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NATIONAL BIOMEDICAL TRACER FACILITY

Project Definition Study

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THE NORTH TEXAS RESEARCH INSTITUTE
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UNIVERSITIES
MEDICAL CENTERS
PRIVATE INDUSTRY
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February 14, 1995

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NATIONAL BIOMEDICAL TRACER FACILITY
PROJECT DEFINITION STUDY

BY A CONSORTIUM OF PUBLIC AND PRIVATE INSTITUTIONS
(In Alphabetical Order)

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Amparo Corporation, Inc., Santa Fe, New Mexico
Bechtel Research and Development, San Francisco, California
Los Alamos National Laboratory, Los Alamos, New Mexico
The North Texas Research Institute, Denton, Texas
Sandia National Laboratories, Albuquerque, New Mexico
Technology Commercialization International, Inc., Albuquerque, New Mexico
The University of Missouri College of Engineering, Columbia
The University of New Mexico Colleges of Engineering and Pharmacy, Albuquerque
The University of North Texas, Denton, Texas
The University of Oklahoma Health Sciences Center College of Pharmacy, Oklahoma City
The University of Texas Southwestern Medical Center, Dallas

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Submitted February 14, 1995

To: **U.S. Department of Energy**
Office of Health and Environmental Research, Office of Energy Research
Medical Applications and Biophysical Research Division, ER-73
Washington, DC 20585

Submitted on behalf of the Consortium by the North Texas Research Institute (NTRI), a not-for-profit corporate affiliate of the University of North Texas

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EXECUTIVE SUMMARY

We request a $25 million government-guaranteed, interest-free loan to be repaid over a 30-year period for construction and initial operations of a cyclotron-based National Biomedical Tracer Facility (NBTF) in North Central Texas. The NBTF will be co-located with a linear accelerator-based commercial radioisotope production facility, funded by the private sector at approximately $28 million. In addition, research radioisotope production by the NBTF will be coordinated through an association with an existing U.S. nuclear reactor center that will produce research and commercial radioisotopes through neutron reactions. The combined facilities will provide the full range of technology for radioisotope production and research: fast neutrons, thermal neutrons, and particle beams (H^-, H^+, and D^+).

The proposed NBTF facility includes an 80 MeV, 1 mA H^- cyclotron that will produce proton-induced (neutron deficient) research isotopes. A second, privately-financed companion facility (part of which is already under construction) will be co-located with the NBTF cyclotron. The companion facility will be an industry-financed commercial isotope production facility with a 70 MeV, 1 mA H^+ linear accelerator (linac) and an intense pulsed-plasma neutron source for producing a limited number of standard commercial radioisotopes, plus a laser-based stable isotope separator. In addition, the NBTF facility will be augmented with a separately funded advanced imaging facility intended to advance the state-of-the-art in medical imaging. The imaging facility will be independently financed and operated. The proposed center — to be comprised of the NBTF, the imaging center, and the commercial production facilities — will be located in North Central Texas near three major airports and the campuses of the University of North Texas (UNT) at Denton and the University of Texas Southwestern Medical Center (UTSMC) at Dallas, whose facilities and existing degree programs will be used for research, training, and education.

Two existing research reactors at Sandia National Laboratories (SNL) in Albuquerque will provide proton-induced radioisotopes for research and provide opportunities for research and reactor-based training. Currently, one of SNL's research reactors and its hot cell facilities are scheduled for modifications to enable production of molybdenum-99 and several other radioisotopes on a commercial scale. The Sandia facilities will be complementary to the accelerator-based facilities in North Texas, with each site producing different radioisotopes.

We propose that the NBTF's research isotopes be processed through the adjacent commercial facility and that their marketing and distribution be coordinated with the existing Isotope Production and Distribution Program (IPDP) of the U.S. Department of Energy (DOE). The linac-based commercial production facility, co-located at the center with the NBTF, will supply a limited number of research isotopes but will concentrate on the business of producing standard raw isotopes and radiochemicals under contract to North American pharmaceutical companies. The commercial facility will assist the NBTF by providing radiochemical processing of cyclotron products under a standard business contract with the NBTF.

We also propose the formation of an NBTF Association whose members will initiate programs in the development of new radioisotopes, radiochemicals, and processing methods. The NBTF and the NBTF Association members' facilities elsewhere will serve as venues for basic, applied, and preclinical research leading to new radiopharmaceuticals. However, the NBTF will not engage in commercial development of radiopharmaceutical products.

Association members — including the University of Missouri, Sandia, the UNT consortium, and two private companies — also will initiate and accelerate existing research and development on methods of separation and enrichment of *stable* isotopes that are used as targets in radioisotope production. The supply of stable isotopes is of crucial importance to the success of the proposed program and the continued advancement of nuclear medicine and research in the life sciences.

Thus, an Association of universities, national laboratories, and private industry in the Central and Southwestern United States will offer a broad scope of research, training, and educational programs that relate to radioisotope applications in medicine, industry, and research. These include the radiopharmacy and radiopharmaceutical R&D programs at the University of New Mexico (UNM) and the University of Oklahoma Health Science Center (OUHSC) and the radiological sciences programs at UTSMC. UNT will provide support through its existing, interdisciplinary programs in accelerator physics and technology, environmental science, organometallic chemistry, materials characterization, and nuclear engineering technology. An on-site program in radiochemistry will be developed by UNT through expansion of existing capabilities, augmented by the existing radiochemistry facilities at UTSMC at Dallas. Both UNM and MU will provide support through their programs in nuclear engineering, health physics, medical physics, and waste management.

The NBTF Association's existing facilities, expertise, and currently-authorized degree programs will be used in lieu of a large, stand-alone research and educational facility at the North Texas site. By using existing facilities and degree programs the NBTF mission will be implemented more rapidly. Distance learning technology, internships, and exchanges among participating institutions (including the national laboratories) will play a strong role in the training and educational program. Industry support and technology transfer will be fostered by a program modeled on other successful programs, such as that of the Missouri University Research Reactor (MURR) and the Tri University Meson Facility (TRIUMF) in Canada.

