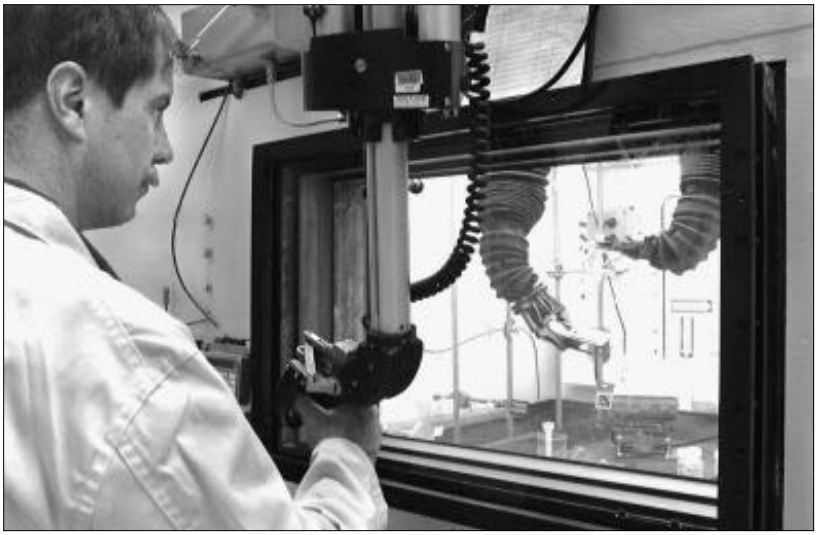
DATELINE LOS ALAMOS

U . S . D E P A R T M E N T O F E N E R G Y
U N I V E R S I T Y O F C A L I F O R N I A

A RACE AROUND THE WORLD

LOS ALAMOS-RUSSIAN TEAM SUPPLIES ONLY SOURCE OF ISOTOPES FOR HEART SCANS

Thousands of heart disease patients nationwide would not be getting important diagnostic tests right now without the efforts of scientists at Los Alamos and a Russian nuclear research institute.



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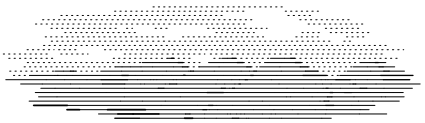
Los Alamos researcher Wayne Taylor inspects a newly arrived strontium-82 "target" in a hot cell at the Laboratory's Radiochemistry Site.



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Los Alamos is providing a precious supply of the medical radioisotope strontium-82, which, when it decays to rubidium-82, is used in positron emission tomography, or PET, a vital imaging technology for diagnosing heart conditions.

Rubidium-82 emits radiation that can be "seen" by special cameras to produce three-dimensional internal images of the heart that show places where circulation is abnormal or blocked.

The three North American facilities — one at Los Alamos' Neutron Scattering Center, one at Brookhaven National Laboratory and one in Canada — capable of producing the irradiated metal sources, or "targets," for the isotope were shut down earlier this year for system upgrades or repairs.

But the collaboration between Los Alamos and the Institute of Nuclear Research in Troitsk, Russia, helped ensure a reliable source of strontium-82 for all the cardiac care clinics doing PET imaging.

The collaboration is a race around the world against the unrelenting decay-rate of the radioisotope itself: with each passing day, another 3 percent of the valuable material is gone.

At the Russian institute, a particle accelerator designed for medium-energy physics experiments is used to irradiate a small block of

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rubidium metal called a "target." The targets — candy bar-sized metal frames that hold the irradiated material inside — are shipped in heavily shielded casks from Moscow to Los Alamos.

After an elaborate chemical extraction process, Los Alamos scientists end up with a precious 13 millionths of a gram of strontium-82 from each source.

The strontium-82 is sent from Los Alamos to Bristol-Myers Squibb in New Brunswick, N.J., where the isotope is mounted on another material to produce a "generator." The generators are distributed to the medical community for use in PET scans by Bristol-Myers Squibb, acting as contract manufacturer for Bracco Diagnostics of Princeton, N.J.

During a PET scan, rubidium-82 is removed from the generator through ion exchange by a normal saline solution and infused directly into a patient. In the bloodstream, rubidium-82 mimics potassium.

Because the heart uses a lot of potassium to do its job, it quickly extracts potassium - and rubidium-82 - from the blood.

The isotope collects in and around the heart and the PET scan reveals places where rubidium-82 piles up. The rubidium-82 decays quickly, so in about 10 minutes the radioactivity in the patient is essentially gone.

Los Alamos first spearheaded a collaboration with the Russian research institute in 1995. The partnership was supported by the Initiatives for Proliferation Prevention program with encouragement from the Department of Energy's Office of Isotope Production and Distribution.

