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GAO Study Finds Lumpectomy Effective As Mastectomy In Trials And In Practice

A data analysis by a Congressional watchdog agency concluded that the effectiveness of breast conservation therapy has, on the average, been similar to that of mastectomy in randomized trials and in community medical practice.

The study performed by the General Accounting Office and released at an NCI-sponsored workshop on treatment of early breast cancer Nov. 15, was greeted by the Institute as confirmation of the results of the controversial National Surgical Adjuvant Breast and Bowel Project B-06 trial.

The workshop also gave the Institute an opportunity to publicly discuss—and defend—its own audit of B-06 patient charts (**The Cancer Letter,** Oct. 21). Also at the workshop, NCI officials were asked to justify their decision not to include tumor size and margin status as data points in the audit.

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In Brief

ACS Board Names McGinnis President; Fuller Re-elected Chairman; Lenhard Is Vice President

LAMAR MCGINNIS was elected president of the American Cancer Society at the annual meeting of the ACS Board of Directors last week in Atlanta. McGinnis, attending surgeon and medical director of the DeKalb Medical Cancer Center in Atlanta, succeeds **Irvin Fleming**. **Larry Fuller**, a retired executive of Southwestern Public Service Co., was re-elected as chairman of the board for another year. **Raymond Lenhard Jr.**, professor of oncology, Johns Hopkins Univ. School of Medicine, was elected vice president and president-elect. **George Dessart**, a communications consultant and executive director for the Center for Study of World TV, was elected vice chairman and chairman-elect. . . . **ALFRED GOLDSON**, professor and chairman of radiotherapy at Howard Univ., has been appointed to the National Cancer Advisory Board, the White House announced last week. Goldson, a fellow of the American College of Radiology, is a leader of the DC Cancer Consortium, which conducts breast and cervical cancer screening in low-income women in Washington, DC. He received an MD in 1972 from Howard Univ. Medical School and was board certified in therapeutic radiology in 1976. . . . **PATRICIA FLEMING** has been appointed director of the Office of National AIDS Policy by President Clinton. She has been interim director of the office. Previously, she worked for Rep. Ted Weiss (D-NY).

GAO Study Confirms Equality Of Lumpectomy, Mastectomy

(Continued from page 1)

The GAO study confirmed the findings of earlier analyses by NCI and the Emmes Corp., an NCI contractor.

"I think we should all be here to praise the findings of this audit—a wonderful job that was done by these people," Bernard Fisher, the ousted head of the cooperative group, said during the public comment period. "[They] went back and looked at findings from 10 to 18 years ago and came up with a high concordance of findings."

Presenting the GAO data, Judith Droitcour, GAO assistant director of program evaluation, human services, said the data in the study showed that breast conservation and mastectomy provided equivalent survival in clinical trials. Just as importantly, the GAO audit indicated that survival rates in day-to-day medical practice matched those in randomized studies, Droitcour said.

"The summary data indicated that five-year survival is similar following the two alternative treatments," she said.

The GAO study was based on a combination of meta-analysis, statistical analysis of records from a medical practice data base, and cross design comparison of results. GAO officials said this was the first time such an approach has been used in the area of breast cancer treatment.

The GAO meta-analysis of six studies from around the world (single-center and multi-center), including the recalculated NSABP data published in the spring of 1994, found the five-year survival rate for breast conservation therapy was 90% compared to 90% for mastectomy.

When the NSABP data were eliminated from the meta-analysis, the survival rate was 91% for breast conservation therapy, and 90% for mastectomy. The meta-analysis was done on node-negative patients.

GAO also analyzed data from NCI's Surveillance, Epidemiology, and End Results data base to determine whether the treatment effect in daily medical practice corresponds to the treatment effects in single-center and multicenter studies.

The SEER data set included more than 5,000 cases believed to be comparable to the participants in randomized studies.

"We believe selection bias in the SEER data set is minimal," Droitcour said.

Using the SEER data set, GAO analysts found that the five-year survival rate was 86.3% for breast conservation therapy, compared to 86.9% for mastectomy, leading to the conclusion that the two treatments produce similar results in day-to-day practice.

"Nearly all the evidence pointed to similar survival for breast conservation therapy and mastectomy," said Droitcour.

One caveat in the GAO study suggested that a minority of breast conservation patients—patients for whom this therapy was relatively unlikely to be used (based on factors such as residence in areas where breast conservation is uncommon)—who did receive breast conservation, would have been likely to achieve "slightly better results" with mastectomy.