The NBTF will be managed by a not-for-profit corporation whose operations will incorporate the best features from a variety of existing public-private partnerships. Contractual agreements between the not-for-profit entities and the for-profit companies will be structured for mutual benefit. For example, the NBTF cyclotron will supply a high intensity beam to back up the commercial linac and vise versa, providing an additional revenue stream to help sustain the operations of the NBTF. An economy of scale will be achieved in certain essential functions, such as radiological safety and waste management, through contractual agreements to provide services between the NBTF and the commercial partner.

The marketing and business plans contained within this study provide for self-sufficiency of the proposed NBTF within five years of the beginning of operations.

> ***Currently, we estimate that the mission and goals of the proposed NBTF could be accomplished through a one-time, government-guaranteed loan from DOE of $25 million (interest-free, with principal repaid over a 30-year period) for construction and initial operations of the NBTF facilities.***

Industry will invest approximately $28 million in constructing the commercial production linac and processing facilities located adjacent to the NBTF site.

Our studies indicate that the NBTF could not be self-supporting if operated in a stand-alone mode. However, when strategically located in a center, along with a commercial production facility and users of the NBTF's products (such as the imaging facility), the resulting complementary relationship can lead to self sufficiency. Therefore, a modest investment in this unique location and the proposed public/private partnership can fulfill the requirements of the NBTF and leverage additional resources and benefits for the advancement of nuclear medicine and related disciplines.

1.0 MISSION, GOALS, AND OBJECTIVES

For the Proposed

NATIONAL BIOMEDICAL TRACER FACILITY

"NBTF"

1.1 Context

This document responds to the requirements and criteria set out in the Department of Energy's October 14, 1993 notice inviting proposals for project definition studies for the proposed National Biomedical Tracer Facility (NBTF). It also addresses issues raised in the 1991 report, *National Biomedical Tracer Facility Planning and Feasibility Study* and in the recently-released study by the Institute of Medicine of the National Academy of Sciences, *Isotopes for Medicine and the Life Sciences*.

The previous studies, DOE's solicitation, and supplementary materials recommended that the NBTF be a particle accelerator-based facility that would produce proton-induced (neutron deficient) radionuclides for research. This proposal defines such a facility, but also suggests the use of an existing research reactor and an alternative technology to produce neutron-induced and proton-induced radionuclides for research.

The mission statement, goals, and objectives below include a provision for the use of existing research reactor facilities in concert with the NBTF in an Association that addresses the full spectrum of needs identified in the reports cited above. We envision the accelerator-based National Biomedical Tracer Facility as one component of a public/private center located in North Central Texas. This center and other affiliated centers of excellence located elsewhere can thoroughly fulfill the mission, goals, and objectives stated below.

1.2 Overall Mission

To establish the National Biomedical Tracer Facility (NBTF) as a world-class research and development facility with linkages among institutions to advance diagnostic and therapeutic health care through cooperation among universities, nuclear medicine professionals, the radiopharmaceutical industry, and the national laboratories.

1.3 Principal Goals

- Establish the NBTF as a key component of a national center for isotope production, research and education, coupled with companion (but independently financed and operated) facilities for commercial radioisotope production and experimental medical imaging.
- Utilize and further develop centers of excellence at the participating institutions for the production of proton rich and neutron-induced radioisotopes for research in nuclear medicine, the life sciences, and potential industrial applications.
- Develop new radiochemicals, processes, and prospective radiopharmaceuticals.
- Establish a public/private NBTF Association of academic institutions, industry, and the national laboratories to provide training, education, and research that advances nuclear medicine, related disciplines, and industrial productivity.
- Use existing facilities and programs as much as possible in supporting the production, research, and educational components of the overall mission.
- Involve the private sector where feasible in supporting the NBTF and achieving the goals of the overall mission, including processing, marketing, and distribution of radioisotopes.

1.4 Primary Objectives of this Study

- Provide a conceptual design and propose a site, method of construction, financing, business plan, and management structure for a particle accelerator-based facility to supply proton rich radionuclides for research and to stimulate research and education.
- Describe an operational framework in which the public and private components of this initiative would provide mutual support for each other's operations and missions.
- Address waste generation/disposal, the regulatory environment, and other potential issues connected with radioisotope production by particle accelerator technology.

1.5 Supplementary Objectives of this Study

- Identify the capabilities of an existing research reactor and other technologies to supply neutron-induced radionuclides for research and to stimulate research and education.

- Address the issue of stable isotope availability and define the existing and potential market for research radionuclides and their method(s) of production.

- Address the need to advance medical imaging technology by defining the requirements for a separately-funded, state-of-the-art experimental medical imaging center to be located near the NBTF facility.

1.6 Proposed Future Efforts

If the Department of Energy's reviewers find merit in this proposal, the Association is prepared to initiate a continuation of the study that would define the implementation of the plan in detail. The following, we believe, are key objectives of a continuing study.

1.7 Objectives of Future Efforts

- Establish a site-specific interim governance structure and an implementation team.

- Provide a detailed, site-specific design, site plan, and operational structure for the proposed NBTF.

- Provide a detailed implementation plan and resource-loaded schedule for the accelerator based facility in partnership with a private sector engineering firm.

- Define key contractors and develop definitive, detailed fixed-price bids and delivery schedules for site-specific construction of the particle accelerator based facility.

- Provide a marketing program and distribution system that involves the private sector and is coordinated with the Department of Energy's Isotope Production and Distribution Program

- Institute definitive institutional linkages and a staged implementation plan to initiate the research and educational mission of the NBTF.

