News & Views
SAIC-Frederick, Inc.
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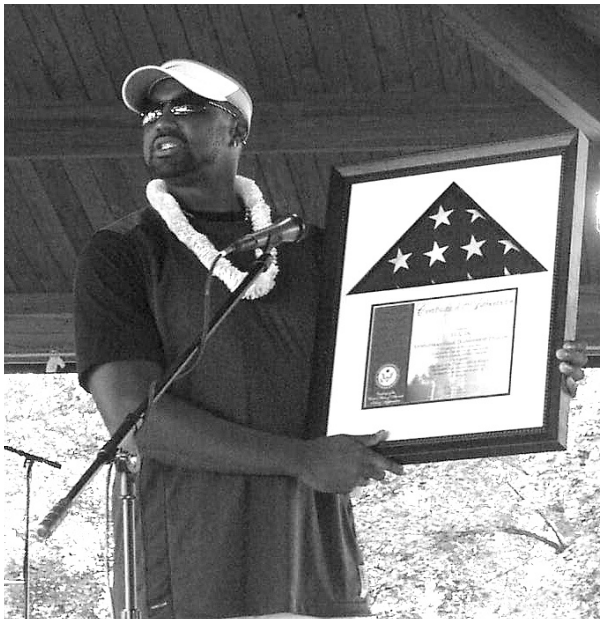
US Flag from Operation Enduring Freedom Presented to BDP

Staff Sergeant Gillis M. Bolden, Jr., U. S. Army, fiancé of Ms. Lydia Lopez, Secretary, Biopharmaceutical Development Program (BDP), SAIC-Frederick, Inc., was stationed at the U.S. Embassy, Kabul, Afghanistan, from October 2002 through April 2003 in support of Operation Enduring Freedom, the War on Terrorism. Upon Staff Sergeant Bolden's return to the United States, he presented BDP with a United States flag that has flown in front of the U.S. Embassy in Afghanistan. A signed certificate by Robert Finn, U.S. Ambassador to Afghanistan, accompanies the flag. As noted on the certificate, *"The National Colors continue to be a beacon of Freedom, Hope and Democracy to people all over the world."*

BDP management requested Staff Sergeant Bolden to again present the flag at the opening of the Summer Annual Staff Meeting/Picnic on September 10th so that all BDP staff could be a part of the presentation. The flag will "tour" NCI-Frederick from September through November and will then be displayed in Building 458.



Staff Sergeant Gillis M. Bolden, Jr., U.S. Army, presented BDP with a United States flag that has flown in front of the U.S. Embassy in Afghanistan.

Cell-Free Protein Expression Now a Practical Option

Traditionally, in vivo has been the only practical way to express protein. It has drawbacks in that it's a slower method and that certain proteins are too toxic for live cells; proteases inside the cell can break other proteins into pieces.

Dr. Deb Chatterjee

Since joining SAIC-Frederick, Inc., Dr. Deb Chatterjee and his colleague, Kala Sitaraman, have been developing an improved method of cell-free protein expression technology to provide recombinant proteins to NCI scientists in both Bethesda and Frederick. The two comprise the Cell-Free Protein Expression Group, a part of Dr. James Hartley's Protein Expression Laboratory of the Research Technology Program.

Dr. Chatterjee worked in the in vivo methods for many years, and for the past few years has concentrated on the in vitro method as well. He has many years of experience in gene expression (in *E. coli*, yeast and insect cells) and protein engineering (DNA and RNA polymerases, reverse transcriptases, restriction enzymes, and RNase inhibitors). He is interested in making membrane proteins and in protein folding and plans to develop a way to make the proteins more stable and more soluble when cloned.

While the in vitro protein expression method still needs to be refined, it has many advantages, Dr. Chatterjee says. It is faster and allows you to test many proteins at a time. It can be used in any type of experiment involving proteins. Also, since the cells are already killed, the system is perfectly suitable for producing toxic proteins that usually kill live cells.

"In the cell-free system you can supplement anything while the protein of interest is being synthesized—protease

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Arthur's Corner

On the Cutting Edge: The Technology Enhancement Fund

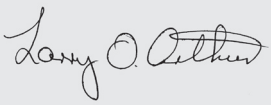
SAIC is a science-based company, founded by scientists and run by scientists, so naturally it has a great interest in scientific technology and innovation. When we prepared the proposal for the current contract, SAIC Corporate suggested that we needed the flexibility to study types of technology that could be useful here at the National Cancer Institute at Frederick but that NCI could not readily fund. So the corporate office provided the SAIC-Frederick, Inc., Principal Investigator with an annual discretionary fund of $500,000 to be used in assessing and bringing in new types of technology to SAIC scientists at NCI-Frederick.