However, the observed difference was not statistically significant, the report said.

Results "Reassuring"

William Wood, professor of surgery at Emory Univ. School of Medicine, described the GAO results as "reassuring."

Wood said the GAO study and the results of the NCI audit confirm the findings of the 1990 NIH consensus development conference on early stage breast cancer.

Wood was the chairman of that conference.

The consensus panel at that conference concluded that breast conservation treatment is an appropriate method of primary therapy for the majority of women with Stage I and II breast cancer, and is preferable because it provides survival equivalent to total mastectomy and axillary dissection while preserving the breast.

The panel said the recommended technique for

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Editors: **Kirsten Boyd Goldberg**
Paul Goldberg

Founder & Contributing Editor: **Jerry D. Boyd**

P.O. Box 15189, Washington, D.C. 20003
Tel. (202) 543-7665 Fax: (202) 543-6879
E-Mail: 73322.2044@compuserve.com

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breast conservation includes local excision of the primary tumor with clear margins and level I-II axillary node dissection, followed by breast irradiation.

"I personally found striking that the level of error and discrepancy found was as slight as it was," Wood said. "I think that's extremely reassuring. Furthermore, we've now heard from an additional trial, the GAO, and we have also heard ongoing results from the trials that form the basis of the original conclusion.

"I think it's very interesting that the conclusion of the 1990 consensus panel—that breast conservation therapy does provide equivalent survival—appears to stand on the basis of these data," Wood said.

The NCI Chart Audit

Presenting the NCI audit results, Michaele Christian, acting chief of the Clinical Trials Monitoring Branch of the Cancer Therapy Evaluation Program at the Div. of Cancer Treatment, said NCI audited the NSABP B-06 data because of the far-reaching implications of the study.

Christian said the publicity about the inclusion of fraudulent data from one participating NSABP institution and failure of the NSABP to follow up on these charges "led to an erosion of public confidence in the overall quality of the data and concerns about the validity of the conclusions of the conclusions of this very important study."

In April, NCI requested a reanalysis, which was performed by the Emmes Corp. under contract from NCI. That audit confirmed the NSABP's original findings, said Christian.

However, because of continuing concern, NCI followed up with its own audit, Christian said.

In its early stages, the NCI audit focused on detection of fraud and carelessness. However, in later stages, the audit focused on verification of eligibility and outcomes.

The audit involved site visits to 37 institutions and examined eligibility data on 83% of patients and endpoint data on 86% of patients. More than 50 NCI auditors participated, including 36 physicians.

All relevant information was presented to a data resolution panel consisting of three NCI physicians who reviewed all cases with discrepant, unverified or ambiguous data.

Christian said eligibility was assessed in 1,493 patients. She said eligibility status was completely verified in 1,416 or 95% of patients. Auditors were unable to verify eligibility in 76 or 5% of patients. The results were obtained using eligibility criteria different from those of NSABP.

Verification rates across the treatment arms were similar, she said: 95%, 94% and 96% of the audited charts (**The Cancer Letter**, Oct. 21).

In terms of the total audited endpoint items, Christian said more than 7,500, or 98%, were verified. The greatest number of discrepancies, she said, was in the identification and date of first event.

Informed consent issues presented a greater challenge, she said.

"There were complex issues surrounding the process of obtaining informed consent," said Christian.

The panel chose to limit its decision making to issues of consent withdrawal, which could have an impact on the re-analysis, she said.

The panel did not declare patients ineligible or remove their data because of a lack of documentation of an informed consent, given the complexity of the process. "Issues other than consent withdrawal, therefore, were not addressed," she said.

The NCI auditors eliminated followup on 36 patients who were identified by the auditors as having given consent, been included in the data base, and, subsequently, having withdrawn consent.

Patients were excluded from the re-analysis if any one item was not verified, said Christian.

In summary, Christian said, of 1,554 of the targeted patients, 1,329 patients, or 85.5%, had all data items verified, including eligibility.

Similar verification rates were observed across the three arms of the study, she said. In terms of outcome endpoint data items. All items were verified in 1,432 patients, or 92.1%, Christian said.

"There was no evidence of any systematic attempt to manipulate the data" that was discovered as a result of the NCI auditing process, said Christian. Many audits, especially the earlier ones, "were conducted under difficult conditions, not the least of which was the unprecedented level of scrutiny and suspicion surrounding this trial," Christian said.

