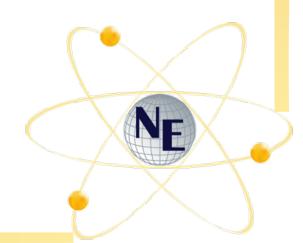
U.S. Department of Energy

The Nation's Needs for Isotopes

Present and Future

John Pantaleo
Program Director
Isotope Program
Office of Nuclear Energy

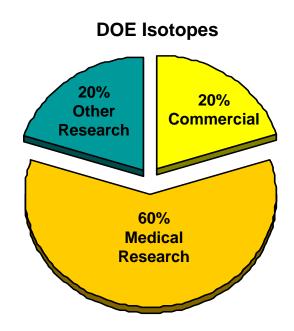
August 5-7, 2008





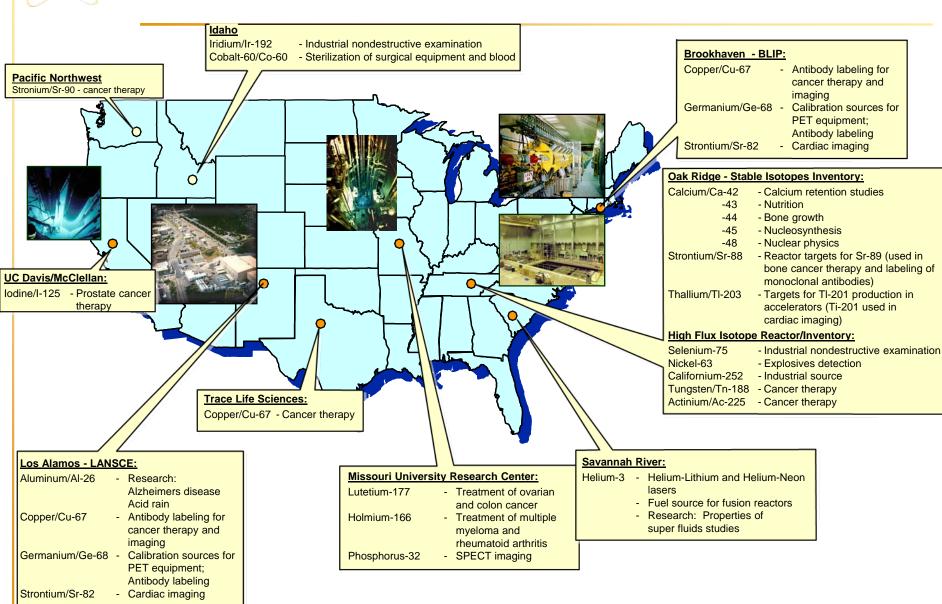
Mission of DOE's Isotope Program

- Produce and sell radioactive and stable isotopes, associated byproducts, surplus materials, and related isotope services.
- Maintain the infrastructure required to supply isotope products and related services.
- Served over 160 customers in FY 2007 and made 484 shipments, most to universities and hospitals





Production Locations





Brookhaven Linac Isotope Producer (BLIP)

Brookhaven National Laboratory

Major Medical Isotopes and Their Applications

| Copper-67 | Antibody labeling for cancer therapy |
|------------------------------|---|
| Germanium-68 | Calibration sources for Positron Emission Tomography equipment, antibody labeling |
| Strontium-82/ Rubidium-82 | Cardiac imaging |

Advantages of BLIP for isotope production

High energy beam with flexible access (200 MeV proton beam)
Well-equipped hot cell facility
Target insertion and retrieval





Isotope Production Facility (IPF)

Los Alamos National Laboratory

Medical Isotopes and Their Applications

| Germanium-68 | Calibration sources for Positron Emission Tomography equipment, antibody labeling |
|------------------------------|---|
| Arsenic-73 | Biomedical Tracer for Arsenic Uptake |
| Strontium-82/ Rubidium-82 | Cardiac imaging |

Advantages of IPF for isotope production

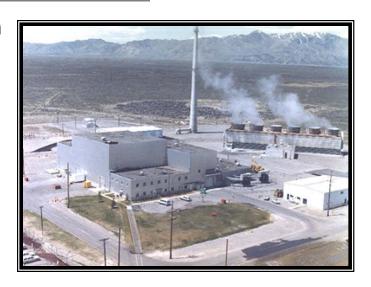
High energy beam with flexible access (100 MeV proton beam)

State-of-the-art facility – target insertion and retrieval

Well-equipped and staffed Hot Cell Facility

Available 30-40 weeks per year

Will enhance short-lived isotope supply





High Flux Isotope Reactor (HFIR)