2.0 PROJECT OVERVIEW

We propose a public and private partnership that will use existing facilities and create a new, accelerator-based facility, the National Biomedical Tracer Facility (NBTF), for the production of research isotopes for medicine, life sciences, and industry.

We propose to construct the NBTF at a site in the Dallas-Fort Worth-Denton Metroplex of North Central Texas (Figure 2.0-1). The NBTF will become a national center dedicated to the production of research radioisotopes and related R&D and educational activities. In addition to the NBTF, the North Texas center will include an independently financed and operated commercial isotope production facility and an advanced medical imaging facility, also independently financed and operated.

The NBTF and its partners at the North Texas center will affiliate with other centers of excellence through a new organization, the **NBTF Association** (hereinafter referred to as the *Association*), which will be chartered by the consortium of institutions submitting this proposal and whose membership will be open to any North American institution. The Association will provide a national venue for advanced research on isotope production and applications and will promote centers of excellence for training and education in nuclear medicine and related disciplines.

We request a one-time loan guarantee from the U.S. Government for $25 million to build and to provide initial assistance to operate the proposed National Biomedical Tracer Facility (NBTF) and to support research and education in nuclear medicine and related fields.

The cyclotron-based NBTF facility, as well as the advanced imaging center, will be managed as not-for-profit entities and will be open to individual users and user groups from throughout North America (and elsewhere, on a time-available basis). An adjacent facility, based on a high-current linear accelerator (linac), will be built and operated by the private sector to supply a limited range of standard radionuclides in commercial quantities to the radiochemical/radio-pharmaceutical industry.

2.1 Association Membership

The current Association membership includes, in alphabetical order: **Advanced Isotope Technologies, Inc.** (AITI), a for-profit Texas corporation; **Amparo Corporation**, a for-profit New Mexico corporation with technical strengths in accelerator systems design and technology; **Bechtel Research and Development**, a Bechtel Corporation subsidiary, which is

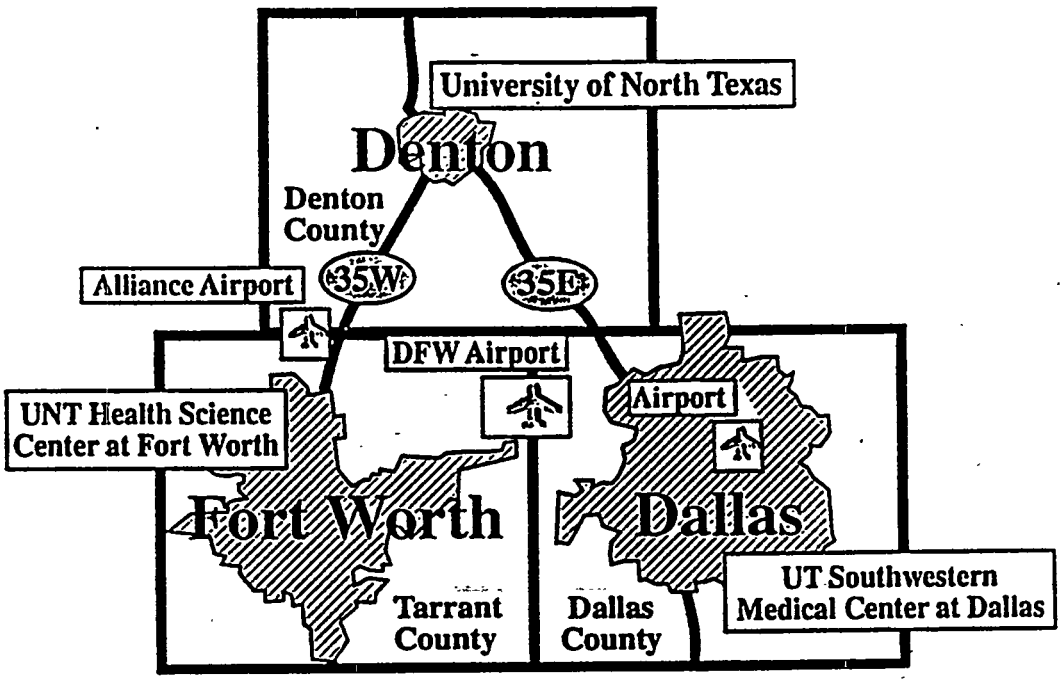

Figure 2.0-1 Dallas-Fort Worth-Denton Metroplex

The proposed NBTF and associated facilities will be located at the northern city limits of Denton, Texas, about five miles north of the University of North Texas campus. The site has easy access via Loop 288 to I-35N to Oklahoma City, I-35E to Dallas, and I-35W to Fort Worth.

a for-profit engineering company with extensive experience in the design and engineering of nuclear facilities, including particle accelerators; **Los Alamos National Laboratory** (LANL); the **North Texas Research Institute** (NTRI), a not-for-profit corporate affiliate of the University of North Texas (UNT); **Sandia National Laboratories** (SNL); **Technology Commercialization International, Inc.** (TCI), a New Mexico-based for-profit corporation dedicated to technology transfer and pharmaceutical development and commercialization; the **University of Missouri** (MU) **College of Engineering**; the **University of New Mexico** (UNM) **Colleges of Engineering and Pharmacy**, the **University of North Texas** (UNT), the **University of Oklahoma** (OU) **Health Science Center's College of Pharmacy**; and the **University of Texas Southwestern Medical Center at Dallas** (UTSMC). If the NBTF becomes a reality, the Association will be broadened to include institutions, individual users, and user groups from other medical and general academic institutions throughout North America (Canada, Mexico, and the U.S.).