Challenge to NCI Chart Audit

In the coming weeks, NCI is likely to be forced to justify its report of the chart audit on the B-06 trial, sources said to **The Cancer Letter**. The likely issues of contention include the audit report's discussion of the patients' tumor size and margin

status, sources said.

Responding to a question during the workshop last week, Christian described the circumstances that resulted in NCI's inability to confirm these variables:

"We had a panel of physicians review all the eligibility criteria and select what we felt were the key eligibility criteria for verification," Christian said, responding to a question from Suzanne Hadley, an NIH scientific fraud investigator who, until recently, was on detail at the Subcommittee on Oversight and Investigations of the House Energy and Commerce Committee.

"The issue of suitability for lumpectomy was evaluated by a variety of criteria," Christian said. "It was felt that there was potentially so much variability in the evaluation of tumor size on site, given the fact that it would be measured by multiple observers—attending physicians, resident physicians, by mammogram, by physical exam, by pathology report—and trying to rectify those would be unnecessarily complex."

Asked by Hadley whether the auditors were able to confirm the margin status, Christian said the margins could not be independently verified.

"The reason for this is that many of the pathology reports from that period did not comment specifically and clearly on the tumor margins," Christian said. "Apparently that was not a common practice at that time."

The B-06 study accrued patients between 1976 and 1984.

The original eligibility check list used by NCI auditors included 25 data points, tumor size among them, but the item did not make the short list of 11 eligibility data points to which the audit was ultimately narrowed down. However, the summary of the NCI audit of B-06 characterized tumor size as a "critical" eligibility criterion.

According to NCI's summary report on the audit, the earlier audits reviewed all the 25 eligibility criteria, but emphasized the "critical eligibility criteria which might be expected to influence outcome, such as the size and characteristics of the tumor and axillary lymph nodes."

At the closing of discussion last week, Wood said the tumor size and margin status defied the capabilities of the audit.

"The size of the tumor and margins were two areas in which the bast data available were those generated for the NSABP, and the NSABP forms were more specific and explicit than those generally carried in the medical records," said Wood.

"The essence of an audit is to look at data that are reported and try to get a better source to validate. Here, the NSABP forms were probably the best source, and it doesn't make make much sense, at least to me, to validate them from the weaker sources," he said.

GAO report "Breast Conservation vs. Mastectomy," is available at no charge from GAO, P.O. Box 6015, Gaithersburg, MD 20884-6015. Tel.: 202/512-6000. Fax: 301/258-4066. Request report number GAO/PEMD-95-9.

Competition For Cancer Center Grants To Be High In FY95

Competition for NCI Cancer Center Support Grants will increase substantially this fiscal year as an unusually large number of funded centers and a group of rising newcomers are expected to submit grant applications.

About 20 applications for new and competing CCSG renewals (P30 grants) are expected in fiscal 1995, according to NCI staff.

The cancer centers will be competing for an FY95 budget that is only 1.1 percent higher than last year. The estimated budget for cancer centers is $132.1 million, an increase of nearly $1.5 million over the FY94 budget of $130.6 million.

"We had several good budget years stemming from an increase in FY92, but that's going to change in FY95 and FY96," Brian Kimes, director of the Centers, Training and Resources Program, said to the NCI Div. of Cancer Biology, Diagnosis and Centers Board of Scientific Counselors last week.

Challenge: New Vs. Established Centers

The expected increase in submission of grant applications is the combination of normal grant cycles and NCI's creation two years ago of a new grant mechanism to help institutions become competitive for full cancer center grants.

In 1993, the Cancer Centers Branch funded the first 14 Cancer Center Planning Grants (P20s). These institutions are expected to compete for full CCSGs or submit renewals for their planning grants between this fiscal year and FY96, NCI staff said.

"With this kind of competition, the challenge of the program will be to provide a certain degree of stability to existing centers and at the same time provide opportunities for new centers of high quality and potential," according to the annual report of the

Cancer Centers Branch. "The likelihood is that a few established centers will be replaced by new centers."

There are 54 funded CCSGs. NCI expects to fund three to five new or renewal P20 grants in FY95.

In FY94, the total actual expenditure for the cancer centers program was $129.15 million.

Cancer Training In "Crisis"

NCI's ability to support cancer training is a "crisis" level, Kimes said to the DCBDC board.

