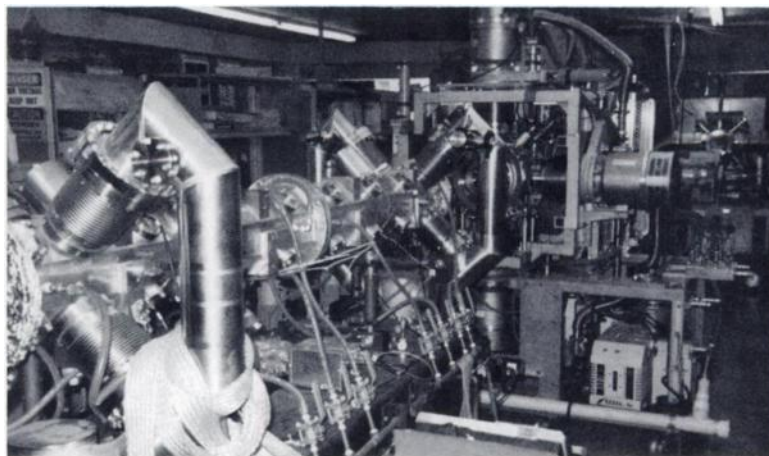


New Isotope Production Company Gearing Up for Nuclear Medicine Industry

In response to the threatened shortage of radioisotopes used in basic and applied research, a new company is preparing to begin manufacturing radioisotopes for the nuclear medicine industry. The company, International Isotopes, Inc. (Denton, TX), will be the first U.S.-based independent commercial manufacturer of pharmaceutical-grade radioisotopes for the nuclear medicine industry. Currently, 70%–80% of all diagnostic nuclear medicine procedures use radioisotopes obtained from sources outside the U.S., accounting for approximately 38% of industry revenue. Moreover, there is no consistent domestic commercial supplier of advanced radioisotopes for use in nuclear medicine basic research and clinical trials—primarily because existing government-owned facilities are committed to other priorities. “The demand from industry is there, and we think we can be considerably more efficient at producing radioisotopes than radiopharmaceutical companies,” said Ira Lon Morgan, PhD, International Isotopes founder and chairman of the board of directors. “At this point, everyone is waiting for us to come on-line and begin manufacturing radioisotopes.”

The company will begin operations by the end of June and will produce 11 radioisotopes, including ^{201}Tl , ^{111}In and ^{123}I , by the end of 1998. The company plans to produce an additional 8 radioisotopes beginning in 1999 (see p. 18N for complete list). So far, International Isotopes has one signed contract, from Imagyn Medical Technologies, a medical device company in Newport Beach, CA. It also has six contracts in the active stages of negotiation and six others in the startup mode, according to Carl Seidel, president and chief executive officer. Seidel emphasized that the company has no intention of becoming a radiopharmaceutical firm. “We’re not going out on the retail market,” said Seidel. “We’ll be making isotopes for other companies who will do the product marketing.”

The biggest appeal of International Isotopes is its acquisition of one of the nation’s most powerful linear accelerators, the injector linear particle accelerator (LINAC). The accelerator was built for the U.S. government’s Superconducting Supercollider project, which was terminated by Congress in 1994. International Isotopes bought the accelerator from the state of Texas in 1996 and moved it piece by piece to Denton. When modi-



fications are completed over the next few months, LINAC will provide 1 mA of current at 70 MeV of energy. In comparison to U.S.-based commercial cyclotrons, LINAC will generate four to five times the beam intensity and more than two times the energy levels.

Six different target stations (with some at intermediate energy levels of 30 MeV and 50 MeV) can be irradiated simultaneously, so several radioisotopes can be produced at once. In its corporate prospectus, International Isotopes predicted that “LINAC will be able to produce 10 to 20 curies of 12 different radioisotopes during a 24-hour period.” The company has also acquired the use of a 42-MeV cyclotron from the University of North Texas for isotope production and special projects and a 2-MW nuclear reactor from Texas A&M University to produce such isotopes as ^{125}I .

Besides LINAC and the cyclotron, the company’s 127,000-square foot administrative and manufacturing facility will house a radiochemistry facility with separate processing equipment for each radioisotope. A radiopharmacy facility that will initially have six suites for processing terminally sterilized products and two suites for aseptically filled processes is also on site and can be expanded to meet increased demand.

There is a major question that remains to be answered, however: Will the company generate enough profits from future contracts to be able to offset its startup costs and operating expenses?

