

NIH Launches Undiagnosed Diseases Program

The National Institutes of Health (NIH) announced on May 19 a new clinical research program intended to provide answers to patients with mysterious conditions that have eluded diagnosis. Called the Undiagnosed Diseases Program, the trans-NIH initiative will focus on the most puzzling medical cases referred to the NIH Clinical Center (Bethesda, MD). “A small number of patients suffer from symptoms that do not correspond to known conditions, making their care and treatment extraordinarily difficult. However, the history of biomedical research has taught us that careful study of baffling cases can provide new insights into the mechanisms of disease—both rare and common,” said NIH Director Elias A. Zerhouni, MD. “The goal of NIH’s Undiagnosed Diseases Program is 2-pronged: to improve disease management for individual patients and to advance medical knowledge in general.”

The new program is the culmination of efforts by William A. Gahl, MD, PhD, clinical director at the National Human Genome Research Institute; John I. Gallin, MD, director of the NIH Clinical Center; and Stephen Groft, PharmD, director of the NIH Office of Rare Diseases. With the program infrastructure now in place, the program is ready to accept patients, the first of whom is expected to be seen in July 2008. To evaluate each patient enrolled in the new program, NIH will enlist the expertise of more than 25 of its senior attending physicians, with specialties including endocrinology, immunology, oncology, dermatology, dentistry, cardiology, and genetics.

Gahl, an expert on rare genetic diseases, will serve as director of the new program. “We have developed a stringent referral process to ensure this program deals with those cases that have truly confounded medical experts,”

Gahl said. “We will be very selective when it comes to patient eligibility. Our focus is strictly on conditions that have not been diagnosed.” To be considered for this NIH pilot program, a patient must be referred by a physician and provide all medical records and diagnostic test results requested by NIH. As many as 100 patients who meet the program’s criteria each year will be asked to undergo additional evaluation during a visit to the NIH Clinical Center that may take up to 1 week. Two nurse practitioners will manage patient recruitment and logistics for the new program.

In organizing the Undiagnosed Diseases Program, NIH has reached out to patient advocacy groups that often serve as resources of information and support for individuals with mysterious ailments. “We hope to build upon our strong working relationships with many patient advocacy groups. These organizations provide a crucial link in our nation’s efforts to improve human health through biomedical research,” said Groft.

For more information about the Undiagnosed Diseases Program, see <http://rarediseases.info.nih.gov/Undiagnosed>. Physicians and patients with specific inquiries should call the NIH Clinical Center clinical information research line, at 1-866-444-8806.

National Institutes of Health

AECL Cuts MAPLE Development

Atomic Energy of Canada Limited (AECL) (Mississauga, Ontario) announced on May 16 that it has discontinued development work on the twin MAPLE reactors located at its Chalk River Laboratories. According to a brief press release, this decision was based on a series of reviews that considered, among other things, the costs of further development as well as the time frame and risks involved with continuing the project. “We are making the

right business decision given the circumstances,” said AECL President and Chief Executive Officer Hugh MacDiarmid. “This was a difficult choice given the tremendous efforts expended by our people on development of the MAPLE reactors. Nevertheless, our board of directors and senior management have concluded that it is no longer feasible to complete the commissioning and start-up of the reactors.”

The decision to discontinue development of the MAPLE reactors will not affect the current supply of medical isotopes through commercial agreements between MDS Nordion and AECL for isotope production at the National Research Universal reactor (NRU) and associated facilities in Chalk River. NRU currently has an operating site licence from the Canadian Nuclear Safety Commission (CNSC) that is valid until October 31, 2011. AECL will work with CNSC and MDS Nordion to plan for requirements for continued production beyond that date.

MacDiarmid added, “We recognize the important role that NRU plays in the supply and delivery of medical isotopes to patients in North America and around the world. AECL is committed to supplying medical isotopes from NRU in a safe and reliable manner.”

After the AECL announcement, Gary Lunn, Canada’s minister of natural resources, and Tony Clement, minister of health, issued a statement that included the observation that: “After 12 years, these reactors have never worked and never produced medical isotopes.” They added that “the Government is contacting provinces and territories and key medical experts to assure them there will be no disruption of supply.” These government representatives cited technical and economic impediments that “crippled” successful completion and start-up of the MAPLE reactors. Among these were:

- Regulatory challenges and commercial disputes that cost hun-

dreds of millions of dollars in private and public funds;

- Technical malfunctions that could not be resolved; and
- Reviews conducted by the auditor general that revealed significant concerns about costs, delays, and technical issues.

On May 22 SNM responded to the announcement of the decision on the MAPLE reactors by noting the need to develop alternative sources of medical isotopes. SNM President-Elect Robert Atcher, PhD, called AECL's decision "terrifically disappointing" but noted that the action has invigorated efforts by the nuclear medicine community to secure other isotope sources outside of the United States and to explore the feasibility of U.S. production of medical isotopes. "For all intents and purposes, there is nothing, which is a sad state of affairs," Atcher said. "Most of the places that have an operating reactor do not have the processing capability in the form of hot cells and a staff that would work 24/7 toward that activity. There are some facilities that have the hot cell capability but don't have the manpower or the reactor nearby." He added that SNM is "leading an effort to examine what capabilities do exist, in any way, shape, or form at any stage of development." At Newsline press time, MDS executives were reported to be in talks with Ottawa authorities to review the potential for resuming development of the MAPLE reactors.