In particular, the National Research Service Awards program "is in trouble and will be for a number of years," Kimes said.

NRSA trainees generally have been more successful than other trainees in eventually winning independent grant support, according to the Cancer Training Branch annual report.

Last year, NCI funded 187 institutional (T32) NRSAs at a cost of $33 million and 168 individual (F31,32, and 33) NRSAs for $4.4 million.

"The lack of any increases in the [NRSA] pool of funds allocated to NCI and the lack of any flexibility within the NCI's FY 1994 budget to shift more resources into this category have resulted in the lowest paylines for T32s in the history of the program and little hope that career development awards (K04s, K07s, K08s, K11s, and K12s) will receive any relief," the annual report said.

"The crisis in training young physicians to pursue basic and clinical research careers is becoming increasingly serious," the report said. "The overall long-term impact of dwindling resources for training and career development is difficult to project, but there are serious questions about whether the NCI will be poised to effectively pursue the most important research opportunities in the future."

Last year, NCI awarded $62.6 million to 623 research training grants.

Prevention Expert Guy Newell, Former NCI Deputy, Dead At 57

Guy Newell, associate vice president for cancer prevention at M.D. Anderson Cancer Center, and a former NCI deputy director, died Nov. 12 in a Houston hospital after a long illness. He was 57.

"Not only was he a respected epidemiologist, but he also was an articulate and enthusiastic proponent of public education to encourage individuals to reduce their risks for cancer," Charles LeMaistre, president of M.D. Anderson, said.

Born in Bogalusa, LA, Newell received a bachelor's degree and medical degree from Tulane Univ. Following postgraduate training at Johns Hopkins Hospital, Newell spent two years as a research planning associate at NCI, and then worked for a year at Peter Bent Brigham Hospital in Boston. He earned a master's degreee in epidemiology from Harvard Univ. in 1968.

Newell held a faculty appointment at Tulane from 1970 until going to NCI as deputy director in 1973.

While at NCI, Newell served as liaison to FDA for the study of saccharin as a possible cause of bladder cancer and coordinated NCI's Diet, Nutrition and Cancer Program. He served as acting NCI director for 10 months from 1976 to 1977.

Newell joined M.D. Anderson in 1979. He was the first chairman of the Dept. of Cancer Prevention and Control.

Prostate Cancer Research Initiative Approved By BSC

Advisors to the NCI Div. of Cancer Biology, Diagnosis and Centers last week approved in concept an initiative to promote the development of new research programs in prostate cancer.

NCI has not decided whether the initiative will be issued as a program announcement with no set-aside funds or as a request for applications with $1.5 million in total costs, program director Jaswant Bhorjee said to the DCBDC Board of Scientific Counselors.

Regardless of the mechanism used, the non-renewable R21 grants would be limited to $300,000 total costs per year per applicant, for four years, and one application per institution, Bhorjee said.

The board also gave concept approval to an trans-NIH RFA for the development of a rat genome map, reducing NCI's contribution from $500,000 to $200,000 in the first year. Up to 12 institutes and centers at NIH may contribute to the program.

The board also approved reissuing RFAs for the Cooperative Network For Evaluation Of Prognostic Markers Of Urinary Bladder Cancer and the Cooperative Human Tissue Network.

The concept statements follow:

Development of New Research Programs in Prostate Cancer. Concept for a new PA or RFA. DCBDC Cancer Centers Branch, Program director: Jaswant Bhorjee.

A major goal of this initiative is to promote development of research relevant to prostate cancer, placing special emphasis on issues of environmental and occupational carcinogenesis, prevention and control, and of unusually high incidence of mortality in underserved minority and other special populations. A strong expectation of this initiative is that it would enhance the interactive, peer-reviewed, funded research base (e.g. R01s) for prostate cancer research at the applicant institution. Each applicant institution must include the following elements:

1. Evidence of credible institutional commitment supporting the development of a research program in prostate cancer, which will benefit from stable leadership and multidisciplinary interactions (i.e., similar to a research program as defined in an NCI-designated cancer center).

2. A qualified Program Leader as the principal investigator who will oversee, conduct planning activities, and provide directions to the developing program.

3. A plan for developing a program with sufficient scientific breadth and depth, which is focused, cohesive and multidisciplinary and takes maximum advantage of the institution's resources and research capabilities. The planned program would be expected to identify and bring together investigators who wish to develop basic, clinical, and prevention and control research projects in prostate cancer. It would also include recruiting new investigators who would bring in special expertise that would strengthen and/or broaden the research base of the program and enhance special emphasis areas, thereby, creating a more productive, interactive research environment.