2.2 Association Expertise and Previous Efforts

Appendix I lists the principal contributors to this study. Appendix II provides institutional profiles with a description of the expertise they bring to this project. The principal contributors to this study represent over 300 years of experience in accelerator technology, reactor technology, and the production, separation, and distribution of radionuclides. To date, members of the Association have amassed a considerable amount of expertise and knowledge about the feasibility of creating a facility which could satisfy the critical national needs identified in the DOE-sponsored *National Biomedical Tracer Facility Planning and Feasibility Study* (1991) and amplified in the *Proceedings of the Purdue National Biomedical Tracer Facility Workshop* (1992) and the recently-released study by the Institute of Medicine of the National Academy of Sciences, *Isotopes for Medicine and the Life Sciences* (1994). In addition, several members of the Association participated in the preparation of the extensive study of the proposed Regional Medical Technology Center (RMTC), which was submitted to DOE by the Texas National Research Laboratory Commission in September, 1994. The role of AITI, NTRI, and UNT in the RMTC study was to design a commercial radioisotope production facility based on the lower energy (70 MeV) section of the Superconducting Super Collider's (SSC) injector linac.

Previous efforts (and the efforts expended on this study) by AITI, NTRI, and UNT over the past three years have included technological analyses, cost analyses, and consideration of siting, design, architecture, and construction of both commercial and research/educational facilities in this field. A key component of these prior efforts have been three independent research and market analyses to determine the conditions necessary to ensure the economic viability of such a combined facility. We have visited a number of academic institutions, radiopharmaceutical manufacturers, private medical R&D firms, national laboratory facilities, and DOE offices and laboratories during previous work and for this study. Radioisotope

production facilities visited include Amersham (England), Du Pont Merck (North Billerica, MA), the Institut National des Radioéléments (Belgium), the Institute of Nuclear Medicine and Radiopharmacies (Shanghai), the Los Alamos Meson Physics Facility (LAMPF, Los Alamos, NM), Mallinckrodt (St. Louis, MO), Medi+Physics/Amersham (Chicago), Nordion (Canada and Belgium), the Tri University Meson Facility (TRIUMF, Vancouver, Canada), plus several minor producers and the facilities of Association members Sandia National Laboratories (NM) and the University of Missouri (Columbia).

We have also visited and consulted numerous times with a number of commercial companies and federal agencies involved in the design and manufacture of particle accelerators suitable for radioisotope production. These include: AccSys, Inc., the California linac manufacturer that manufactured part of the SSC injector; Ebco Technologies, Inc., a Canadian accelerator manufacturer associated with Vancouver's TRIUMF consortium; Ion Beam Applications s.a., a Belgian cyclotron manufacturer; Los Alamos National Laboratory's Accelerator Operations and Technology Division; and the Paul Sherrer Institut (PSI), a Swiss research institute that operates high current cyclotrons. We have definitive quotations and designs from selected vendors, with guaranteed specifications and costs.

2.3 Proposed New Facilities

We propose to construct the NBTF in North Central Texas near the existing university facilities at UNT in Denton and academic medicine facilities at UTSMC at Dallas. The North Texas center will have three contiguous, but physically and financially separate facilities:

1. **The NBTF — a cyclotron-based research and educational facility,** operated by the public sector, with an 80 MeV, 1 mA cyclotron that will produce research radioisotopes and specialty radiochemicals under conditions of Good Laboratory Practice (GLP) and/or Good Manufacturing Practice (GMP) and support research on isotope production and applications;

2. **A commercial production facility,** *financed and operated by the private sector,* based on a 70 MeV, 1 mA linear accelerator (linac) and an intense neutron source that will supply a limited range of radioisotopes for the U.S. radiopharmaceutical industry under FDA-mandated requirements of GMP; and

3. **An Advanced Medical Imaging Center,** *financed and operated independently of the NBTF and the commercial production facility,* intended to advance the state-of-the-art in medical imaging.

The linac-based commercial production facility must be physically and operationally separate from the research, educational, and imaging facilities to sustain GMP and fulfill its contracted, commercial obligations. However, the cyclotron-based research facility, operating under GLP and/or GMP, will produce research isotopes that could be used in human clinical studies. We must stress that routine 24-hour-per-day, 365-day-per-year commercial production of radioisotopes, which are provided on a definitive schedule to industry using GMP in a dedicated commercial facility, is not compatible with research and development activities. It *is* possible, however, to provide contracted backup to the linac-based commercial facility for both planned downtime and emergencies.

The envisioned Advanced Medical Imaging Center, to be located near the NBTF facilities, will be augmented with animal and human clinical facilities to accommodate research populations and will be separate from the cyclotron and linac-based facilities. The imaging center could ultimately serve as a Southwestern regional imaging facility to provide potential research subjects and a clinical revenue stream in support of its operations.

2.4 Existing Site for the NBTF and Affiliated Facilities

Both the production linac and the research cyclotron will be installed in an existing UNT facility in Denton, the *Nike Site*. This site, a former Nike Hercules launch site, has three large, highly-shielded underground vaults that, with some modifications, will accommodate the proposed production facility and the related research and educational activities discussed below, and will additionally reduce costs for shielding, construction, etc. The 20-acre site is surrounded by farm land, which could be leased or purchased for future expansion of the center or co-location of compatible industrial and not-for-profit entities.

2.5 Transportation

The proposed NBTF site at Denton, Texas, is served by a four-lane divided highway, Loop 288, which joins with I-35 (to Oklahoma City), I-35W (to Fort Worth), and I-35E (to Dallas). The site has excellent access via these interstate highways to DFW International Airport (35 minutes away and hub for American and Delta Airlines and UPS) and Alliance Industrial Airport (25 minutes away and a recently-announced hub for Federal Express). Dallas Love Field, the hub of Southwest Airlines, is 40 minutes away. The North Central Texas site provides an ideal point in the Central U.S. for radioisotope distribution and human travel. Direct airline flights are available to each of the current Association's members from DFW International or Dallas Love Field.

