunity to save today's children from the ravages of tomorrow's cancer. The President's action will especially protect our 10 and 12-year-olds from the lure of tobacco use," the statement said.

NCI Contracts

Advisors Ok Recompetition Of Chemoprevention Contracts

Advisors to NCI recommended the continuation of a $22.1 million per year project that tests compounds for chemopreventive activity.

The NCI Board of Scientific Advisors unanimously approved recompetition of seven contracts that support studies for the testing and development of potential chemopreventive agents. The contracts, together worth nearly $115 million over five years, are issued by the Chemoprevention Branch in the Division of Cancer Prevention and Control.

The board recommended the contracts be issued for up to five years, but asked DCPC staff to report on progress made on the studies in no later that two years.

The contracts are due for recompetition at a time when another advisory group, the Cancer Prevention Working Group, is studying the Institute's cancer prevention program. The Working Group is expected to issue a report next year. BSA members were reluctant to either wholeheartedly support the chemoprevention contracts or recommend their discontinuation without the Working Group's recommendations.

"The Working Group is looking at this whole area and its report will be pivotal," said BSA Chairman David Livingston at the board's meeting Aug. 8. "Interrupting any one of these [contracts] would have a dislocating effect."

Gary Kelloff, chief of the Chemoprevention Branch, said the seven contracts "are functionally one program," from agent identification and testing in vitro, to phase I and II studies. Currently, 24 agents are in phase I studies and 15 to 17 agents are in phase II trials, he said.

Several board members were critical of DCPC's presentation of the contract concepts and description of the research program.

"I don't have an appropriate context with which to judge the investment opportunity," said Amy Langer, executive director, National Alliance of Breast Cancer Organizations.

"You have described the whole field of chemoprevention research," Eric Fearon, associate professor of molecular medicine and genetics, University of Michigan Medical Center, said to Kelloff. Fearon asked for more specific information on the research results and publications.

The contracts have led to 100 peer-reviewed publications, Kelloff said. Because phase II trials began only two years ago, data are not yet available, he said.

Livingston appointed a subcommittee of Fearon, Frederick Appelbaum of Fred Hutchinson Cancer Research Center, and Enrico Mihich of Roswell Park Memorial Institute, to prepare a report to NCI staff with suggestions for the presentation of concept statements.

The excerpted text of the concept statements follow:

In Vitro Screening for Chemopreventive Agents. Master agreement contracts; 13 contractors in the MA pool. Proposed funding $9.885 million over five years.

The primary purpose of this project is to use rodent carcinogenesis models (chemically induced or transgenic) for each of the major epithelial types of cancer to screen for organ specific chemopreventive agents. Each year multiple contracts are awarded under the MA for screening candidate agents in animal tumor models and for developing and standardizing new models for characterizing chemopreventive activity at major cancer target sites.

Approximately 20-50 new agents are screened annually and new models are developed as needed to address current clinical chemoprevention research interests. More than 20 animal screening models are new available covering colon, mammary glands, lung, esophagus, prostate, bladder, skin, brain, pancreas and lymphoma.

Each year, the primary objective is to identify the 5-10 top new agetns having sufficient chemopreventive activity to warrant further development in the Chemoprevention Branch program.

Evaluation of Chemopreventive Agents by In Vitro Screening Assays. Master agreement contracts; 14 contractors in the MA pool. Proposed funding $7.8 million over five years.

Purpose: To evaluate large numbers of chemicals in different chemical classes using cell culture and biochemical techniques that demonstrate potential chemopreventive activities. These activities include the inhibition of transformation and related endpoints in primary animal or human cell or organ cultures, and modulation of enzyme activities associated with carcinogenesis. Further drug development decisions are based in part on these essential data. This drug discovery testing provides a scientific rationale for priorritizing and directing the further screening of the agents in appropriate animal models, and is the first step in

identifying and developing new cancer chemopreventive agents.

Scope of the project is to test 50-100 new agents per year in a minimum of 200 and a maximum of 400 assays, representing a battery of cell culture and molecular mechanism assays. This project also provides for the development, standardization, and validation of the in vitro mechanistic and screening assays.