4 A significant aspect of the plan should consider initiating novel pilot projects or feasibility studies that will stimulate basic, clinical, and prevention and control research in prostate cancer. It is expected this would help build the peer-reviewed, funded research base in support of prostate cancer, and at the same time enhance the research capabilities of the institution in special emphasis areas.

The funds for this initiative would support: (a) Partial salary of the Program Development Leader; (b) Funds for special retreats to enhance the development of a prostate cancer research program; (c) Pilot projects for feasibility studies in cancer of the prostate; (d) Recruitment of new scientists to the institution who will pursue prostate cancer research and contribute to multidisciplinary objectives.

Construction of a High-Resolution Map of the Rat Genome. RFA for R01 grants, one to two awards, five years, approximate total cost $2.46 million in the first year, NCI contribution will be $200,000. Cancer Immunology Branch, Program director: Grace Shen.

The objective of this initiative is to construct a high resolution genetic map of the rat genome. In addition, a large insert DNA library of the rat genome is to be constructed to facilitate the cloning and analysis of disease genes that have been mapped genetically. This will be a trans-NIH initiative, with support deriving from 12 Institutes and Centers.

The National Center for Human Genome Research (NCHGR) currently supports projects aimed at mapping the human and mouse genomes, as well as selected non-mammalian genomes. However, due to a lack of sequence identity and specificity, only 5 to 10% of mouse and human genetic markers can be used to screen the rat genome.

Mapping a mammalian genome other than those already targeted by the NCHGR is a costly task and would be difficult for any one Institute or Center to support entirely. Substantial reductions in cost have been demonstrated in mouse and human genome mapping by using a concerted, centralized approach.

The idea for the rat genome mapping project stems in part from the NHLBI's 1993 Report of the Expert Panel on Genetic Strategies for Heart, Lung and Blood Diseases.

Cooperative Network For Evaluation Of Prognostic Markers Of Urinary Bladder Cancer. Concept for RFA, six awards (cooperative agreements), four years, total $5.52 million. Cancer Diagnosis Branch, Program director: Roger Aamodt.

The objective of this initiative is to continue the Marker Network for Bladder Cancer. The goal of this inter-institutional network is to identify biochemical immunologic, genetic and other quantifiable diagnostic and predictive markers for urinary bladder cancer, to evaluate their potential and define appropriate clinical applications and to validate the usefulness of the most promising markers. The Network has initiated and stimulated significant research aimed at diagnosis and prognosis of bladder cancer and already identified and evaluated several promising bladder cancer markers. Additional efforts are needed to complete ongoing studies and to identify and evaluate new markers.

The Marker Network for Bladder Cancer was formed in 1992 with the following investigators: Carlos Cordon-Cardo, Memorial Sloan-Kettering Cancer Center; Yves Fradet, Laval Univ.; H. Barton Grossman, M D. Anderson; George Hemstreet, Univ. of Oklahoma; Fred Waldman, Univ. of California at San Francisco; and Leon Wheeless, Univ. of Rochester.

Network investigators evaluate scientific needs and opportunities in the areas of bladder cancer diagnosis and prognosis, set research priorities, design Network protocols and share tissues, reagents, and techniques to implement their studies. Individual Network laboratories carry out studies to demonstrate the feasibility of new markers. Network laboratories work together on larger

scale preliminary studies, interlaboratory variability studies, and studies to determine whether the assays can be exported to other laboratories. Once a promising assay has been well developed, the Network designs and carries out large scale retrospective or prospective validation studies to confirm its clinical potential.

Cooperative Human Tissue Network. Concept for RFA, five awards, five years, total $13.54 million. Cancer Diagnosis Branch, Program director: Roger Aamodt.

This is a concept to maintain the Cooperative Human Tissue Network, established January 1987. The CHTN was established in response to the perception by the biomedical research community that lack of access to appropriate human tissues posed a major obstacle to cancer research, particularly molecular genetics which was being applied to cancer biology and diagnosis. CHTN has experienced rapid growth and provided thousands of specimens to hundreds of researchers.

