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# Secondary AML In High-Dose Chemo Trial Cause For Careful Monitoring, NCI Says

NCI and the National Surgical Adjuvant Breast & Bowel Project have issued a joint statement on the identification of five cases of secondary acute myeloid leukemia in a trial involving high dose chemotherapy for breast cancer.

Patients and physicians participating in B-25, an NSABP trial for node-positive breast cancer, were informed in letters last week that the incidence of AML in the trial was higher than expected.

NCI acted swiftly to head off the kind of criticism the Institute received

(Continued to page 2)

*In Brief*

## NCAB Task Force Supports Group-Led Data And Safety Monitoring Committees

**DATA AND SAFETY** monitoring committees for phase III clinical trials conducted by NCI-supported cooperative groups should consist of members of the cooperative group and a few independent reviewers, a task force of the National Cancer Advisory Board has recommended. The Clinical Trials Task Force, at a recent meeting, voted 9-1 to approve a motion by **Sharon Murphy**, chairman of the Pediatric Oncology Group, supporting recommendations made by **Ross McIntyre**, chairman of the Cooperative Group Chairs Committee. In a letter to NCI, McIntyre suggested that 20 percent of the voting membership of monitoring committees include persons not affiliated with the group. Completely independent monitoring boards would be costly, McIntyre wrote, because groups would have difficulty finding and training independent reviewers. The nay vote was cast by **Fran Visco**, president of the National Breast Cancer Coalition, who said monitoring boards should be independent. . . . **FEDERAL TRADE COMMISSION** has asked NCI to convene an expert panel to evaluate methods used to determine cigarette tar and nicotine levels. In a letter to NCI Director **Samuel Broder**, FTC Chairman **Janet Steiger** said health groups have challenged whether the testing methods result in tar and nicotine ratings that are accurate measurements of the health risks of smoking. . . . **ROSS DONEHOWER** has been named director of the Div. of Medical Oncology at Johns Hopkins Oncology Center. Donehower has been acting director of the division since 1992. He joined the faculty in 1980, after a fellowship in the NCI Medicine Branch and Clinical Pharmacology Branch. . . . **MOODY WHARAM JR.** was named director of the Div. of Radiation Oncology at Johns Hopkins. He joined the division in 1975 and served as acting director since 1990.

## Secondary AML Tests NCI's New Communication Approach

(Continued from page 1)

last spring from members of Congress and patient advocates for delay in discussing the risk of endometrial cancer due to tamoxifen.

"This is the new way of doing business," Bruce Chabner, director of the NCI Div. of Cancer Treatment, said to **The Cancer Letter**. "We should have done this for the uterine cases in tamoxifen."

Prior to sending the letters, NCI and NSABP officials met with researchers from academia and the pharmaceutical industry, clinical trialists, patient advocates, and FDA officials.

At the July 29 meeting in Rockville, some physicians said NCI should be careful not to cause panic and questioned the need for a letter to patients.

Patient advocates countered that cancer patients deserve more information, not less. They encouraged NCI to provide a full account of what is known about the leukemia cases.

"In the past, the lack of information has added to the hysteria," said Deborah Collyar, a board member of Breast Cancer Action, based in San Francisco. "People have to feel like they are getting the whole story."

NCI officials agreed. "Cancer patients are our main concern," Chabner said in the July 29 statement. "That is why we are committed to keeping patients informed of new findings—even while we are investigating the significance of the finding."

**Unknown Risk, Unknown Benefit**

In the B-25 trial, 2,548 women received higher than standard doses of chemotherapy to prevent disease recurrence. The women received doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan), as well as G-CSF. Women over 50 also received tamoxifen.

The trial increased the dose of cyclophosphamide two to four times above the standard dose while maintaining the standard dose of doxorubicin in three treatment groups. Patients in each group received a different dose of cyclophosphamide, all higher than the standard dose. Patients were enrolled from April 1992 to February 1994.