Funded by DOE, the IPP program teams U.S. industry, universities and national laboratories with institutes in the former Soviet Union to develop potential commercial partnerships.

The medical isotope program has now become a source of revenue for all the partners and a success story for the IPP. The Russian institute is incorporated into the global isotope market while its scientists are dissuaded from selling their nuclear expertise to rogue nations.

←

Positron Emission Tomography scans of a heart.

Linda Jacobson (left) and Jason Kitten manipulate samples with remote mechanical arms behind 18-inch-thick leaded-glass windows.

Technology Commercialization International, an Albuquerque, N.M., company, is the member of IPP's business coalition that represents INR, the Russian institute, in the United States. TCI, which manages a number of joint ventures and partnerships with Russian institutes, helped get FDA approval and imports the rubidium targets. The company is pursuing diagnostic and therapeutic applications of other isotopes INR could produce.

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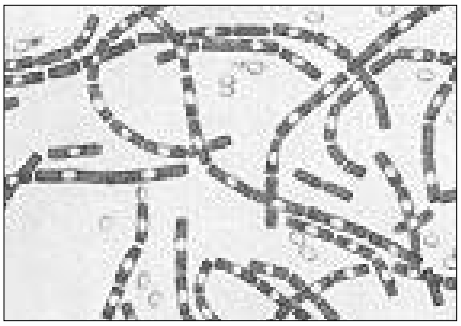
DATELINE: LOS ALAMOS

CATCHING CLUES TO DREAD DISEASES

SCIENTISTS LOOK AT DIFFERENCES IN GENOMES THAT ARE LESS THAN ONE THOUSANDTH OF ONE PERCENT

Los Alamos researchers have advanced a genetic analysis technique to quickly identify diseases in forensic tissue samples and, for the first time, distinguish differing strains of disease that could be present, even if the samples are decades old.

The technique helps pinpoint the source of a disease during a current outbreak, with significant implications for human health and international trade. Forensic samples were analyzed from victims of a human anthrax outbreak that occurred in Russia in 1979.



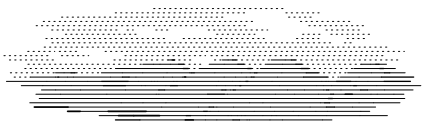
Bacillus anthracis

Los Alamos drew on its extensive background in the separation and analysis of genetic material to test small tissue samples from humans or animals for pathogens and identify slight variations in the genetic fragments of those pathogens.

"To distinguish different strains of a pathogen, we analyze DNA fragment lengths and sequences of specific fragments," said project leader Paul Jackson. "We are looking at differences in the genome that are far less than one thousandth of one percent. And we can detect them readily."

The technique uses the polymerase chain reaction, or PCR, and DNA sequencing. PCR, which replicates DNA fragments in huge volumes, makes current genetic studies possible by producing many identical copies of a single fragment for study.

In a cell, DNA polymerases play an important role in duplicating DNA. In PCR, researchers first heat the double strands of DNA to separate the strands. Then they add a DNA polymerase, along with short DNA fragments called "primers" that start or "prime" the reaction. The reaction



builds a complementary strand of DNA using the information on each of the original strands.

From the two identical copies of double-stranded DNA, four copies are made the same way, then eight, then 16 and so on, taking advantage of exponential duplication — quickly resulting in thousands of copies for study. Thus, all the targeted genetic material necessary for a complete analysis can be gained from one or a very few dead bacteria in a sample.

Los Alamos researchers have taken PCR to another level of precision. A double PCR strategy increased the sensitivity of the procedure while specifically selecting the pathogen under investigation. DNA products of a first PCR amplification were used as templates in a second reaction primed by primers that differentiate among strains of a species.

The technique has been tested on many pathogens. For example, there are many strains of the common bacteria *Escherichia coli*, but the strain *E. coli* Q157 causes food poisoning. The Los Alamos technique could quickly identify that particular strain.

The technology is not limited to human diseases. Analysis also can identify the source of diseases in livestock, poultry and plants. Identifying a disease source or vector is critical to its control.

For example, following an outbreak of anthrax in Norwegian cattle, analysis showed the *Bacillus anthracis* strains came from Third World countries.

The list of possible source countries matched the list of countries from which the fodder supplement bone meal had been imported. Processing bone meal does not kill notoriously hardy *B. anthracis* spores. With a likely source of contamination identified, officials in Norway were able to reduce a serious commercial threat.

Alternately, if an analysis shows a group of samples are infected by exactly the same strain of a disease and the strain is indigenous to that location, it suggests the cause is a natural outbreak and not a food-borne infection, as was recently found in samples from Australian cattle. Such evidence can be crucial to international trade.

Los Alamos does not maintain any live *B. anthracis* culture or any other pathogenic organisms. All DNA is extracted from certified dead tissue and research is conducted on genetic fragments.