Oak Ridge National Laboratory

Medical Isotopes and Their Applications

| Californium-252 | Cancer therapy |
|--------------------------|---|
| Nickel-63 | Gas sensing devices |
| Tungsten-188/Rhenium-188 | Bone pain palliation, from liver cancer therapy |
| Selenium-75 | GAMMA Radiography sources |

Advantages of HFIR for isotope production

Neutron flux (~2.6 x 10¹⁵) 3 Easy-access hydraulic tubes Several hot cell facilities

Future

Capacity exists to produce many more isotopes





Advanced Test Reactor (ATR)

Idaho National Laboratory

Isotopes Produced and Their Applications

| Co-60 | Irradiators for sterilization of | |
|-------|----------------------------------|--|
| | medical equipment, etc. | |

ATR Advantages

Moderately high flux neutron flux $(~3 \times 10^{14})$

Many irradiation positions available Hot cell facilities

Future

In 2008, install hydraulic tube for short-lived isotopes

Lutetium-177 and Cesium-131





Chemical and Materials Laboratories

Oak Ridge National Laboratory

Stable Isotope Services

| Chemical physical forms | Metal and ceramic powder |
|---|------------------------------------|
| Pyrochemical conversion – oxides to high purity metal | Wire rolling/swaging (hot or cold) |
| Drop casting | Target fabrication |

These laboratories are available to provide unique stable services and dispense over 200 different isotopes in a wide variety of chemical and physical forms.



Materials Laboratory



Separated Isotopes

• In addition to extensive capabilities for the reactor and accelerator production of radioisotopes, a number of isotopes are also available from the decay of long-lived stock materials or as fission products resulting from the processing of nuclear materials.

Such isotopes include:

Ac-225 Am-241 (currently unavailable)

Cm-248 He-3

Sr-90 U-234



Quality Products and Services

cGMP Radioisotopes

Current Good Manufacturing Practice (cGMP) capabilities have been developed at the national laboratories and are now available for Strontium-82 and Germanium-68 (BNL and LANL) and for Tungsten-188/Rhenium-188 generators (ORNL). These products are provided nonsterile as Bulk Pharmaceutical Products under the cGMP programs.

ISO 9001

Over 200 Stable Isotopes are provided from ORNL as off-the-shelf products in various chemical forms. Custom chemical conversions and physical form preparations are available using metallurgical, ceramic, or vacuum process to provide most stable isotopes in the desired forms for customer applications. Enriched stable isotopes are also often used as the precursor for the production of various radioisotopes. The preparation and distribution of enriched stable isotope products has been ISO 9001 registered through Underwriters Laboratories, Inc., since 1996.



Isotope Development

- Lutetium-177 high specific activity used in peptide radiolabeling emits a low beta energy, which reduces radiation side effects and produces a tissue-penetration range appropriate for smaller tumors, colon, bone, liver, lung cancer.
- Barium-131 is the parent isotope in a Ba-131/Cs-131 generator, an alternative used for the manufacture of seed implants used for prostate cancer therapy.
- Yttrium-86 is a positron emitter which can be used for PET imaging prior to cancer immunotherapy with yttrium-90. Yttrium-86 labeled tumor-seeking monoclonal antibodies (Mab) can be used for evaluating effective tumor uptake and radiation dose.



National Isotope Data Center

- The Department of Energy National Isotope Data Center (formerly the Isotope Business Office) is located at Oak Ridge National Laboratory and coordinates the distribution of all DOE isotope products and services available from DOE facilities.
- Information and quotations for products and services can be obtained by contacting: National Isotope Data Center, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6158, Phone: (865) 574-6984, Fax: (865) 574-6986, Email: isotopes@ornl.gov





| <u>Isotope</u> | <u>Half-Life</u> | Examples of Important Applications | <u>Production</u> | |
|----------------------|------------------|---|--|---|
| Actinium-225/Ac-225 | 10 days | Radioisotope used as the starting material for the Ac-225/bismuth-213 generator. Bismuth-213 is used for targeted alpha therapy for treatment of a variety of cancers, including acute myelogenous leukemia | ORNL - extract Th-229 from U-233, and recover Ac-225 daughter. Production also possible from reactors or accelerators. | 1 |
| Actinium-227/Ac-227 | 21.8 years | Parent of Ra-223, which is used for treating skeletal metastases from breast and prostate cancer | ORNL/PNNL - purify Ac-227 from Ac/Be sources | 2 |
| Silver-110m/Ag-110m | 250 days | Use in combination with other radioisotopes for measuring blast furnace performance. | ORNL - Neutron capture on Ag-109 target | 2 |
| Aluminum-26/Al-26 | 7.2 E+5 years | Medical research on Alzheimer's and environmental research on acid rain | LANL(TRIUMF) - proton spallation on potassium chloride target | 2 |
| Americium-241/Am-241 | 432.7 years | As gamma source, Am-241 is used for well- logging in oil exploration, for analyzing sulfur content in oil, and in home smoke detectors | LANL/PNNL - recovery from operations associated with plutonium production or excess materials dispositioning | 2 |
| Barium-133/Ba-133 | 1.6 days | Calibration source for radiation measurement instrumentation | ORNL - neutron capture on Ba-132 target | 2 |
| Beryllium-7/Be-7 | 53.3 days | Berylliosis studies | BNL - proton irradiation of water | 1 |
| Berkelium-249/Bk-249 | 320 days | Heavy element radiochemistry | ORNL - multiple neutron capture on Cm-244 | 2 |