Institute of Medicine Report Spurred Idea for Company

The idea to privatize the production of radioisotopes came to the forefront about 5 years ago when the Department of Energy (DOE) called on uni-

Superconducting Supercollider project LINAC being modified by International Isotopes, Inc., to produce radioisotopes for nuclear medicine diagnostics, therapeutics and research.

Radioisotopes to Be Produced by International Isotopes, Inc.

The following products will be available in the second half of 1998:

Thallium-201
Indium-111
Iodine-123
Iodine-125
Gallium-67
Cobalt-57
Strontium-89
Lead-201
Fluorine-18
Palladium-103
Yttrium-90

The following additional radioisotopes will be available in 1999:

Copper-64
Copper-67
Tin-117m
Cadmium-109
Germanium-68
Samarium-153
Iodine-131
Strontium-82

Additionally, in 1998, the company will provide contract manufacturing, labeling, final packaging and distribution for finished radiopharmaceuticals under customer FDA investigational new drug application- or new drug application-approved processes.

versities and industries to present proposals on how its radioisotope production facilities could be better used by the business and scientific communities outside of government. Morgan, then president of International Digital Modeling Corporation and an adjunct professor at the University of North Texas in Denton, submitted a proposal to the DOE in an effort to get financing to start a research organization in which universities and companies would construct facilities for radioisotope production. In 1994, he presented his proposal to a panel from the Institute of Medicine, which was convened by the DOE to examine whether the supply of medical isotopes in the U.S. was adequate. (The panel recommended the establishment of a national isotope program, a national biomedical tracer facility and additional support for some government and university research reactors, but subsequent congressional budget cuts to DOE programs put most of the proposals on hold.)

"Before the budget cuts, the DOE was considering five proposals that were submitted by the private sector," said Seidel, who served as an advisor to the DOE committee evaluating the proposals. "Dr. Morgan's proposal had the best chance of being commercially viable." When Congress canceled funding for the Superconducting Supercollider in 1994, the state of Texas was given permission to sell off components of the incomplete facility to recoup some of the \$1 billion that it had sunk into the project. With LINAC on the auction block, Morgan decided to form a private company, International Isotopes, that would use the linear accelerator to produce radioisotopes for the nuclear medicine community. The company purchased LINAC for \$2.9 million in 1996 and is spending \$6 million to upgrade the accelerator. "We formed this company to satisfy all the recommendations from the Institute of Medicine report," said Morgan. "We plan to produce those radioisotopes listed in the report as being threatened by supply shortages, and we'd like to be a reliable supplier to any company or research institution that needs radioisotopes."

First Signed Contract

On January 26, 1998, International Isotopes signed its first contract to produce radioisotope brachytherapy implant seeds for Imagyn Medical Technologies. Imagyn committed to pay \$1 million for the development of the proprietary seeds (used to treat prostate cancer and other malignancies) and manufacturing processes. The device company also signed on for a minimum 3-year supply contract, which is estimated to be valued at several million dollars. "We felt comfortable with the management team at International Isotopes and felt they would be the most responsive

to our needs," said Susan Dubé, senior vice president at Imagyn. "We also felt they were offering a competitive price for our brachytherapy seeds."

International Isotopes is also offering a unique service in that it is helping Imagyn design the best formulation for the seeds. "At this point, we're in the throes of debating a number of seed designs," said Dubé. "We could develop a new product that potentially could be patented." Researchers at International Isotopes are providing the scientific knowledge. Since the ^{125}I for the seeds will be produced in a nuclear reactor owned by International Isotopes, Imagyn will not have to contend with the possibility of delays in the startup of LINAC. According to Dubé, Imagyn plans to begin marketing the seeds this summer. "We've already heard from several hospitals expressing interest in purchasing the seeds," she said. "It's very difficult for doctors to get access to these seeds, and there currently is a high demand for a reliable supplier."

Future Plans

Executives at International Isotopes are currently in the process of negotiating contracts with radiopharmaceutical companies and are keeping an open mind and preparing to broaden the company's mission to satisfy market needs. "At first we thought we would only be making radiochemicals, not the completed radiopharmaceuticals," said Seidel. "But a number of companies have indicated that they may want us to provide them with a finished product." The company plans to submit a Drug Master File with the Food and Drug Administration (FDA) in June for each radioisotope it plans to produce. "We're currently working with the FDA to make sure there are no objections to our manufacturing practices, and we expect that they will come to inspect the facility after we are on-line," said Seidel. He added that no formal FDA approval is needed for the company to begin manufacturing. Thus, he does not foresee any startup delays resulting from regulatory requirements.