“We deal exclusively with the DNA — the genetic blueprint of an organism,” Jackson said.

For the study that showed the technique works on even decades-old samples, Jackson's team performed the analysis on pencil-eraser-sized, formalin-fixed tissue samples from human anthrax victims. The study also included anthrax-infected cattle and primate samples.

The human samples came from forensic studies of an anthrax outbreak that occurred in Sverdlovsk, Union of Soviet Socialist Republics, now Ekaterinburg, Russia, in April 1979. The event has been reported in Russian and English-language media, including a paper in *Science* in November 1994.

At the time, Soviet officials attributed the outbreak to consumption of contaminated meat. But evidence shows that most victims worked or lived in a narrow zone extending from a military microbiology facility in the city to the southern city limit. The zone paralleled the prevailing northerly wind.

Results from the Los Alamos analysis confirmed that tissues from all victims contained fully virulent *B. anthracis*, not a vaccine strain. Analysis further showed the Sverdlovsk victims were infected by a mixture of different *B. anthracis* strains.

All natural outbreaks of anthrax studied resulted from a single strain. While mixtures of strains of anthrax might overcome or confuse defensive therapeutic strategies, there is no experimental data or evidence to suggest that such a mixture is resistant to the AVA licensed anthrax vaccine used by the U.S. military. However, continuing analysis of the samples is addressing this issue.

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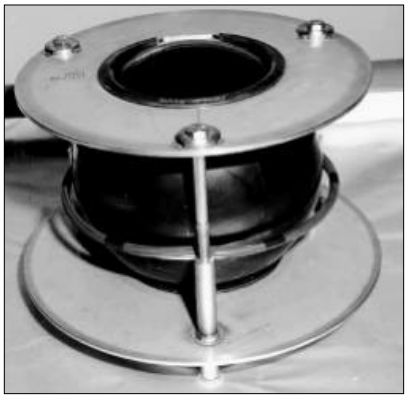
LOS ALAMOS MAKES PLUTONIUM PIT

FIRST WEAPONS CORE PRODUCED IN UNITED STATES IN SEVEN YEARS

Los Alamos weapons scientists have made a plutonium pit like those inside U.S. nuclear weapons, the first produced since 1989. Pits are hollow spheres of plutonium encased in layers of steel and other metals. These metallic shells are located inside the fission component of modern nuclear weapons, including the W88, which sits atop a Trident II missile.

The fabrication of the demonstration pit in February is the first step toward re-establishing the nation's ability to make nuclear weapons to replace those removed from the stockpile for analysis or to fix any defects in the stockpile that affect the safety, security and reliability of the nation's nuclear weapons, said Paul Cunningham, director of the Laboratory's Nuclear Materials and Stockpile Management Program.

"This is a major milestone in our assignment from the Department of Energy to carry out science-based stockpile stewardship to ensure the safety, security and reliability of the nation's nuclear deterrent without nuclear testing," Cunningham said.



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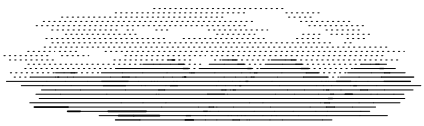
A bowling ball demonstrates a holding fixture for use in a pit storage container.

Mason & Hanger Corp., Pantex Plant

The DOE asked Los Alamos to take over on a limited basis the manufacturing of pits, a job done at DOE's Rocky Flats plant in Colorado until 1989, when it discontinued its plutonium production.

In making the early development plutonium pit, the Laboratory demonstrated that it can perform the complex steps necessary to make this weapon component for the stockpile.

The 1996 Programmatic Environmental Impact Statement for Stockpile Stewardship and Management assigned Los Alamos the tasks of



processing plutonium for fabrication and making pits, in part because Los Alamos has the nation's only full-capability plutonium facility. The PEIS called for Los Alamos to develop the capability to make 20 to 50 pits a year eventually.

"The Laboratory made devices used in the first pits in the 1940s and produced a dozen or so a year for the Nevada testing program," Cunningham said. "But this is the first Los Alamos pit that is in the same configuration and made with many of the same methods as those in the modern U.S. stockpile."

Los Alamos plans to make a few more development units and then produce a replica of a pit from a stockpile weapon. By 2001, Los Alamos plans to produce a pit that will serve as a replacement for a weapon in the stockpile.

These so-called "war reserve pits" will require an extensive birth certificate that documents every detail of their fabrication so that weapons scientists and engineers can track any subsequent changes that might affect the safety and reliability of the weapon far into the future. Los Alamos has experience with these processes through its manufacture for the DOE of war reserve detonators and other non-nuclear weapon components.