Notes: 1. Limited Quantities Available 2. Currently Not Available

3. Customer Inquiries; Not in Production



| <u>Isotope</u> | <u>Half-Life</u> | Examples of Important Applications | <u>Production</u> | |
|------------------------|------------------|---|--|---|
| Californium-252/Cf-252 | 2.6 years | Primarily used as a neutron source for reactor start-up, for detection of presence of nitrogen based chemical explosives, and for analysis of sulfur content of petroleum. Technology also being developed for use in brachytherapeutic treatment of cervical cancer | ORNL - multiple neutron capture on Cm-244 | 1 |
| Cesium-131/Cs-131 | 9.7 days | Treatment for prostate cancer | INL - daughter product of Ba-131 decay. Ba-131 made by neutron capture on Ba-130 | 2 |
| Cesium-137/Cs-137 | 30 years | As a gamma source for cargo imaging systems, as a brachytherapy source for intracavitary cancer treatment, as a calibration source in medical imaging systems and radiation protection instrumentation, as the gamma source for blood irradiators, sterilizers, and in research irradiators | Fission product of U-235, recovered from spent nuclear fuels | 2 |
| Cobalt-60/Co-60 | 5.3 years | As the gamma source for industrial and agricultural irradiators and sterilizers, external beam teletherapy machines, and gamma knife systems for brain cancer treatment | INL - neutron capture on Co-59 target | 1 |
| Copper-67/Cu-67 | 2.6 days | As a therapeutic agent for cell-targeted radioimmunotherapy of cancer | LANL/BNL - proton irradiation of zinc oxide targets. Material currently available from Trace Life Sciences | 3 |
| Gallium-67/Ga-67 | 3.3 days | Medical imaging | LANL - proton irradiation of Zn-68 | 3 |
| Gadolinium-153/Gd-153 | 241.6 days | Line sources for PET imaging quality assurance, bone density measurements for osteoporosis detection | INL - Neutron capture on Eu-151 and Gd-152 | 3 |

Notes: 1. Limited Quantities Available 2. Currently Not Available

3. Customer Inquiries; Not in Production



| <u>Isotope</u> | Half-Life | Examples of Important Applications | Production | |
|--|---------------|---|---|---|
| Holmium-166/Ho-166 | 1.12 days | Beta emitting radioisotope studied as a therapeutic agent for rheumatoid arthritis, metastatic liver cancer (microspheres), and hepatoma. | ORNL - Neutron capture on Ho-165 (natural holmium) | 2 |
| Iridium-192/Ir-192 | 73.8 days | Gamma radiography inspection of welds and localized brachytherapy for treating cancer | ORNL - neutron capture on iridium-191 metal | 3 |
| Iron-52/Fe-52 | 8.3 hours | Blood metabolism and blood disease studies | LANL/BNL - proton irradiation of Ni metal | 3 |
| Krypton-85/Kr-85 | 10.7 years | Low pressure beta sources for thickness gauges | Fission product | 2 |
| Lutetium-177/Lu-177 High Specfic Activity | 6.7 days | As a therapeutic agent for cell-targeted radioimmunotherapy of cancer | ORNL - neutron capture on enriched Lu-176 target | 4 |
| Magnesium-28/Mg-28 | 20.9 hours | Research in biometabolic studies and plant nutrient uptake | BNL - proton irradiation on potassium chloride | 3 |
| Mercury-197/Hg-197 | 2.7 days | Medical research and diagnosis in lung and kidney | LANL - proton irradiation of Au-197 | 3 |
| Mercury-203/Hg-203 | 46.6 days | As a brain imaging agent, kidney imaging agent, and as an assay for metallothioneins | ORNL - neutron capture on Hg-202 | 3 |
| Molybdenum-99/Mo-99 | 2.7 days | Starting generator material for the Tc-99m generator used in medical imaging | Fission product. Possible reactor production by neutron capture on Mo-98 target | 2 |
| Neptunium-237/Np-237 | 2.1 E+6 years | Neutron dosimetry and criticality safety and nuclear nonproliferation experiments | Fission product | 2 |