2.6 Accelerator-Based and Reactor-Based Radioisotope Production

We propose that the National Biomedical Tracer Facility (NBTF), located at the North Texas center, be supplemented by the facilities and expertise of an Association of academic institutions, companies, and national laboratories in the Central and Southwestern United States. Existing facilities in Louisiana, Missouri, New Mexico, Oklahoma, and Texas — augmented by a new accelerator-based center located in North Central Texas — will provide the full range of technologies for radioisotope production and research: fast neutrons, thermal neutrons, and particle beams (H^-, H^+, and D^+).

The Association brings together the proposed accelerator facilities, to be located in North Central Texas, with existing research reactors at Sandia National Laboratories (SNL) at Albuquerque, New Mexico, where DOE plans to modify an existing reactor and hot cells for radioisotope production. Reactor-produced neutrons will be employed in the production of radioisotopes that cannot be made (or made efficiently) with accelerator-produced particle beams. In addition, an intense neutron source, located at the Texas site and operated by the for-profit company, will provide a source of fast neutrons, epi-thermal neutrons, and deuterons for radioisotope production.

2.7 Production Facilities

The Association's production facilities will include the existing nuclear reactor at Sandia, two particle accelerators (the NBTF cyclotron and the commercial linac), and an intense neutron source. The particle accelerators and the intense neutron source will be located near the University of North Texas (UNT) at Denton and the University of Texas Southwestern Medical Center (UTSMC) at Dallas. The Association and its facilities will supply critical medical research radioisotopes to users throughout North America, including medical and life science researchers, the U.S. pharmaceutical industry, and other industrial users. The North Texas center's facilities will produce the following categories of products and services:

1. **A wide variety of research radioisotopes** and specialty radiochemicals for life science and medical researchers;

2. **Basic and applied research** on stable isotope and radioisotope production and applications; and

3. **A limited range of commercial radioisotopes** for industry under commercial contracts.

The North Texas center's facilities and expertise, including the NBTF, will also be available for proprietary R&D through contractual agreements with industry on a time-available basis.

The Association's existing facilities and the proposed North Texas center will lay the cornerstone for a broad national consortium dedicated to research and education in nuclear medicine and allied disciplines.

The Sandia reactor and hot cell facilities, currently scheduled for an upgrade by DOE, will produce molybdenum-99 and a limited range of commercial radioisotopes. The Sandia reactor's annular core provides an ideal configuration for research and research isotope production using low-energy and epithermal neutrons.

A commercial intense neutron source, based on dense plasma focus technology and located at the North Texas center, will provide a source of fast neutrons for commercial radioisotope production and research. Los Alamos National Laboratory (LANL) currently provides equipment and personnel in support of the neutron source development through a Cooperative Research and Development Agreement (CRADA) with AITI. This activity, which has progressed in experiments at Los Alamos to the stage of commercial development, moved from LANL to UNT's Nike site in January 1995 under the agreement between AITI and LANL. The intense neutron source is based on dense plasma focus technology that uses deuterium or deuterium/tritium to create a neutron flux sufficient to convert stable isotopes to radioisotopes in commercial quantity.

2.8 Rationale for the Advanced Medical Imaging Center, its Capabilities, and Funding

The Radiological Sciences program at UTSMC at Dallas is heavily engaged in research and development of advanced medical imaging technologies, as well as basic, preclinical, and clinical research in nuclear medicine. The UTSMC nuclear medicine faculty therefore propose to develop a basic/preclinical experimental imaging unit adjacent to the NBTF at the Denton site.

> ***The proposed Advanced Medical Imaging Center will be separately financed and operated, independent of the NBTF and the commercial production facility.***

The Advanced Medical Imaging Center will be managed by UTSMC personnel under the umbrella of UTSMC and the NBTF Association. Like the NBTF, the imaging center's facilities will be open to Association members and other users for basic and preclinical research. The laboratory will include both anatomic (CT) and functional (PET and SPECT) imaging devices specialized for small animal imaging at high resolution and sensitivity. A special focus of the imaging center will be the design, development, and building of advanced, high resolution prototype imaging devices for special applications.

Development of the imaging center will be staged; i.e, first located in existing facilities with

small animal support facilities in nearby Dallas, and later augmented in a specially designed facility at the Denton site. The Denton imaging facility will be adjacent to a unique source (the NBTF) of radioisotopes with a wide range of energies, half-lives, and chemical/biological properties that will enable research that otherwise could not be done at any existing center in the U.S. Separate financing for the Denton imaging center will be sought from the state, federal agencies, and the private sector.

2.9 Stable Isotopes

In addition to radioisotope R&D, the facilities and expertise of Missouri, Sandia, and the North Texas group will provide the base for an accelerated R&D program in *stable isotope* separation and enrichment. This activity will be funded through public sector grants and private sector R&D contracts. Research on laser-based stable isotope separation currently is underway at MU's College of Engineering and at AITI/UNT. Association member Technology Commercialization International, Inc. (TCI), a New Mexico-based corporation, has obtained exclusive marketing and distribution rights for both stable and radioactive isotopes from several Russian institutes. TCI will assist the NBTF and the Association in obtaining stable isotopes and in technology transfer from foreign sources, particularly Russia. TCI is awaiting DOE's approval of a proposal submitted through the United States Industry Coalition (USIC) as a joint project with Sandia for the purpose of developing and commercializing an improved process for the generation and separation of molybdenum isotopes (and potentially other isotopes) for medical applications. The availability of stable enriched isotopes for radioisotope production and life sciences research is of great importance to the success of the proposed program and the continued advancement of nuclear medicine and related disciplines.