The five cases of AML occurred in women age 50 and older and represented 0.2 percent of patients. The leukemia occurred in all three of the treatment groups. Two of the women have died from leukemia. The women all were diagnosed with AML from nine to 19 months following their first course of chemotherapy.

Secondary leukemia has long been recognized as an uncommon risk of chemotherapy, according to the NCI-NSABP statement. Women with breast cancer have one tenth of 1 percent risk of contracting leukemia.

"With the detection of five cases within two years of beginning treatment, NSABP and NCI officials feel there may be an increased risk of secondary AML linked to higher doses of certain cancer drugs," the statement said. "Neither the precise risk nor the possible benefits of the treatment are known at this time."

The benefit of standard chemotherapy for node-negative breast cancer patients is a 10 percent improvement in 10-year survival, compared to patients who undergo surgery alone, according to the statement. "Patients should in no way be discouraged from accepting standard adjuvant treatments, which clearly reduce recurrence of disease," the statement said.

Trials using higher than standard doses are an effort to improve a patient's chances of survival, NCI and NSABP said.

"We anticipate that the benefits against breast cancer will far outweigh the leukemia risk, though we may not be able to document the answer for some time," Ronald Herberman, interim NSABP chairman, said in the statement. "Careful patient monitoring, which can be accomplished only in the context of a well-designed clinical trial, has allowed us to rapidly detect the AML cases and has provided a better understanding of the risk of AML after receiving these medications for breast cancer."

**THE CANCER LETTER**

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**Monitoring Plan**

During the NCI meeting, the following monitoring plan was adopted:

- A review to ensure the adequacy of model informed consent documents for each NCI-supported clinical trial involving similar chemotherapeutic regimens.
- A requirement that all NCI-supported investigators report to NCI within 30 days of diagnosis any cases of secondary AML for other cancers.
- Development of a monitoring plan to expeditiously obtain reliable estimates of the risk of secondary AML following specific regimens of dose-intensive chemotherapies.

At the meeting, researchers encouraged NCI to establish a repository for biological materials from patients diagnosed with secondary AML. Future research could identify exactly how secondary AML occurs and possibly identify patients most at risk of the disease.

Cyclophosphamide, an alkylating agent, and doxorubicin, an anthracycline, are commonly used anticancer drugs. Some of the most active anticancer regimens combine these two types of agents.

In a letter to investigators, Jeffrey Abrams, senior investigator in the NCI Cancer Therapy Evaluation Program, said further research must find the best combination of these drugs.

"Given the significant therapeutic benefit that may result from dose-intensive therapy, considerations for limiting evaluation of this strategy because of an increased risk of secondary AML must be carefully balanced against the possibility of significant benefit in terms of improved survival," Abrams wrote. "This implies a critical need to define as quickly as possible the risk of secondary AML following therapy which employs higher than standard doses of cyclophosphamide and/or anthracyclines, and to define the relevant contributions of each agent in order to select the combination with the most favorable therapeutic index."

Recently, an increased incidence of AML following treatment with epipodophyllotoxin-containing regimens has also been documented, Abrams wrote.

**"Watch This Carefully"**

Experts at the NCI meeting said it was disputable whether the five cases in the B-25 trial represented an increased risk.

Abrams agreed that the statistical issues were controversial, however, the problem should be monitored. "This is very different than we expected," said Abrams. "It does represent a difference compared with what you would expect with standard dose therapy."

Clara Bloomfield, chairman of the DCT Board of Scientific Counselors, said the general oncologist does not have much information on secondary leukemia and needs to be informed. "We have to watch this carefully," she said. "Secondary leukemia is a disease in which we haven't had a lot of success. These patients do relapse. The only thing curative has been [bone marrow] transplantation."

**"Once the Media Distorts This..."**

Charles Schiffer, of Univ. of Maryland and chairman of the FDA Oncologic Drugs Advisory Committee, questioned NCI's plan to send a letter to patients. "The issue is how much alarm do you want to cause among the patients and physicians, once the media distorts this," he said.