Notes: 1. Limited Quantities Available 2. Currently Not Available

3. Customer Inquiries; Not in Production



| <u>Isotope</u> | Half-Life | Examples of Important Applications | <u>Production</u> | |
|-----------------------|------------|--|---|---|
| Nickel-63/Ni-63 | 100 years | Beta emitter used for as an ionization source in scientific instruments and as a miniature power source for remote instrumentation | ORNL - neutron capture on enriched Ni-62. Less than a five year supply of Ni-62 exists | 1 |
| Promethium-147/Pm-147 | 2.6 years | Beta emitter used as a miniature power source for military electronics | Fission product. Reactor production by neutron capture on Nd-146 target | 2 |
| Selenium-75/Se-75 | 119.8 days | Gamma radiography | ORNL - neutron capture of Se-74 | 3 |
| Silicon-32/Si-32 | 104 years | Research on oceanic circulation, atmospheric circulation, groundwater flow, and dating of marine siliceous biota | LANL (TRIUMF) - proton spallation on potassium chloride target | 4 |
| Strontium-85/Sr-85 | 64.8 days | Evaluation of bone metastases and for brain scans | LANL - proton irradiation on natural molybdenum targets | 3 |
| Strontium-89/Sr-89 | 50.5 days | Treatment for pain relief from skeletal metastases of breast and prostate cancer | ORNL - neutron capture of Sr-88 | 3 |
| Technetium-95m/Tc-95m | 61 days | Radioactive tracer in medical research | BNL - proton irradiation on molybdenum or rhodium targets | 3 |
| Thorium-228/Th-228 | 1.9 years | Parent of Bi-212 for monoclonal antibody labeling used in cancer research and therapy | PNNL - extracted from U-232 | 3 |
| Tin-117m/Sn-117m | 13.6 days | Treatment for pain relief in bone cancer | ORNL - neutron capture on enriched Sn-117 target. Production by accelerator being developed | 4 |
| Titanium-44/Ti-44 | 47.3 years | Parent for Sc-44 used in positron emission tomography | LANL - proton irradiation on manganese chloride target | 3 |

Notes: 1. Limited Quantities Available 2. Currently Not Available

3. Customer Inquiries; Not in Production



| <u>Isotope</u> | <u>Half-Life</u> | Examples of Important Applications | <u>Production</u> | |
|-------------------|------------------|--|--|---|
| Uranium-234/U-234 | 2.5 years | Neutron detection instrumentation | ORNL - recovered as a daughter product from Pu-238 | 1 |
| Vanadium-48/V-48 | 15.9 days | Nutritional and environmental research | LANL - proton irradiation on zinc oxide target | 3 |
| Yttrium-86/Y-86 | 14.7 hours | As a photon-emitting surrogate for yttrium-90 in various cancer treatment applications | BNL - proton irradiation on Sr-88 target | 4 |



DOE Isotopes in Short Supply

Enriched, Stable Non-Radioactive Isotopes used for various applications including as target materials for production of radioisotopes. Although a large inventory of various stable isotopes is available, this List summarizes key examples which have been provided to the academic, research and industrial communities.

| <u>Isotope</u> | Examples of Important Applications | <u>Production</u> |
|---|---|--------------------------------|
| Boron/B-10 | Biomedical labeling and shielding and neutron detection | LANL - ICON |
| Boron/B-11 | Biomedical labeling and production of borosilicate glasses in rad-hard elctronic applications | LANL - ICON |
| Gadolinium/Gd-157 (2 nd pass)/Gd-154 | Nuclear fuel studies | ORNL - calutron enrichment |
| Helium-3/He-3 | Commercially used in Helium-Lithium (HeLi) and Helium-Neon (HeNe) neutron detectors and lasers. Possible fuel source for fusion reactors. Used as a research isotope to study properties of super fluids. Some medical applications | SRO - He-3 processing facility |
| Lead/Pb-204/Pb-207 | Lead poisoning studies | ORNL - calutron enrichment |
| Mercury-202/Hg-202 | Analysis for mercury pollution | ORNL - calutron enrichment |
| Ruthenium-96/Ru-96 | Precursor to Ru-97 which is used as a spinal fluid imaging agent and diagnosis of liver disease | ORNL - calutron enrichment |
| Samarium-150/Sm-50 | Nuclear science studies | ORNL - calutron enrichment |
| Tantalum-181/Ta-181 | Electronic industry research | ORNL - calutron enrichment |
| Tungsten-180/W-180 | Precursor to W-181 used in medical research | ORNL - calutron enrichment |
| Vanadium-51/V-51 | Metal alloying research | ORNL - calutron enrichment |
| | | Pantaleo/5_a |