2.10 Fiscal Realities of the Proposed NBTF

Our financial and market analyses indicate that a **stand-alone** National Biomedical Tracer Facility (NBTF) producing only research isotopes could not be self-sustaining as required by the conditions of the DOE solicitation for proposals and supplementary information issued by DOE. Our analyses also suggest that a **stand-alone** NBTF could not fully address the current and future needs of the nuclear medicine community as addressed in previous studies and in the recently-released report of the Institute of Medicine (IOM) on *Isotopes for Medicine and the Life Sciences*. However, our studies also indicate the following:

> ***If the NBTF is constructed as part of a center that also contains a state-of-the-art commercial production facility, which can supply processing, waste handling, and other support, as well as isotope consumers (such as the imaging center), the NBTF can be both self supporting and meet the needs defined in the IOM report.***

Thus, the management structure we propose is based on fiscal realities that require a mix of mutually-supporting facilities at the NBTF site.

2.11 Proposed Oversight Structure

As stated at the beginning of this section, we propose that the NBTF be constructed and operated as one of two key components of the center located in North Central Texas. The other key component of the proposed center is a privately-funded, state-of-the-art commercial production facility already underway by Advanced Isotope Technologies, Inc. (AITI). The center will be further enhanced by the addition of the Advanced Medical Imaging Center, also independently funded.

> ***We also propose the formation of a* National Biomedical Tracer Facility Association *(the NBTF Association or Association), which will tie together the NBTF, the other North Texas facilities and affiliated centers of excellence throughout North America.***

The new Association, open to both the public and the private sector, will address all isotope-related issues raised in the IOM report. The Association will be both a forum for the discussion of such issues and an instrument for solving problems through the proposed NBTF and through Association member facilities throughout North America. The NBTF and associated facilities will be advised by a Scientific Advisory Committee and an Industrial Advisory Committee organized by the Association.

2.12 Management and Operations of the NBTF and its Affiliates

We considered a number of alternative management structures, including the following: state ownership and operation, not-for-profit corporate ownership and operation, for-profit corporate ownership and operation, for-profit consortia, not-for-profit consortia, and multi-partner university consortia. The operational structures we propose are based, in part, on that of the Missouri Research Reactor center (MURR) and the Houston Advanced Research Center (HARC), and the Tri University Meson Facility (TRIUMF).

We propose that the NBTF be managed as a division of NTRI, the not-for-profit corporate affiliate and technology transfer arm of the University of North Texas. The director of the NBTF will be appointed by the executive director of NTRI and ratified by the NBTF Association and NTRI boards of directors. Alternatively, a new, not-for-profit corporation could be founded, or the NBTF Association could be appropriately incorporated to manage the NBTF. The NBTF will be directed by an executive director, assisted by scientific and technical staff. The director and the scientific and technical staff will be full time employees

of the NBTF, but those with the appropriate experience and credentials will be eligible for joint faculty appointments to the graduate faculties of nearby UNT and UTSMC, and other Association members, as appropriate.

The cyclotron-based research and educational facilities of the NBTF will operate as a not-for-profit entity, open to individual users and user groups from throughout North America. The linac-based commercial production facility will be operated by a private sector company (AITI) that will serve industry through standard business contracts with its industrial customers. The combined isotope production facilities of the center will permit the NBTF to eventually be self-sustaining. The two components will reinforce each other's missions through mutually supporting contractual arrangements. For example, the cyclotron will provide a high intensity beam to back up the linac, an arrangement that will provide an additional revenue stream to help sustain the operations of the cyclotron-based research and educational unit. As recommended in the recent study by the Institute of Medicine of the National Academy of Sciences, *Isotopes for Medicine and the Life Sciences*, high activity research isotopes produced by the cyclotron will be processed by the commercial operator under contract with the NBTF management entity. An economy of scale could be achieved in certain essential functions (such as radiological safety, product shipping, and waste management/handling) through contractual agreements to provide certain services between the NBTF and the commercial company.

2.13 Product Demand and Specific Products

Considerable effort was expended in this project definition study to define the likely market for research radioisotopes, retail radioisotope products, and wholesale radiochemicals. Sections 4 and 7 incorporate such information, as does Appendix IX. Appendix IX discusses estimates of the general market, including the 1993 U.S. radiopharmaceutical and radiochemical markets and the 1993 bulk wholesale radiochemical market. Candidate radioisotopes were identified through the existing literature, through personal interviews with approximately 40 recognized experts in the field, and through the list of radionuclides suggested in the *Proceedings of the Purdue National Biomedical Tracer Facility Workshop* (1992).

> *Note: The following list of candidate research radionuclides includes a number of positron emitters, not because we expect an upsurge in PET cameras and PET usage, but because of an apparent trend to use positron emitters for gamma imaging with cameras equipped with special high energy collimation. New cameras are also being developed for high resolution imaging with higher energy gamma photons.*

The radionuclides and generator systems identified in the Purdue report are the following (in alphabetical order): (1) high priority radioisotopes, including Antimony-118, Arsenic-72, Arsenic-73, Arsenic-74, Barium-128, Beryllium-7, Bromine-77, Bromine-80m, Cesium-128, Copper-61, Copper-62, Copper-64, Copper-67, Fluorine-18, Gallium-68, Indium-113m, Indium-114m, Iodine-122, Iodine-124, Iodine-125, Iron-52, Lutetium-172, Magnesium-28, Manganese-56, Rubidium-82, Ruthenium-97, Sodium-22, Tantalum-179, Technetium-95m, Technetium-96, Vanadium-48, Xenon-127, Yttrium-88, and Zirconium-89; and (2) radioisotope generators to produce some of the above radioisotopes (in alphabetical order of the daughter isotope), including Tellurium-118/Antimony-118, Selenium-72/Arsenic-72, Barium-128/Cesium-128, Zinc-62/Copper-62, Germanium-68/Gallium-68, Tin-113/Indium-113m, Hafnium-172/Lutetium-172, and Strontium-82/Rubidium-82. Some of the isotopes on the Purdue report list were excluded from consideration as NBTF product candidates because of one or more of the following reasons: (1) difficult to produce; (2) no clearly demonstrated clinical or research need; or (3) more attractive alternative isotopic candidates are available. Those radioisotopes excluded from further consideration here are the following, listed in alphabetical order: Astatine-211, Bromine-75, Bromine-76, Bromine-80m, Calcium-45, Cesium-137, Cobalt-60, Gadolinium-153, Gold-198, Iodine-131, Iron-55, Lutetium-177, Magnesium-28, Manganese-54, Molybdenum-99, Platinum-193m, Potassium-43, Silver-111, Tellurium-123m, and Tin-117m.