Bloomfield said that NCI and the cooperative group could be blamed for not informing patients. "We do not want to put ourselves in a position that could be criticized that patients were misled," she said. "If I were a patient, I would choose the high dose therapy and take the risk of secondary leukemia. But I still think patients should be informed that this puts them at risk."

She noted that in the five cases of AML, every patient's white blood cell count had fallen to 30,000 before the secondary AML was diagnosed. "Monitoring should be in place so that you find it before a patient comes in with a white count of 30,000," Bloomfield said.

"I would be concerned about the alarm," Schiffer said.

"I disagree strongly," Bloomfield said. "The patient has the right to know and make the decision. They ought to be informed about the options."

Specific monitoring issues would be left up to the cooperative groups, said Michael Friedman, CTEP director. "We want to establish minimal norms," he said. "We will take your advice. We think patients should know about this."

Collyar said patients and the public should be informed, and the letter would not cause alarm if it were worded in a way that related the AML risk to other risks and benefits. "The basis for the hysteria is when people get incomplete information that is

taken out of context," she said.

Schiffer said he understood the importance of releasing the information, but was not convinced that NCI should send a letter to patients, thereby seeming to usurp the patient-doctor relationship.

"Everyone knows you can get leukemia," he said. "I'm not sure a patient letter is warranted." In addition, he said, "I don't think meetings of this type should replace the cooperative group and the doctor who gave the drugs. There should be some perspective here. Compared to endometrial cancer [risk due to tamoxifen], this is much less important."

Collyar and other patient activists said they were pleased at NCI's action. "This meeting is a good step in the right direction," she said. "You are opening to patient groups. The public trust has to be there or we run into the problem of researchers fearing taking risks. We want more research to be done."

Amy Langer of the National Alliance of Breast Cancer Organizations said the meeting "opened a new era in dealing with toxicities and trial problems."

"It is appropriate to communicate with patients, and it does not have to create hysteria," Langer said. "My main concern is that we do not want to give women a reason to opt out of the standard regimens."

She suggested NCI use this situation as a model for further communication with patients.

## Saratov, An Industrial Town In Russian Heartland, Is Site For Breast Cancer Conference

As she traveled through Russia last fall, psychosocial oncologist Barrie Cassileth realized that few of the cancer specialists she met had any knowledge of modern drugs and modern technology.

"Top level oncologists in Moscow and St. Petersburg are up on the developments in the West," said Cassileth. "But thousands of physicians in the rest of the country are working with nothing. No equipment. No drugs. No information about what has happened in the past half-century."

Hence, Cassileth's idea: hold a breast cancer conference that would bring top scientists from the US (as well as Moscow and St. Petersburg) closer to the Russian heartland. For the conference, Cassileth chose the city of Saratov, located about 450 miles southeast of Moscow, along the banks of the Volga.

After a hectic year of lining up sponsors and presenters, Cassileth is able to say with certainty that the conference will take place on June 7 through 9, 1995.

The conference, designed for Russian and American physicians and researchers, is being sponsored by NCI, the Russian Ministry of Health, the US State Department, the Univ. of North Carolina, the Saratov Medical Univ., the Russian National Oncology Center in Moscow and the New York-based National Alliance of Breast Cancer Organizations.

"Physicians in Russia are eager to collaborate on studies in the treatment of cancer," Cassileth, adjunct professor of medicine at Duke Univ. and the Univ. of North Carolina, said to **The Cancer Letter**. "For them, collaborations present the best opportunity to learn what's new in the treatment of cancer, and to obtain cutting edge drugs for their patients.

"For American physicians, such collaborations present a great opportunity for access to research subjects—as well as an opportunity to help bring Russian medicine into the twentieth century," Cassileth said.