The Technology Enhancement Fund enables SAIC-Frederick, Inc., scientists to access emerging or cutting-edge research technologies relevant to the NCI-Frederick research mission in cancer and AIDS. For example, the Fund can be used to establish a beta test site for relevant prototype instrumentation or software; to do technology enhancement research; to support a visiting scientist with unique expertise in a relevant technology development area; to provide training grants for OTS employees to work in the laboratories of leading scientists in your area who are involved in the development of relevant technology, development of Cooperative Research and Development Agreements (CRADAs); or to invest in technology development in selected biotechnology companies. Relevant topic areas include (but are not limited to) bioinformatics, robotics, proteomics, and genomics.

Any SAIC-Frederick, Inc., employee may apply for funds. The proposals should be innovative and technology-based, preferably with a clear description as to how the effort in the proposal will benefit the general scientific aims and goals of NCI-Frederick. Dr. Jeff Lifson coordinates the Technology Enhancement Fund, while Dr. Robert Wiltrout, Dr. Lifson, and I are the standing members of the Technology Enhancement Fund Oversight Committee. If there are requests in areas outside of our expertise we ask ad hoc reviewers to study the proposals and make recommendations. The Technology Enhancement Web site (<http://web.ncifcrf.gov/intra/tef/>) contains a brief description of the Fund and includes application forms.

Most of the applications so far have come from the Basic Science Program and the Research Technology Program. However, all SAIC-Frederick, Inc., employees are eligible to submit proposals for funding. Many applications have involved purchase of specialized equipment that was not readily available through NCI funding mechanisms. All equipment and other physical assets that are purchased by this funding mechanism are assigned to NCI. A good example of funding which was not equipment-related is our support of integrating a laboratory information management system (LIMS) in the Laboratory of Molecular Technology (LMT) to manage the core services, sample tracking, and data retrieval. The LIMS was originally designed by SAIC for Dr. Kenneth Beutow, a member of NCI's Genetic Annotation Initiative. It is now being customized and expanded to support the needs of the LMT. Since the LIMS is designed in a modular form, it is expected that it can be adapted by other laboratories at NCI-Frederick, at little cost for the expansion, thus fitting the request that the technology funded by this process have broad application to cancer and AIDS research. Finally, this fund is also used to recognize outstanding employees by supporting the achievement awards in the Winter Staff Meetings.

Using Technology Enhancement Funds to explore new research opportunities enables us to get "ahead of the curve" in cutting-edge technology development and to provide our partner, the NCI, with an opportunity to evaluate the technology's usefulness. It's an important area of funding, and we encourage all of you to consider the Technology Enhancement Fund as you plan your programs.



Benefits Corner

Health & Welfare Open Enrollment

It's that season once again—Open Enrollment season, that is. This is the time you are allowed to add dependents, change coverage, and enroll in new plans for the 2004 calendar year.

We anticipate that health and dental premiums will increase again this year. National average increases are predicted at over 15%. As this newsletter goes to print (October), we are working with consultants, negotiating rates, and considering year-round feedback from our employees as well as employee input from last autumn's Employee Survey. We are committed to offering the best value and benefits possible to our employees.

Open Enrollment packets will be mailed to the home addresses of all eligible employees by the first week of November. Please review the packets carefully for changes and important information about the plans. Anyone who wishes to take advantage of the Flexible Spending Health or Dependent Care plans MUST RE-ENROLL for 2004. Your 2003 election WILL NOT carry over into 2004. Open Enrollment meetings for employee questions and presentations from plan representatives will be held in the Conference Center Auditorium, Bldg. 549, at Ft. Detrick during November. Dates and times will be in your packet. Deadline for 2004 changes is December 5, 2003.