In a separate exercise, the North Texas group's own team of industry professionals separately identified additional potential research isotopes and generator systems. They also identified the stable isotopes needed for accelerator targets, nuclear reactions, excitation functions, needs for target development, and other R&D issues. The radionuclides identified through this process include (in alphabetical order): (1) research isotopes, including Bismuth-205, Bismuth-206, Bismuth-207, Cerium-139, Chromium-51, Iron-52, Iodine-125, Rhenium-186; and (2) isotope generators, including Iron-52/Manganese-52m, Neodymium-140/Praseodymium-140, Rubidium-81/Krypton-81m, and Tungsten-178/Tantalum-178.

The team also explored the possibilities for supplementing the production of existing products now produced at the national laboratories but on an infrequent basis. These radionuclides include the following products that are currently in demand but not produced by industry: Strontium-82, Germanium-68, Copper-67, Cadmium-109, Xenon-127, Cobalt-57, and Fluorine-18. If produced, Fluorine-18 will be distributed regionally due to its short, two-hour half life. Additionally, the NBTF will study lower cost methods for producing some existing commercial products, such as Lead-201, Iodine-123, etc. See Sections 4 and 7 for more complete discussions of candidate nuclide products.

2.14 Marketing and Distribution of Products and Services

We propose that production and distribution of research isotopes be coordinated with the U.S. Department of Energy's Isotope Production and Distribution Program (IPDP) to ensure that the IPDP and NBTF programs are complementary and mutually supportive. Advisory oversight through the Association, the Scientific Advisory Committee, and the Industrial Advisory Committee will include broad representation from the concerned communities, including professional societies, industry, academe, and government.

2.15 Outreach and Technology Transfer

Distance learning technology, student internships, postdoctoral training, and faculty/staff exchanges among participating institutions will play a strong role in the training and educational program. Industry support and technology transfer will be fostered by a program modeled on other successful public/private partnerships, particularly that of Canada's Tri University Meson Facility (TRIUMF). Industry also could access NBTF facilities and expertise for proprietary R&D through contractual arrangements. The proposed NBTF technology transfer program will likely favor industries of the North American Free Trade Agreement (NAFTA) group. However, non-NAFTA industries will not be excluded. Like TRIUMF, the NBTF technology transfer program will have two objectives:

- *Dissemination of technology transfer opportunities to industry in support of economic development, and*
- *Provide additional revenues through royalties and technology licensing to support the research and educational missions of the NBTF and the Association.*

Finally, TRIUMF and other research centers have amply demonstrated the importance of international participation in research. Hence, both North American and all international users and user groups will have access to the NBTF's research facilities, with priority determined through peer review involving the Association. Proprietary research under contract with industry will be individually considered and approved by the NBTF management aided by the Association's Scientific Advisory Board. Proprietary research will be accommodated on a time-available basis that does not disrupt nor displace basic research nor the production of research isotopes.

Both Sandia and Los Alamos will add a breadth of other technologies in support of research in nuclear medicine and related disciplines. They will also provide for a sharing of technology, facilities, and research that will complement the accelerator-based installation in North Central Texas and other members of the Association.

2.16 Use of Existing Facilities at Other Locations

We envision that the Association will ultimately offer a broad scope of research, training, and educational programs that relate to radioisotope applications in medicine, industry, and research. However, the business plans for the NBTF and its commercial partner indicates that the NBTF could not sustain the overhead of a large, stand-alone research and educational facility at the North Central Texas site. This will not be wise nor tenable in our opinion. Instead, we propose to use existing facilities, expertise, and currently-authorized degree programs at the collaborating academic institutions and the national laboratories.

2.17 Research and Educational Contributions of Association Members

The contributions of the reactor facilities at Sandia to radioisotope production are desirable because they contribute capabilities that the NBTF will not have. Sandia's two reactors and the Reactor Engineering and Technology Center's processing facilities provide ample opportunities for research as well as the current DOE plan for commercial production of molybdenum-99. Sandia, MU, UNM, and UNT will also contribute expertise in nuclear technology, nuclear engineering, nuclear engineering technology, health physics, and related areas.

The University of Texas Southwestern Medical Center at Dallas (UTSMC) has existing, excellent facilities for radiochemistry, radiolabelling, medical imaging (both anatomical and functional), animal studies, continuing education, graduate education, and postgraduate research. This facility is located approximately 40 minutes by car from the proposed NBTF site and the University of North Texas and offers many doctoral programs, including Radiological Sciences. The educational and research program in Nuclear Medicine will be centered in the facilities of UTSMC at Dallas, within the departments of Radiology and Radiation Oncology, both involving the graduate program in Radiological Sciences. The educational and research program in Radiochemistry will be centered in the NBTF facilities, the facilities of UTSMC in Radiological Sciences, and UNT's graduate program in Chemistry. UTSMC will staff and manage the proposed Advanced Medical Imaging Center and related on-site animal research and clinical research facilities.

The University of North Texas (approximately ten minutes by car from the proposed site) has existing, excellent faculty and facilities in the physical, life, and computational sciences. UNT's role will be education and R&D in the basic sciences and engineering technology, including programs in accelerator technology, accelerator operations, and health physics. UNT grants bachelor's, master's, and doctoral degrees in all of the natural science and computational sciences. UNT will draw on its existing articulation agreements with community colleges to develop technical training programs in the disciplines that support nuclear medicine and related industrial areas. Both UTSMC and UNT offer strong

continuing education programs, and each has administrative offices and facilities to support these efforts which draw on the expertise of the faculty and other professionals.