Saratov, an industrial city with a population of one million that until recently was closed to foreigners, is an unusual choice for an international conference. Cassileth selected it because of its long insolation from the West, its 5,000-student medical university, and its sister-cities affiliation with Chapel Hill, NC, where she lives.

"Saratov gave me the opportunity to experience the richness of cultural life of provincial Russia that is otherwise inaccessible to foreigners," Cassileth said. "It's a place very different from Moscow and St. Petersburg."

However, in the course of making arrangements, Cassileth realized that Saratov is also a city devoid of accommodations for international tourists.

What to do?

Cassileth made arrangements for a clean, well-lighted (and German-built) 180-cabin river cruise ship to be docked off the city for the conference. Now Cassileth is considering chartering a jet for a direct flight from the US to Saratov, the first such flight ever.

There are still i's to dot and t's to cross: Cassileth is working to raise $70,000 to cover travel stipends for Russian doctors and is trying to convince Russia's ministry of defense to allow the secretary of the conference, who is a colonel in the air force, to travel to the US.

Vassily Vlassov, the secretary, is a professor of aerospace medicine at Saratov Medical University and the founder of Russia's first institutional review board. Recently, he was told that he would not be allowed to travel to the US.

"We were looking forward to his visit—and so was NCI," she said. "I hope we can still work it out."

US conference participants include Martin Abeloff, director, Johns Hopkins Oncology Center; Bruce Chabner, director of the NCI Div. of Cancer Treatment; Norman Coleman, chairman, Harvard Joint Center for Radiation Therapy; Kathleen Foley, professor of neurology, Memorial Sloan-Kettering Cancer Center; Robert Hoover, chief of the NCI Environmental Epidemiology Branch; David Kinne, professor of surgery, Columbia-Presbyterian Comprehensive Cancer Center; Edison Liu, principal investigator of the breast cancer SPORE grant at the Lineberger Comprehensive Cancer Center at UNC; Virginia LiVolsi, director of surgical pathology at the Univ. of Pennsylvania Comprehensive Cancer Center; and Kent Osborne, interim chief of the Div. of Medical Oncology and principal investigator of the breast cancer SPORE, Univ. of Texas Health Science Center.

Russian participants include N.N. Trapesnikov, member of the Russian Academy of Medical Sciences and Director of the National Oncology Center in Moscow; E.A. Koreckiy, professor at the National Cancer Institute of the Ukraine; V.F. Semiglazov, corresponding member of the Russian Academy of Medical Sciences and professor of oncology at the N.N. Petrov Research Institute of Oncology in St. Petersburg and K. P. Hanson, director of the Petrov Institute.

**For additional information,** contact Cassileth, 919/967-2184 or conference coordinator Svetlana Lisanti at the Center for Biomedical Communications, 201/385-8080.

## Medenica Patients Drop Suit Against Hilton Head Doctors

Patients of the controversial Hilton Head physician Rajko Medenica dropped their suit against three doctors who, the suit claimed, attempted to use the peer review system to drive Medenica off the island..

The plaintiffs, who included Denver businessman Chuck Stevinson, boxer Muhamad Ali and a member of the Coors family, moved to dismiss the case last month.

Acting on their motion, US District Court Judge Cameron McGowan Curris on July 20 dismissed the case with prejudice, thereby preventing the patients from refiling, and leaving open the dispute over who will pay the six-figure attorneys' fees incurred by the underwriters for the three defendants.

The dismissal came soon after Hilton Head Hospital sent a letter to the Denver area hospital where Medenica was facing sanctions.

Earlier this year, St. Anthony Hospital in Denver downgraded Medenica's privileges from full to provisional, after being informed that his privileges had been changed at Hilton Head (**The Cancer Letter**, March 18).

However, a subsequent letter from Hilton Head, a copy of which was obtained by **The Cancer Letter**, stated that Medenica was never the subject of a professional review action.

Following receipt of the letter from Hilton Head, St. Anthony returned Medenica's full privileges.