Foundations for Tomorrow…

Supporting Clinical Research

The Clinical Research Support Services (CRSS) is now the Regulatory Compliance and Human Subjects Protection Program (RCHSPP). Comprising the Regulatory Group, the Safety Group, and the Clinical Trials Management team, RCHSPP provides dedicated regulatory and clinical monitoring support to a variety of clinical trials conducted by the Basic Research Program within NIAID. These Phase I, II, and III trials run the gamut from natural history to gene therapy and intervention studies, and cover a wide range of infectious disease states. While many clinical studies are conducted at NIH, the staff also travels to remote sites such as Mali, Uganda, and South Africa, and plans to visit South America, Australia, and Europe. The group also participates in major initiatives involving biodefense and bioterrorism clinical trials. SAIC-Frederick, Inc., anticipates staffing approximately 40 clinical research professionals and support staff for these efforts.

The Regulatory Group provides regulatory support in safety and Investigational New Drug (IND) applications. Its 10 team members have diverse backgrounds, including nursing, Good Laboratory Practice, Good Manufacturing Practice, medical technical writing, medical devices, and industry experience. Several members have obtained certifications, including Regulatory Affairs Certification (RAC), Certified Clinical Research Associate (CCRA), and Certified Clinical Research Coordinator (CCRC).

In support of IND applications, the Regulatory Group draws on its extensive experience with the Food and Drug Administration (FDA) to compile, prepare, and submit IND applications, prepare IND annual progress reports, assist investigators with writing investigators' brochures, and provide a comprehensive protocol review to the principal investigator. Currently, the RCHSPP provides support for approximately 15 INDs, which include protocols conducted at domestic and international sites.

To ensure compliance with FDA regulations, the Safety Group oversees the reporting processes for serious adverse events (SAEs) that occur on research studies. This team also reviews informed consent documents to ensure compliance with the Code of Federal Regulations and the International Conference on Harmonization/Good Clinical Practices (ICH/GCP) Guidelines. The Safety Group was instrumental in the formation of the NIAID Intramural Data Safety Monitoring Board (DSMB) and continues to provide support as the Executive Secretary to the DSMB, which currently reviews approximately 10 protocols.

The Clinical Trials Management (CTM) team plays a key role in the success of performing well-controlled clinical research trials that the RCHSPP sponsors. The team's main responsibility is to monitor the clinical research studies and ensure the studies are conducted in compliance with an Institutional Review Board/Ethics Committee (IRB/EC)-approved protocol, applicable FDA and DHHS regulations, and ICH/GCP guidelines.

The key to the CTM team's success is in the services they provide in the areas of protocol/informed consent form review, case report forms design, study initiation visits, routine monitoring visits, and study close-out visits. Detecting, reporting, and resolving discrepancies that occur during the study period and communicating with principal investigators and other study personnel are major challenges for the CTM team. The CTM team is on the front line of clinical research, and they play a major role in the protection of the human subjects, quality of the data, and success of the clinical trials research.

RCHSPP Staff front row(left to right): Marilyn Powers, Terri Deal, Margaret Moos, Shelby Ainsley, Kim Teska, Keren Kessner; 2nd row: Patty Price-Abbott, Jen Imes, Beth Baseler, Tammy McCracken;3rd row: Amy Adams, Julie McLaren, Julie Solarczyk, Shelly Simpson, Susan Maxwell, Corrine Keen; 4th row: Mary Smith, Jill Thompson, Laurie McMahon, Mike Galcik; 5th row: Scott Garrand, Danny Owens, Michael Gay, and Laurie Lambert. Not pictured: Lea Ann Lehmann

Cell-Free Protein Expression

(continued from page 1)

inhibitors, lipids, chaperones [helper proteins that are required for proper folding of other proteins]—depending on the experiment and the scientist's needs," he says. The Cell-Free Protein Expression Group specializes in helping NCI scientists by expressing difficult proteins, including G protein-coupled receptors (GPCRs). GPCRs are an important class of more than 1,000 proteins that are involved in many diseases from asthma to HIV and play a part in about 20 marketed drugs valued at $30 billion per year in sales. According to an August 1, 2003, on-line article in Drug Discovery and Development about Dr. Chatterjee, their toxicity makes the receptors nearly impossible to produce in cells. "Not a single GPCR has been produced in any recombinant protein expression system, in *E. coli*, or any other cells—yet," Dr. Chatterjee is quoted as saying in the article. Thus, he has focused on cell-free systems.