*Atomic Energy of Canada Limited
SNM*

ANSTO Cuts Threaten NM Infrastructure

On May 19, the Australian Nuclear Science and Technology Organisation (ANSTO) announced restructuring that will result in \$10 million in annual savings but will require 80 staff cuts from its workforce of 1,009 individuals. The move came as a result of decreases in government funding and a need to meet "core operational, scientific and research objectives in an environment of increasing costs and budget constraints."

Some Australians viewed the government cuts as related to the antinuclear stance of the Australian Labor Party. Opposition senator Eric Abetz told the Australian press that the job cuts will constitute a major setback for nuclear medicine in the country. "There will be a very real impact in the health area for ANSTO and that is going to put at risk a lot of the very valuable diagnoses and treatments that ANSTO's developed for cancer, Alzheimer's, and Parkinson's disease," he said. In addition to early retirements and "involuntary redundancies" (layoffs), the budget decreases will end a number of ANSTO graduate programs in nuclear medicine-related research.

Opposition MP Danna Vale was more pointed in her criticism of government budget cuts. "Not only do these cuts mean local job losses but the massive cut in funding is a blow for the research industry with key studies into health, climate change, and industry to be cut," she said. "Disturbingly, the cuts, which arise from Labor's ideological opposition to nuclear power, will affect not only ANSTO's materials research program, but also their nuclear medicine program. These cuts are a direct result of Labor's \$13.6 million in ideologically driven budget cuts to ANSTO. It is ideology gone mad that Labor will allow its antinuclear agenda to affect work in the nuclear medicine field."

The cuts come at a time when nuclear medicine, including PET and PET/CT, are making greater inroads in routine practice in Australia. A study published in the May issue of the *Australian Health Review* (2008;32:282-291) by Adams et al. from the University of Sydney looked at the nuclear medicine technologist workforce in the country over the past decade. The authors concluded that in that period "service provision increased while workforce size decreased and the nuclear medicine technologist workforce is at risk of failing to meet the anticipated rise in health service needs."

*Australian Nuclear Science and
Technology Organisation
Australian Health Review*

DOE INCITE Resources Available

The U.S. Department of Energy (DOE) announced on May 13 it is accepting proposals through August 11 for a program to support high-impact scientific advances through the use of some of the world's most powerful supercomputers at 4 of DOE's national laboratories. Through the Innovative and Novel Computational Impact on Theory and Experiment (INCITE) program, the DOE Office of Science plans to award approximately 680 million supercomputer processor hours at its laboratories.

"Over the past 5 years since we launched INCITE, the program has achieved some remarkable discoveries," said Raymond L. Orbach, PhD, DOE undersecretary for science. The INCITE program encourages proposals from scientists and engineers from universities, industry, and other research facilities for large-scale science projects requiring the use of high-performance computing systems not commonly available in academia or the private sector. The number of processor hours expected to be awarded in 2009 is more than double the amount allocated in 2008 and is made possible by the new 550 teraflop/s IBM BlueGene P supercomputer recently installed at Argonne National Laboratory (Chicago, IL).

The term "processor hours" refers to allocation of time on a supercomputer. A project receiving 1 million processor h would take 500 h (about 21 d) on a 2,000-processor supercomputer. The same project performed on a single-processor desktop computer would take more than 114 y.

For 2009, the INCITE program provides the only opportunity for researchers to request allocations on the Cray XT4 supercomputer at Oak Ridge National Laboratory (TN) and the IBM Blue Gene supercomputer at Argonne. Other available computing resources are the Cray XT4 supercomputer at Lawrence Berkeley National Laboratory (CA) and the Hewlett-Packard massively parallel system at Pacific Northwest National Laboratory (Richland, WA).

“Although these supercomputers provide tremendous capabilities, a key component of INCITE is the technical expertise provided by our staff members at the centers. In many cases, with the help of our center staff, the applications will run on 10 times or 100 times as many processors to yield results in unprecedented detail,” Orbach said. “But getting to this level of computational readiness can be a high hurdle for even experienced computational scientists. The support provided to INCITE researchers is a key factor in their scientific success.”

Winning proposals will be selected through a peer-review process and are expected to be announced later this year. Current DOE sponsorship is not required for this program. More information is available at <http://hpc.science.doe.gov>.

U.S. Department of Energy

Imaging Trends and Insurance Coverage

In an article in the May issue of *Medical Care* (2008;46:460–466), J.M. Mitchell from Georgetown University (Washington, DC) reported on utilization trends for advanced imaging procedures, drawing on data from individuals with private insurance coverage in California. Using data from a large private insurer, the author documented trends in utilization for MR, CT, and PET imaging from 2000 through 2004 and calculated relative changes in use rates by provider type (self-referring physicians, radiologists, hospitals, and independent diagnostic testing facilities). He found that PET utilization increased by almost 400% (from 2.4 to 12 per 10,000 enrollees) during the study period, whereas MR and CT imaging increases each exceeded 50%. These

increases varied greatly by demographics, types of providers, and areas of the state. The findings suggested that “physician self-referral arrangements and independent diagnostic testing facilities seem to be contributing to this greater use of advanced imaging, especially for MRI and PET,” whereas relative changes in use of advanced imaging performed at hospitals were small. The author concluded that the widely varying utilization rates in northern and southern California and among different providers suggest that reimbursement may be driving unnecessary imaging among the well-insured. He concluded, “Use of highly reimbursed advanced imaging, a major driver of higher health care costs, should be based on clear clinical practice guidelines to ensure appropriate use.”

Medical Care