"Now he is able to treat patients in Hilton Head and in Denver, and that meant there was no sense in pursuing the case," Stevinson said to **The Cancer Letter**. Since the case was filed, the three defendants—oncologist Jane Gehlsen, neurologist Dan Howley and neurosurgeon Alfred Higgins—have moved from Hilton Head.

The letter that led to St. Anthony's decision to restore Medenica's privileges stated that Medenica was never subject of any sanctions, but instead entered a contractual agreement with Hilton Head Hospital, accepting a different peer review structure.

Such contractual agreements don't have to be reported to the National Practitioner Data Bank, Hilton Head Hospital president and CEO Curtis Clayton wrote in the June 13 letter to St. Anthony. The data bank includes reports of professional review actions that may adversely affect the physicians' clinical privileges.

"Based upon the advice of counsel, the [Hilton Head] Hospital considered that the Agreement and Guidelines and all Board [of Trustees] action taken in connection with those documents did not constitute a professional review action which was required to be reported to the data bank," Clayton wrote.

"Dr. Medenica applied for oncology privileges, and these were granted," the document continued. "Our board did not consider that the agreement and its action approving the two-year appointment in oncology adversely affected Dr. Medenica's clinical privileges.

"Accordingly, it should not be a surprise that Dr. Medenica would assume that his privileges at Hilton Head Hospital had not been changed, modified or adversely affected, or that it was necessary to report a change of status to your institution," Clayton wrote.

At St. Anthony, Medenica has been granted privileges in oncology immunology, hematology and internal medicine, but, according to documents, he will be limited to practice in accordance with standard protocols.

According to a resolution of St. Anthony's board of trustees, a copy of which was obtained by **The Cancer Letter**, unconventional therapies would have to be reviewed in advance by the hospital's institutional review board.

Medenica's existing patients will be exempt from the limitations of the agreement.

The hospital also urged Medenica to set up his own "research facility" in Denver. "Since [St. Anthony] is not primarily a research facility and is incapable of supporting large volume basic clinical research, [Medenica is] encouraged to establish a clinical research center in the community, where his patients may be treated in an appropriate setting, with the required controls and monitoring to assure patient safety and compliance with external agency requirements," the resolution states.

**Hospital To Be Sold**

In a related development, Hilton Head Hospital is expected to be sold to a partnership that includes American Medical International Inc. and the University Medical Associates of the Univ. of South Carolina.

Following two victories in disputes over hospital privileges, Medenica is scheduled to face another challenge—a trial scheduled for Sept. 7 in a case in which a breast cancer patient at Hilton Head claims medical malpractice (**The Cancer Letter**, April 30, 1993).

## No Cancer Letter for 2 Weeks; Next Issue Dated September 9

**The Cancer Letter** will take its annual summer publishing break over the next two weeks. The next issue, Vol. 20 No. 34, will be published on Sept. 9.

The August issue of **Cancer Economics** will be mailed to subscribers at the end of this month.

The office will be open; subscription and editorial staff will be available during this time.

## The Cancer Letter's First Ever Inventory Reduction Sale

**The Cancer Letter's** closets are bulging with copies (real ones, not photocopies) of 1994 issues and other publications. Substantial savings are available on the following items:

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*Editor's note: The 1993 Index is in production and should be in the hands of subscribers and available for purchase by non-subscribers in September. We appologize for the delay.*

## The Cancer Letter FAX: Because You Need The News Sooner

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# Program Announcement

**PA-94-086**
Title: **Investigator-Initiated Interactive Research Project Grants**
National Institutes of Health
Application Receipt Dates: Feb. 15, June 15, Oct. 15

This is to rescind NIH PA-93-078, on Investigator-Initiated Interactive Research Project Grants [issued in April 1993] and replace it with the following Program Announcement. The purpose of this revised PA is to clarify several important aspects of the Interactive Research Project Grant (IRPG) program. The full text of the PA is available by contacting the address under Inquiries. The key clarifications in this revised Program Announcement are as follows:

1. The important characteristics of IRPG applications and their differences from Program Projects are explained more clearly.