Although the in vitro technology has been around for about 40 years, the amount of protein produced is not as great as that produced in vivo. However, Dr. Chatterjee says, it won't be long until they can equal the in vivo method. Even now, enough is produced for use in many applications, including protein structure determination. Dr. Chatterjee has applied for a patent to protect the method he has developed at SAIC-Frederick, Inc. This will bring to 25 the patents he holds on protein expression, protein engineering and purification.

Dr. Chatterjee says that he finds this work rewarding, challenging, and frustrating. Each protein is different, "an individual beast," he says, just like people. "One size doesn't fit all. That makes proteomics a difficult field. But, after all," he says with a laugh, "research is 95% frustration and 5% satisfaction."

10 Ways You Can Make NCI-Frederick a Better Place to Work!

Protective Services wants to provide a safe and secure working environment for all employees and guests at NCI-Frederick. While we attempt to provide the most secure surroundings possible, all employees and visitors should take responsibility for their own personal safety when on campus.

Most crimes committed at NCI-Frederick are crimes against property, not people. When property is unsecured, a thief can simply walk off with it. We need your cooperation and assistance to make the NCI-Frederick campus a safer and more secure place to work. You are urged to practice the following tips:

1. Always wear your ID badge.
2. Report suspicious individuals immediately to Protective Services (x1091).
3. Never loan your cardkey or building keys to anyone else.
4. To ensure accountability in the event of an emergency, make sure each person enters a building separately, using their own cardkey.
5. Report lost keys and cardkeys immediately to Protective Services (x1092).
6. Do not prop doors open.
7. Never leave your purse or wallet unattended.
8. Secure petty cash in a locked desk or safe.
9. Secure your laptop computer in a locked area or desk, or take it home with you. (Contact the SAIC-Frederick, Inc., Property Accountability Department at x5822 for property loan documentation.)
10. Safeguard all government property. If you notice any government property missing, report it to Protective Services at x1091 immediately!

Translational Research: Taking a Product to Clinical Trial

The National Cancer Institute at Frederick has long been known for translational research, getting products from the laboratory to the patient. Have you ever wondered just what takes place before you receive that prescription drug or take that shot your doctor says you need? This article will follow one such product, a new anthrax vaccine, from the time it was accepted as a project for the Biopharmaceutical Development Program (BDP) to the time it was released for clinical evaluation.

The BDP provides SAIC-Frederick, Inc., biological drug development expertise and production capability to government-supported investigators through the Biological Resources Branch (BRB) branch of the NCI. Following current Good Manufacturing Practices (cGMPs), as outlined in the Code of Federal Regulations, the BDP manufactures parenteral biologics to produce therapeutics, vaccines, viral vectors, and natural products.

In this case, a study conducted at the United States Army Medical Research Institute of Infectious Diseases (USAMRIID), determined the protective effect of the active pharmaceutical ingredient, known as recombinant Protective Antigen (rPA), in a new anthrax vaccine. rPA is produced as a secreted protein in a recombinant, non-virulent, non-spore-forming strain of *Bacillus anthracis*. The animal studies showed that vaccination with rPA protected the animals against mild exposures to virulent *B. anthracis* and greatly increased the time frame for which antibiotics could be successfully

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LASP Employees Keep Up to Date Through Certification

Like many groups on the NCI-Frederick campus, Laboratory Animal Sciences Program (LASP) employees maintain efficiency and constantly refine their expertise through national certification by the American Association for Laboratory Animal Science (AALAS), the highest recognition technicians can achieve.

An AALAS flyer states that the testing "was developed to recognize professional achievement and provide an authoritative endorsement of a technician's level of competence in laboratory animal technology," and that "AALAS certification is recognized by other professional organizations as evidence of a highly educated staff. It demonstrates that continuing education is important in your facility, that technical competence is valued, and that the animal care staff is dedicated to this profession."

Julie Bullock, Veterinary Associate in Laboratory Animal Medicine, Laboratory Animal Sciences Program (LAM, LASP) coordinates the LASP's training program, along with her other duties. Julie teaches 20-week courses to prep employees for certification and notes that the employees "work very hard to study for tests and quizzes and balance all that study time with home and career demands." Often, these courses mark the first time in many years that they have been back in the classroom.