Making development pits will help researchers thoroughly understand each step. Once they start manufacturing stockpile pits, their goal will be to duplicate each manufacturing process precisely, Cunningham said.

Los Alamos wants to maintain expertise in pit fabrication as part of an integrated approach to stockpile stewardship. Cunningham said researchers will improve their ability to understand and predict problems in the stockpile by integrating small-scale manufacturing with weapons surveillance, non-nuclear experiments and complex computer simulations.

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DATELINE: LOS ALAMOS

SAFER DRINKING WATER

LOS ALAMOS RESEARCHERS TEST AND TREAT WATER IN GUATEMALAN VILLAGE

The drinking water in the village of San Miguel de Uspantán in Guatemala will be safer to drink thanks to the efforts of two Los Alamos researchers and the Española Valley Rotary Club of Española, N. M., a small community about 20 miles north of Los Alamos.

The Española Valley Rotary Club annually takes on an international charitable project. For a number of years, some members of the civic group have been traveling to the Guatemalan village.

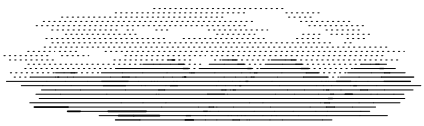
Sondra Cantrell, president of the group, in her trip to the village last year, was told by local doctors that about 80 to 85 percent of the illnesses they treated were related to poor water conditions.

"I thought it would be a lot smarter to treat the problem," Cantrell said. So, she contacted Los Alamos hydrologists Bill Turney and Steve McLin, who got involved with the ongoing project.

The civic group partially funded the trip and Los Alamos' Water Quality and Hydrology Group as well as Johnson Controls Northern New Mexico provided equipment and support. Both researchers spent 10 days in San Miguel de Uspantán last October. Turney's wife, Camille Flores-Turney, also accompanied the researchers where she served as the Spanish-speaking translator.

The village, about 135 miles from Guatemala City and 50 miles from the Mexican border, is home to about 4,000 people. The village sits at the base of mountains where water is drawn from three springs. Researchers concluded that two of the three springs were free of

➔ Los Alamos researcher Steve McLin empties water from a bottle next to Nacimiento Cotoxac spring in Guatemala. The waterfall in the background only flows during rainstorms. The waterfall and a nearby spring where the village of San Miguel de Uspantán in Guatemala draws its water were contaminated with coliform and *E. coli* bacteria.



any nitrates or bacteria. The third spring showed the presence of *E. coli* and coliforms. The absence of nitrates suggests little or no use of pesticides or herbicides.

To test the village's water, Turney and McLin used portable nitrate-testing kits. They also measured chlorine levels in the water, as well as the acid level, and tested for *E. coli* and coliform bacteria. Coliforms were tested by adding a reactive agent to samples taken from the reservoirs.

These samples were then placed in vials that sat for 24 hours. After this period, the samples were placed under an ultraviolet lamp. Researchers were able to detect *E. coli* and coliforms by the darkness of the water when exposed to the ultraviolet light. Related tests also showed the absence of chlorine, which kills bacteria in water.

"Most adults can withstand the presence of nitrates," Turney said. "But for infants less than six months old, nitrates rob their blood's oxygen-carrying capacity."

The village's infant mortality rate is between 50 and 80 percent. This is due to *E. coli* and other toxic bacteria and viruses. The closest fully staffed hospital is in Guatemala City. With no automobiles or bicycles, villagers don't have access to medical treatment in times of emergencies.

Village officials received a demonstration of Turney's and McLin's findings so that they could see the problems of the water supply and so that they could learn how to provide treatment with their existing water testing equipment and the nitrate-test kits left by the researchers.

"Getting the chlorination working was achievable in a short period of time," McLin said. "All these conditions (hepatitis, polio and cholera — contractible through bacteria- or virus-laden water) are life-threatening."

Turney and McLin would like to return to the village to see what progress has been made in addressing the high infant mortality rate and improvements on the water system.

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DATELINE: LOS ALAMOS

BRIEFLY ...


Marion Timm

LOS ALAMOS DIVERSITY DIRECTOR MARION TIMM RECEIVED THE HILDA DAVIS AWARD FOR EDUCATIONAL LEADERSHIP FROM THE NATIONAL ASSOCIATION FOR WOMEN IN EDUCATION. Timm was recognized during the Advancing Women in Higher Education national conference in Baltimore. This award is named after 92-year-old educator and organizational leader Hilda Andrea Davis. The National Association for Women in Education is a professional association that addresses issues in higher education, scholarship and broad advancement of women educators and students. Before coming to Los Alamos, Timm ran the Office of Equal Opportunity and Diversity at the University of California at Irvine and held similar jobs at the University of Vermont, the state University of New York at Stony Brook and the University of New Mexico.

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