2. The section on study populations has been updated to reflect the latest NIH policy required under the NIH Revitalization Act of 1993 and announced in the Federal Register of March 28, 1994. All applications received on or after June 1, 1994 must conform to this new policy.

3. The requirements for format and layout of each application in the IRPG group have been stated more clearly.

4. The procedures for submission of applications and the receipt dates for applications, including AIDS and AIDS-related applications, have been clarified.

5. The guidelines for requesting limited shared resources for projects in the IRPG group have been clarified.

6. The special instructions for preparation of Section 7, Consultants/ Collaborators, of the Research Plan have been clarified.

7. Table II, Distribution of Effort of All Personnel in the IRPG, is no longer required.

8. The process for referral of the applications and the review criteria for the collaborative arrangements have been clarified.

**Purpose:** Certain questions in biomedical and behavioral research require research efforts that extend beyond the level practicable in a single project or require a variety of technical approaches beyond the means of a single investigator. There may be areas of investigation that are under-represented in individual research project grant (R01) and First Independent Research Support and Transition (R29) award applications because of the lack of available collaborative effort on a local level.

NIH has used many ways to encourage strong collaboration among research scientists. These have ranged from specific interaction of the Federal government with academia/industry through contract or cooperative agreement solicitations to RFAs that solicit research applications involving various forms of cooperation among applicants. This PA provides for a new kind of formal interaction, based on the initiative of applicants, to enhance existing interactions with colleagues or to develop new collaborative relationships.

The IRPG program encourages the coordinated submission of related research project grant (R01) and, to a limited extent, FIRST award (R29) applications from investigators who wish to collaborate on research, but do not require extensive shared physical resources. These applications must be scientifically interrelated in some manner and must describe the objectives and scientific importance of the interchange of, e.g., ideas, data, and materials, among the collaborating investigators. A minimum of two independent investigators with related research objectives are encouraged to submit concurrent, collaborative, cross-referenced individual R01 and/or R29 applications. The proposed projects must not be dependent upon each other to the extent that one could not be accomplished in the absence of the other. Applicants may be from one or several institutions. Applications will be reviewed independently for scientific merit. Applications judged to have significant and substantial merit will be considered for funding both as independent awards and in the context of the proposed IRPG collaboration.

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations. Foreign institutions, however, are not eligible for the R29 award. Applications may be submitted from one or more institutions. Applications from or involving minority institutions, minority individuals, and women are encouraged. Applicants for IRPG awards may not concurrently submit additional R01 or R29 applications (either investigator-initiated or in response to an RFA) that represent significant duplication of the efforts described in the IRPG. Concurrent submission of program project (P01) or cooperative agreement (U01, U10, U19, etc.) applications requesting support for essentially similar work also is prohibited.

The IRPG group must consist of a minimum of two independent applications. An IRPG package may consist of a combination of R01 and R29 applications, or R01 applications only, but may not consist solely of R29 applications. Applications for new (Type 1) and competing renewal (Type 2) awards may be submitted as IRPGs.

Occasionally, Institutes and Centers of the NIH may issue additional PAs that include IRPGs. The RFA also may be used, in limited circumstances, to solicit applications for IRPG awards in a discrete scientific area. Although the level of interaction for IRPGs between or among applicants in these solicitations will conform to those outlined here for the investigator-initiated IRPG, there may be minor differences outlined in the RFA. For example, all RFA solicitations will specify a single receipt date that will be different from those listed in this

program announcement.

This revised program announcement supersedes any previous program announcements regarding IRPG awards.

NIH encourages qualified independent investigators to develop and submit coordinated R01 and R29 applications that address any research area supported by the Institutes or Centers. The IRPG program could be used constructively to support collaborative efforts designed to accelerate the development of fundamental knowledge and/or enhance the clinical application of that knowledge. The IRPG award may fit well with clinical applications that propose limited, testable research questions or focused therapeutic and related correlative laboratory studies. However, the IRPG program is not appropriate for large epidemiologic studies or multi-institutional clinical trials using common protocols.