The objective is to identify the 10-20 best new agents per year having sufficient in vitro effectiveness to warrant further testing in animals.

Preclinical Evaluation of Intermediate Endpoints and their Modulation by Chemopreventive Agents. Master agreement contracts; 22 contractors in the MA pool. Proposed funding $13 million over five years.

Purpose: To evaluate a wide range of intermediate biomarkers in organ specific animal tumor models. Classes of biomarkers being examined include histopathologically defined preinvasive lesions and abnormal cytology as analyzed by computer assisted image morphometry and cytology, apoptosis, specific enzymes and DNA adducts induced by carcinogents. The ability of known chemopreventives to modulate these markers is being examined in a variety of model systems.

Each year, 6-10 studies are initiated to identify, characterize, and validate intermediate biomarkers as surrogate endpoints for cancer. These studies are carried out in a various target organ systems using agents of known chemopreventive efficacy for the specific organ system.

Objective: To identify, optimize and validate surrogate endpoint biomarkers for cancer which may be applicable to clinical chemoprevention trials. Also, to develop biomarker endpoints for more efficient preclinical efficacy screens and for preclinical models mimicking clinical carcinogenesis.

Preclinical Toxicology of Chemopreventive Agents. Master agreement contracts; 8 contractors in the MA pool. Proposed funding $13 million over five years.

Purpose: To use multiples of the anticipated human dose in order to define toxicological and pharmacological dose-related effects. The data are used to prepare the IND and the Investigational Drug Brochure. The data includes clinical observations, growth rates, food consumption, plasma drug levels, complete clinical and anatomic pathology, and study-specific endpoints.

Objective: To conduct GLP toxicity evaluations that will support the safe clinical administration of the drug, regulatory requirements, and NDA approval for chemoprevention.

Efficacy Studies of Chemopreventive Agents in Animal Models. Master agreement contracts; 11 MA holders. Proposed funding $9.885 million over five years.

Purpose: To perform detailed chemopreventive efficacy testing in organ-specific animal tumor models of major human cancers. An important aspect of this project is the measurement of blood levels versus efficacy, providing critical information for future clinical studies. To this end, the evaluation of dose-response effects of promising agetns at their intended cancer targets, characterization of chemopreventive activity of agent combinations, and exploration of chemopreventive activity in animal models designed to approximate human carcinogenesis (e.g., induced by inhaled cigarette smoke or "Western" diet, occurring in mature or aging animals, or in animals bearing genetic lesions associated with carcinogenesis) are also important components of this project.

Each year 10-20 agents and agent combinations are tested in appropriate animal efficacy models. Efficacy testing may include detailed dose reponse, bioavailability, organ site response, and potential toxicity.

Phase I Clinical Trials of Chemopreventive Agents. Master agreement contracts; 16 MA holders. Proposed funding $19.25 million over five years.

Purpose: To conduct single-dose, dose-escalation pharmacokinetic and toxicological evaluations of chemopreventive agents in well individuals and to conduct repeated, daily-dose evaluations in individuals at risk for cancer. Data from repeated dosing studies (for approximately three months) includes pharmacokinetics, pharmacological blood and tissue biomarker evaluations, and toxicology.

Scope: Up to 10 phase I studies on single agents and agent combinations are initiated each year. The single-dose pharmacokinetic study usually constitutes the initial IND protocol submission and leads to regulatory review of the development program for that drug.

Phase II Clinical Trials of Chemopreventive Agents. Master agreement contracts; 20 MA holders. Proposed funding $42.16 million over five years.

Purpose: To evaluate in humans the chemopreventive efficacy of drugs under development by the Chemoprevention Branch. Protocols have been designed for 11 cancer targets: prostate, breast, colon, lung, bladder, cervix, esophagus, oral cavity, skin, multiple myeloma, and liver.

Scope: Multiple contracts are awarded under the MA for phase II trials to support the development plans for Chemoprevention Branch sponsored INDs. Up to 10 studies may be initiated each year, the priority and timing depending primarily on the promise of the drug for marketing approval as a chemopreventive agent, requirements of collaborations with the pharmacetical industry, and availability of adequate cohorts.