Certification is awarded at three levels: Assistant Laboratory Animal Technician (ALAT), Laboratory Animal Technician (LAT), and Laboratory Animal Technologist (LATG), with the latter being the highest level. To be certified at each level you must meet certain prerequisites in education and experience and pass a certification examination, after which you are listed in a Technician Certification Registry for two years. To continue, you must take continuing education units (CEUs) on a 1-year schedule, maintain your AALAS membership, and pay Registry fees every two years (when submitting your CEUs), according to the AALAS flyer.

The following people, from both NCI-Frederick and NCI-Bethesda, have recently been certified:

Mary Albaugh	LAT	Mary May	LAT
Ranee Baker	LAT	Matthew McCollum	ALAT
Katharine Bergstrom	ALAT	Catherine Morgan	ALAT
Carrie Bonomi	ALAT	Tamara Morgan	ALAT
Suzanne Borgel	ALAT	Stephanie Newborg	ALAT
John Buckley	LATG	Raul Santacruz	ALAT
Lisa Craig-Davis	LATG	Karen Shankle	ALAT
Kelly Dougherty	ALAT	Charlene Shaw	LATG
Angie Hackley	ALAT	Carol Smith	ALAT
Victoria Keck	ALAT	Lori Warg	LAT

Clinical Trial

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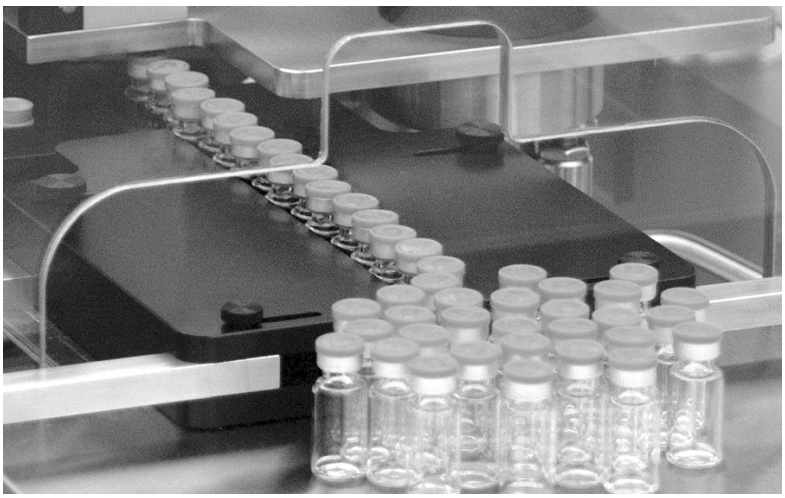
administered after large exposures of virulent *B. anthracis*.

Every BDP project begins with representatives from the BDP, the BRB, and the principal investigator (PI) discussing various aspects of the project, such as data on the current fermentation/purification protocols. This information is critically important because it provides the BDP with a logical starting point. As is often the case, this project required some changes in the original process since the material was to be used in a human clinical trial.

The first BDP group to initiate work on the rPA Project was the Fermentation Development Laboratory. USAMRIID submitted the cell bank to the BDP Quality Control group to isolate the plasmid-encoding rPA and then confirm the DNA sequence prior to any further work with the bacterial strain. The Fermentation Development Laboratory started generating and qualifying a Master Cell Bank from which they would then generate a Working Cell Bank.

Media optimization was also required for the rPA project; the fermentation media employed at USAMRIID contained tryptone, an animal (bovine)-derived media component, as a carbon source. Because of concerns regarding bovine spongiform encephalitis (BSE), also known as "mad cow disease," the Food and Drug Administration (FDA) requires extensive data, including country of origin and herd information, from companies using animal-sourced media components. Experimenting with tryptone replacements during fermentation optimization, the Fermentation Development Laboratory discovered that soytone, a plant-derived protein source, would be effective and have no detrimental effects on the overall process.

From the Fermentation Development Laboratory, the rPA project moved to the Purification Development Laboratory, which scales up processes from bench-scale to pilot-plant level and, if necessary, modifies the purification procedure to achieve the required level of cGMP compliance. As with any drug, it is also desirable to improve final product purity and yield as much as possible. The original laboratory purification procedure for the rPA project required some modifications, revolving around chromatographic resin selection, since one resin used by USAMRIID was no longer in production, and another resin would have made large-scale manufacture prohibitively expensive. When the process was finalized, the Purification Development Laboratory performed a 1:5 scale production purification and trained people from the Clinical Manufacturing Group in the purification methodologies. In addition, the pilot-scale material served as an in-house rPA standard and was also used to generate preliminary real-time stability data in the final formulation buffer.