The IRPG application consists of a number of investigator-initiated projects that share an aspect of relationship of objectives. The projects may involve several institutions and may be interdisciplinary. The IRPG program is intended to promote collaborative efforts between or among projects, while providing a record of independently acquired awards credited to each individually funded investigator and allowing retention of research autonomy by the named Principal Investigator (PI) of each project. Each grantee will have the ability to submit on his/her behalf competing supplements as appropriate to incorporate promising new directions of research as they evolve. The freedom to establish collaborations on an equal footing at separate sites (including foreign locations, with the exception that only domestic organizations are eligible to receive FIRST (R29) awards), and the transferability of awards made to individual investigators, are other benefits.

Thus, the IRPG application must demonstrate a sense of collaboration toward related goals. It must describe how the participants intend to take the opportunity to participate in mutually-beneficial interactions, while maintaining the independence of their projects. The IRPG application may involve utilization of shared resources in advancing effective collaborations. It is important for each individual application comprising a portion of the overall IRPG to describe the proportion of the shared resources needed for that individual project.

Since each component R01 and R29 is an independent application, it should be prepared in the same level of detail and with the same care as a traditional R01 or R29 application. Each project also should be able to stand on its own scientifically; the projects proposed must not be dependent on each other, but should be designed so that they could be accomplished independently. For example, one project should not be completely dependent on another project for provision of a critical chemical or reagent, testing or processing of key samples, or interpretation of data.

**Comparison with Program Projects:** Historically, the NIH has relied on multi-component awards, such as program projects (P01), center grants (P30, P50), and cooperative agreements (U01) to encourage multi-disciplinary collaboration in areas requiring integration and coordinated direction of basic and clinical research components. Such awards include the provision of extensive core facilities/resources and appointment of a program director to manage the overall effort.

However, for many research areas it may be appropriate to consider an intermediate level of collaboration that is beyond that practicable for single projects. For such scientifically originated collaborative efforts, the exchanges of data, materials, and ideas, rather than shared extensive physical resources or central oversight, are the primary requirement. The IRPG is meant to facilitate this class of research activity.

The IRPG allows interaction to be initiated among applicants, as is the case with a program project grant (P01) application, but the IRPG differs from the P01 in important ways. The IRPG group consists of investigator-initiated applications on related but independent topics, with a formalized agreement to collaborate in specific ways. The collaboration may include limited shared scientific resources. The IRPG program can be useful where interdependency among efforts is not a requirement, but where the intended collaboration would enhance goal achievement. The IRPG application must provide for interaction between or among the investigators arising from their desire to collaborate as independent investigators. The scope of research in each component of a successful IRPG group should be greater than could be achieved without the collaboration. The proposed collaborations should have a demonstrable impact on ability of the investigators to achieve the projects' goals.

In contrast, the P01 has a well-defined major objective or central theme, most commonly incorporates collaborative efforts among investigators from the same institution, may involve significant core resources, and is under the control of a central principal individual with authority over research direction and budget. If significant core resources beyond a limited amount are needed, applicants should consider applying for a P01.

Each application in an IRPG Group will be referred to the most appropriate Initial Review Group (IRG). The IRG could be either a DRG Study Section or an Institute or Center-managed review committee, depending on the referral guidelines for the particular research proposed.

Additional instructions are available in "Special Instructions for Preparing Applications for Investigator-Initiated Interactive Research Project Grants," from the Office of Grants Information, Div. of Research Grants, NIH, 301-594-7248. Not all Institutes or Centers are participating in this program.

Inquiries (NCI): Dr. Marvin Kalt, Deputy Director, Div. of Extramural Activities, NCI, Tel: 301/496-4218.