Editor's note: NCI contract concepts precede the development of Requests for Proposals by several weeks or months. Concept statements are published here for informational purposes. ***The Cancer Letter*** *will publish the text of the RFPs as soon as NCI issues them.*

NCI Revises Procedures For Contract Concept Review

NCI has revised its procedures for reviewing contracts that fund research, development and support services.

Since 1981, all NCI contracts were submitted to one of the four Boards of Scientific Counselors for concept review. Each contract concept statement was review individually.

Under the new procedure, the Board of Scientific Advisors and the Board of Scientific Counselors—the two groups that replaced the four BSCs—will review each program, laboratory or branch every four years. The review will include the portfolio of contracts.

During intervening years, the NCI Executive Committee will review new and renewal contracts. The EC will decide whether BSA review can be waived for renewals that contain no major changes.

The new policy is designed to reduce the amount of time NCI advisors spend reviewing contract concepts, Philip Amoruso, associate director, Office of Extramural Management, said at the Aug. 7 meeting of the BSA.

Text of the **NCI Concept Review Policy** follows:

Role and composition of the Executive Committee: The Executive Committee is the corporate decision making body of the Institute and is composed of 16 members: the Division Directors, the Associate Directors for Intramural and Extramural Management the Chair Persons of the Intramural and Extramural Advisory Boards and 5 non-Federal members from the scientific community. Three of these non-Federal members serve as Chair Persons for the Board of Scientific Advisors and Board of Scientific Counselors and two serve as scientific advisors to the Director. The EC approves all new and renewals of contracts prior to submission to the BSA or BSC for concept approval. "Renewals" may be either a recompetition of the project, or, with appropriate approval, non-competitively awarded to a particular institution or company.

NIH Policy for Contract Concept Review: NIH policy requires that all new and renewals of research and development and support to research and development contracts be concept reviewed. The specific questions for review include purpose, scope, objectives, scientific rationale, requested resources, the need to use the contract mechanism and relative priority. Concept review of a contract renewal may be waived by the Director, NCI, or his designee if there are no major changes in the scope of the contract since the last time it was concept reviewed.

Current NCI Policy for Contract Concept Review: Since 1981 it has been Institute policy that all NCI contracts (both new and renewals) were to be submitted to Divisional Boards of Scientific Counselors for concept review. Each contract concept was individually presented to the BSC for concept review approval. The Institute did not waive concept review for any contracts. Issues:

—NCI has reorganized its Board structure. The four Divisional Boards of Scientific Counselors have been abolished and one Board of Scientific Advisors for extramural programs and a Board of Scientific Counselors with 2 subcommittees for the intramural programs have been established.

—Concerns were raised by the previous BSCs that review of individual contract concepts was not effective since it was difficult to relate the review back to the Divisional program that it was supporting.

—Each year approximately 25 new contracts and 50 contract renewals required concept review by the previous BSCs.

New Approved NCI Policy for Contract Concept Review: The BSA and BSC will review each extramural program or intramural laboratory or branch every 4 years to include the portfolio of contracts and the BSA and BSC will be charged with making recommendations on the contract program in relation to the overall program review. The review will include judgements on the scientific rationale, the contract resources, how the contract program is fulfilling the program objectives and the quality of performance. This will serve as the concept review for the contracts for that specific scientific program and will serve as guide for the EC in the management and funding decisions

During the intervening years the following reviews will be effected to comply with NIH policy:

—The NCI Executive Committee will review new R&D and support to R&D contract concepts, both new and renewal. However, renewals with no major change in the workscope, the Executive Committee will decide if the concept will be sent to the BSA or if concept review by the BSA Will be waived. It is estimated that this change in policy will reduce the number of concept reviews referred to the BSA and BSC from 75 per year to approximately 20.

—The BSA and BSC are required to concept review all new R&D and support to R&D contracts and contract recompetitions which involve a major change in the workscope. This is an NIH requirement.

—BSA and BSC recommendations on the contract program resulting from a specific program review will be acted upon by the Director and the EC.

—Contracts with no research component do not require concept review by the BSA or BSC. However, they will be included in the program review which will be conducted every four years.