Now the project was ready for the clinical manufacturing step. The Clinical Manufacturing Group wrote the Batch Production Record that served as the "instruction manual" for how to purify the rPA in a cGMP-compliant fashion. Only after a meticulous technical review by the Purification Development Laboratory and compliance review by Biopharmaceutical Quality Assurance (BQA) was the clinical manufacture of rPA allowed to begin, in preparation for the manufacturing campaign. The Clinical Manufacturing Group packed, tested, and cleaned all the columns, and cleaned and tested all the chromatography equipment. The buffers were all made in a cGMP-compliant fashion. The manufacturing suites were cleaned, monitored, and cleared by BQA for production. BQA-approved disposable materials (i.e., pipettes, gloves, and bottles) were supplied from BDP's Materials Management and Inventory Control (MMIC) group. Once these preparations were in place, production could begin.

The result of all the planning, preparation and constant review required to perform purifications following cGMP guidelines is that the actual purification is usually uneventful and (hopefully) unexciting. During the clinical manufacture of the rPA, samples were taken throughout the process and examined by Biopharmaceutical Quality Control (BQC) for protein content and purity. After purification, another team within the Clinical Manufacturing Group vialed the rPA, then the Central Repository performed a "rate freeze." Samples of the clinical lot of rPA, now

vialed and frozen, were removed for BQC testing and stability. The remainder of the rPA was submitted to MMIC for storage at -70°C under cGMP conditions.

Although the physical manufacturing work was completed, much still had to be done before the product could be used in a clinical trial. BQA and the customer reviewed the documentation generated during the clinical production of rPA in real time. BQA also reviewed the testing results. The Regulatory Affairs Group assembled the manufacturing data into a Chemistry, Manufacturing, and Control document, several hundred pages in length and describing everything the FDA needed to know about how the product was made and what was used to make it. The document was sent electronically to NIAID, where it was merged with the other sections of the Investigational New Drug (IND) submission.

As with all projects, the BDP's work did not stop with the completion of fermentations and purifications. The BDP worked closely with NIAID to address FDA questions about proper mixing and handling of the product at the clinic, e.g., how stable the product was in a syringe. We will conduct regular stability assessments of the product for at least two years or longer, if necessary, to ensure that the product is safe to use during the course of the trial.

Each product is unique and comes to the BDP with its own set of challenges. Nevertheless, the BDP as an organization is committed to conducting first-class science as well as to addressing all relevant aspects of regulatory compliance and quality. In this way, each product, such as rPA, can be fairly evaluated for safety and effectiveness.

Take Your Child To Work Day (July 23)

The annual summer "Take Your Child to Work Day" was held July 23. The weather cooperated as children attended 23 sessions in labs and departments across the campus. Children got a chance to hold mice, run their own experiments, and even meet the campus police dog.

Important Telephone Numbers

Ethics Hotline 1-800-435-4234
Human Resources Department . . . . . (301) 846-1146
Benefits Questions, HR Department . . . . . (301) 846-1146
SAIC Stock Programs 1-800-785-7764
SAIC Stock Price 1-888-245-0104

Important Dates

Winter Staff Meeting . . . . . Wednesday, December 17, 2003
Spring Research Festival. . . . Wed. & Thurs, May 12 & 13, 2004

SAIC Stock

The price for SAIC stock was set by the SAIC Board of Directors on October 10, 2003. The new price is $31.79 per share, up $1.29 from $30.50.

Stock Price Set	Future Trade Dates*
October 10, 2003	October 17, 2003
December 10, 2003	December 17, 2003

**Dates are subject to change.*

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Reminder: Change in Holiday Policy

By the time you read this, you will have had a new holiday, with Columbus Day (Monday, October 13, 2003) having been a scheduled holiday for all NCI-Frederick employees. Remember that Columbus Day replaces the day after Thanksgiving as a holiday for SAIC-Frederick, Inc., employees. That day—Friday, November 28, 2003—will be a scheduled workday.

If you would like vacation leave that day, you should request approval from your supervisor as far in advance as possible so that a vacation leave schedule can be developed that is compatible with your organization's work requirements. Approval of such requests is subject to the operational requirements of each program.

If you have any questions, please call Human Resources, extension 1146.

News & Views
Operations and Technical Support

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