Although the biggest radiopharmaceutical companies are holding off on signing contracts with International Isotopes, industry executives are hopeful and eager for the company to succeed. "Clearly there is a shortage of key research isotopes that had been provided by government facilities in the past and are no longer being provided," said Roy Brown, director of regulatory compliance at Mallinckrodt, Inc., in St. Louis, MO. "International Isotopes seems to be in a good position to provide isotopes to the radiopharmaceutical community." Although Mallinckrodt is considering using the company as a potential supplier, no contract will be signed until the facility goes on-line, according to Brown.

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Government Relations Committee Meeting Highlights

The ACNP/SNM Government Relations Committee met on January 31, 1998, in Las Vegas, NV, to review its 1997 accomplishments and discuss goals for 1998. As outlined in the 1997 Government Relations Committee annual report (available on the SNM Web site at www.snm.org), the Government Relations Office either completed or made significant progress toward accomplishing each of its 1997 goals. These goals were as follows:

- Pushing for general licensure for diagnostic and therapeutic agents regulated by the Nuclear Regulatory Commission (NRC).

- Implementing "fast-track" approval from the Food and Drug Administration (FDA) for diagnostic cancer agents.
- Implementing legislation governing the approval process for radiopharmaceuticals and other issues such as pharmacy compounding and PET.
- Monitoring and disseminating information on issues pertinent to nuclear medicine.

Looking forward for 1998, the committee discussed a variety of issues affecting nuclear medicine and established new goals for the year. Following discussions

on the FDA, the NRC and the Department of Energy (DOE), the committee set the following goals for 1998:

- To continue to work with the NRC to eliminate unnecessary regulations affecting diagnostic and therapeutic nuclear medicine.
- To work with the FDA to implement the portions of the 1997 FDA reform bill affecting nuclear medicine.
- To increase nuclear medicine research funding governed by the DOE.
- To continue to monitor and disseminate information on issues pertinent to nuclear medicine.

NRC Update

The NRC has finished receiving comments from the regulated community and other stakeholders, completing the drafting stage of the process of revising 10 CFR Part 35. As reviewed by Catherine Haney, chair of the NRC 10 CFR 35 working group, at the SNM House of Delegates Meeting February 1, 1998, the draft rulemaking contained several important changes to the current 10 CFR 35. The document was reviewed by a task force chaired by SNM president H. William Strauss, MD, to develop positions on such important issues as training and experience for authorized users. The task force, which worked right up until the March 1 deadline, concluded that the NRC should remove itself from evaluating clinical competence and focus only on radiation safety. The SNM made

three recommendations to the NRC on training and experience:

1. SNM identified 10+ topics that users should be educated in to ensure competency in radiation safety only.
2. SNM would ensure competency in these 10+ topics through an examination developed and administered by a third party. In recognition of the fact that individuals' aptitudes vary, neither a minimum nor a maximum number of hours was included for this section.
3. SNM also felt it was important to require some handling and practical experience for nuclear medicine. This could be accomplished through either an Accreditation Council for Graduate Medical Education-approved

course or a graduate-level course at an accredited institution. Once again, a specific number of hours was not prescribed; instead, the focus was on subject areas deemed important to understanding radiation safety.

The NRC working group now has approximately 2 months to collate comments and develop a proposed rule for Commission approval. It is expected that the NRC will publish an official proposed rule in the *Federal Register* in May 1998. It is likely that there will be another series of workshops over the summer, with the comment period closing in the fall. The Government Relations Office will continue to closely monitor this topic and provide regular updates through the SNM Web site (www.snm.org).

—David Nichols is the director of the ACNP/SNM government relations office.

New Isotope Production Company (Continued from page 18N)

For now, the nuclear medicine industry will reserve judgment on International Isotopes until the company is up and running and delivers on its expectations of "being able to ship to anywhere in the U.S. within 4 hours" and meeting industry demand for a varied number of isotopes. Stockholders, however,

seem to have already placed their faith in the company. When International Isotopes went public last August, its shares were priced at \$9 per share. As of press time, the stock was trading on the NASDAQ SmallCap Market (under the symbol INIS) for \$19.25 per share.

—Deborah Kotz