The original CHTN then consisted of Univ. of Alabama at Birmingham, the National Disease Research Interchange and Ohio State Univ. Pediatric tumor tissues were provided by the Children's Cancer Study Group under a subcontract from Ohio State. The Network was recompeted in 1989. Five of the ten applications received scored high in the competitive review. These included the three original groups, the pediatric tissue group at Columbus Children's Hospital (Previously Children's Cancer Study Group) and a group at Case Western Reserve Univ. These were funded on January 1, 1991.

The CHTN is directed by a coordinating committee which consists of the Principal Investigator and one additional representative from each of the participating institutions and a representative from NCI. The Network has five Divisions, each with primary responsibility for one geographic area of the US.

By January 1994 the Network had distributed more than 65,000 tissue specimens to more than 500 investigators. No expansion of the Network is anticipated.

RFPs Available: ASCUS Trial

RFP NCI-CN-55040-05

Title: **Randomized Trial on Clinical Management Of ASCUS And LSIL of the Uterine Cervix—Clinical Centers**

Deadline: Approximately Jan. 30

The proposed project is a three-armed clinical trial of 6 years duration involving 7,200 females aged 16 and over. The subjects will be randomized to one of three arms, each containing 2,400 females. Each clinical center should be able to recruit a minimum of 1,200 randomized subjects within a maximum time period of 18 months. Of the 1,200 recruited subjects, 600 subjects shall have recently diagnosed low-grade squamous intraepithelial lesion and 600 subjects shall have atypical squamous cells of undetermined significance. The offeror must document their referral base of ASCUS/LSIL diagnosed patients for 1993. The trial goals and major objectives are: 1) to determine whether human papillomavirus DNA testing can effectively triage women with a cytologic diagnosis of ASCUS or LSIL; 2) to develop clinical management guidelines and provide prognostic information for the ASCUS and LSIL diagnostic categories of the Bethesda System; and 3) to determine whether the cost of screening and treatment for the potential precursor lesions of cervical cancer can be reduced through improved triage.

Request for this solicitation must be in writing and reference the RFP number. Four to six awards are anticipated.

Inquiries: Gary Topper, RCB, PCCS, NCI, 6120 Executive Blvd, Bethesda, MD 20892-7226, Tel: 301/496-8603.

RFP NCI-CN-55042-07

Title: **Colposcopy Quality Control Group for the ASCUS/LSIL Clinical Management Trial**

Deadline: Approximately Jan. 30

The NCI Div. of Cancer Prevention and Control is soliciting proposals for a Colposcopy Quality Control (QC) Group that will be responsible for overseeing all aspects of randomized clinical trial involving colposcopy and the taking of cervical biopsies among 3,600 women with the cervical cytologic diagnoses of atypical squamous cells of undetermined significance (ASCUS) and 3,600 women with low-grade squamous intra-epithelial lesions (LSIL). The group shall be responsible for overseeing the quality of all aspects of the trial involving colposcopies and the taking of cervical biopsies.

The general requirements include: 1) preparation with the other collaborators of the final protocols, data systems, and study forms; specifically, identifying the optimal means to assure the highest possible quality of colposcopic examinations and cervical biopsies; 2) prior to enrollment, optimizing and standardizing clinic colposcopic and biopsy procedures, equipment, and supplies; 3) during the conduct of the trial, monitoring and optimizing all aspects of the protocol related to colposcopy and biopsies including the design and conduct of experiments to assess the accuracy of colposcopic examinations, particularly the assessment of lesion severity and placement of biopsies; 4) ongoing participation in the overall supervision of the trial via the Steering Committee and its subcommittees; and 5) cooperation with all trial administrative functions, including reporting, data management, and proper handling of trial-related biospecimens.

Inquiries: Victor Buyny, RCB, PCCS, NCI, Executive Plaza South Rm 635, 6120 Executive Blvd, MSC 7226, Bethesda, MD 20892-7226, Tel: 301/496-8603.

RFP NCI-CN-55043-05

Title: **Pathology Quality Control Group For The ASCUS/**

LSIL Clinical Management Trial
Deadline: Approximately Jan. 30

The NCI Div. of Cancer Prevention and Control is soliciting proposals for a Pathology Quality Control (QC) Group that will assure the reliable and accurate use of the Bethesda System for cytology and the cervical intra-epithelial neoplasia (CIN) scale for histopathology for a randomized clinical management trial among 3,600 women with the cervical cytologic diagnoses of ASCUS and 3,600 women with LSIL. The Pathology QC Group shall be responsible for overseeing the quality of all aspects of the Trial involving cytology and histopathology.

The general requirements include: 1) preparation with the other collaborators of the final protocols, data systems, and study forms; specifically, identifying the optimal protocol for the collection, fixation, staining, storing, and transport of cytologic and histologic specimens; 2) prior to enrollment, minimizing the intra-and inter-laboratory variability of cytologic and histologic diagnoses from the cooperating pathology laboratories used by the clinical centers during the trial; 3) during the conduct of the trial, continuing to monitor and optimize all aspects of the protocol related to pathology, including review of all 7,200 referral cytology smears, all 7,200 enrollment smears, and a large sample (about 1,000 per year) of the follow-up cytology smears at the clinical centers; 4) review of all histology slides collected in the trial (estimated for budgetary purposes at about 8,000 cases over the course of the study) to standardize clinical outcomes and provide quality control, including the design and conduct or masked quality control experiments; 5) ongoing participation in the overall supervision of the trial via the steering committee and its subcommittees; and 6) cooperation with all trial administrative functions, including reporting, data management, and proper handling of trial-related biospecimens.

Inquiries: Gary Topper, RCB, PCCS, NCI, Executive Plaza South Rm 635, 6120 Executive Blvd, MSC 7226, Bethesda, MD 20892-7226, Tel: 301/496-8603.

RFP NCI-CN-55044-07
Title: **HPV Quality Control Group for the ASCUS/LSIL Clinical Management Trial**
Deadline: Approximately Jan. 30

The NCI Div. of Cancer Prevention and Control is soliciting proposals for an HPV Quality Control (QC) Group that will be responsible for overseeing all aspects of HPV DNA testing for a randomized clinical trial among 3,600 women with the cervical cytologic diagnoses of atypical squamous cells of undetermined significance (ASCUS) and 3,600 women with low-grade squamous intra-epithelial lesions (LSIL). The HPV QC Group shall be responsible for maintaining the quality of the trial's HPV DNA testing.

The general requirements include: 1) preparation with the other collaborators of the final protocols, data systems, and study forms; specifically, identifying the optimal means to collect, store, and transport cervical specimens for HPV DNA testing; 2) prior to enrollment, choosing optimal HPV DNA testing methods, assessing the qualifications of testing laboratories, preparing a list of approved laboratories, and validating the performance of participating laboratories before enrollment; 3) during the conduct of the trial, monitoring and optimizing all aspects of the Trial procedures manual related to HPV DNA testing including the design and conduct of masked quality control experiments and the performance of repeat "in-house testing of specimens; 4) ongoing participation in the overall supervision of the Trial via the Steering Committee and its subcommittees; 5) cooperation with all trial administrative functions, including reporting, data management, and proper handling of trial-related biospecimens; and 6) establishment of Data Management and Quality Assurance systems.

Inquiries: Victor Buyny, RCB, PCCS, NCI, Executive Plaza South Rm 635, 6120 Executive Blvd, MSC 7226, Bethesda, MD 20892-7226, Tel: 301/496-8603.

RFA Available

RFA RR-95-002
Title: **National Gene Vector Laboratories**
Letter of Intent Receipt Date: Dec. 15
Application Receipt Date: Feb. 21

The National Center for Research Resources, together with NCI, the National Heart, Lung, and Blood Institute, and the National Institute of Diabetes and Digestive and Kidney Diseases as cosponsors, invite applications to establish National Gene Vector Laboratories to enhance research leading to successful gene therapy of single- and multiple-gene disorders. The funding instrument to be used for this program will be the NIH Animal Model, and Animal and Biological Materials Resource Cooperative Agreement (U42). Approximately $3.5 million in total costs will be available in fiscal 1995 for the first year. It is anticipated that between one and three awards will be made.

Inquiries: The RFA may be obtained electronically through the NIH Grant Line (data line 301-402-2231) and the NIH GOPHER (gopher.nih.gov) and by mail and e-mail from: Dorothy Sogn, Medical Officer, General Clinical Research Centers Program, National Center for Research Resources, Westwood Bldg Rm 10A-07, Bethesda, MD 20892-4500, Tel: 301/594-7945, Fax: 301/594-7929, E-mail: DorothyS@EP.NCRR.NIH.GOV.

NCI Contract Award

Title: Clinical trials of biological response modifiers, Task A. Contractor: Univ. of Alabama at Birmingham, $2,429,827.