The University of Missouri (MU) will contribute graduate programs (M.S. and Ph.D.) in nuclear engineering with concentrations in health physics and medical physics. MU will also assume a leadership role in continuing education and distance learning technology.

> ***We propose to place the NBTF and the NBTF Association's educational program in the vanguard of institutions creating the electronically-linked*** **virtual university** ***of the 21st Century.***

Both the University of New Mexico (UNM) and the University of Oklahoma (OU) have nationally-recognized educational programs in radiopharmacy and strong programs in radiopharmaceutical R&D. Each also has links to the private sector that will be exploited in technology transfer from the NBTF. MU and UNM's programs in nuclear engineering and UNM's program in waste management also will bolster the educational and research missions of the NBTF.

We envision that the Association will ultimately offer a broad educational program, including performance-based technical training, continuing education, undergraduate and graduate degree programs, and postdoctoral training. Applicable educational programs currently in place at the collaborating institutions include Biochemistry (B.A./B.S., M.S., Ph.D.), Biomedical Engineering (M.S., Ph.D.), Biological Sciences (B.A./B.S., M.A./M.S. Ph.D.), Chemistry (B.A./B.S., M.S., Ph.D.), Doctor of Medicine (M.D.), Environmental Science (M.S., Ph.D.), Hazardous Waste Engineering (M.S.), Nuclear Engineering (B.S., M.S., Ph.D.), Nuclear Engineering Technology (B.S., M.S.), Molecular Biology (M.S., Ph.D.), Molecular Biophysics (Ph.D.), Pharmaceutical Sciences (M.S., Ph.D.), Physics (B.A./B.S., M.A./M.S., Ph.D.), Radiological Sciences (M.A., Ph.D.), and Radiopharmacy (B.S., Pharm.D., Ph.D.). Graduate degree programs in Radiochemistry are included under UTSMC's program in Radiological Sciences.

> *The Scientific Advisory Committee of the Association will annually hold a competition for graduate scholarships, predoctoral internships, postdoctoral fellowships, and grants for faculty/staff exchanges among Association members and the national laboratories. The competition and awards will be managed by the NBTF management entity.*

We also propose training and educational programs in Accelerator Technology, Accelerator Operations, and Health Physics with headquarters in the Ion Beam Modification and Analysis Laboratory (IBMAL) on the nearby UNT campus. IBMAL operates five different accelerators and is the world's leader in atomic mass spectrometry (AMS) of stable isotopes, having perfected the technology to detect uniquely any element in the periodic table except

indium (which has isobaric interferences) at the sub parts-per-billion level, with the expectation to reach the parts-per-trillion level (one part in 10^{12}) in the near future. UNT's Department of Physics has a 25-year history of excellence in the application of accelerator technology to atomic and nuclear physics and, most recently, in accelerator-based materials characterization. Every two years, UNT hosts the *Conference on the Application of Accelerators in Research and Industry*. It is the premier international conference in the field of accelerators as applied to *both* research and industrial applications. For example, in the most recent 13th Conference (November 1994), entire sections were devoted to atomic and nuclear physics, isotope production for medical applications, biological and medical applications of AMS, targetry, accelerator-based neutron sources for barium neutron capture therapy, high energy physics, radiation processing, materials analysis, accelerator technology, radiation safety, and other areas.

Los Alamos National Laboratory (LANL) is providing equipment and personnel in support of development of the intense neutron source through an agreement with AITI to develop an alternative technology for radioisotope production. This development has progressed to the stage of commercial application. Equipment and personnel moved from LANL to AITI's leased facility at UNT's Nike Site in January 1995 under the agreement. This program, based on dense plasma focus technology, will develop a commercial prototype and subsequently, production units that will provide fast neutrons for radioisotope production.

2.18 Business Plan

To summarize, the NBTF will be structured and operated as a key component of the NBTF center, located in North Central Texas. The other key component of the proposed center is a privately-funded, state-of-the-art commercial production facility already under construction by AITI. The center will be further enhanced by the addition of an Advanced Medical Imaging Center, also independently funded and operated by UTSMC.

The NBTF will provide two basic groups of products and five categories of services. The groups of products are:

- *Research radionuclides for the nuclear medicine and industrial communities; and*
- *Specialized commercial radionuclide products.*

The categories of services are:

- *Basic research and development of new isotopes, processes, separations, and radiochemical processes;*

- *Contract research and development for AITI and other companies;*
- *Service irradiation and backup production for AITI and other companies;*
- *Technology transfer of NBTF developed technology; and*
- *Education and training.*

The NBTF is expected to operate at a break-even point within five years after installation and commissioning of the cyclotron and associated facilities. The sources of funds for NBTF construction are a $25 interest free loan, and in-kind facilities donated by UNT. The replacement costs of the donated facilities are estimated in excess of $5 million.

The major sources of NBTF Operating Revenues are the following:

- *Total income from the sale of research radioisotopes is estimated to grow to approximately $3.5 million annually in the fifth year of operation. These radioisotopes include imaging, therapeutic, industrial, and other radioisotopes used in life sciences research and development. The estimate rests on the assumption that isotope production will decrease at the Los Alamos Meson Physics Facility (LAMPF). If DOE chooses to limit commercial production of research isotopes at the Brookhaven Linac Isotope Producer (BLIP), the market penetration will be much greater. The market penetration for imaging research isotopes in the first year of production operations is estimated to be 5% and grows to 40% in year five.*
- *The radiopharmaceutical companies will be a source of R&D contract revenue, service irradiation, revenue from production contracts for specialized products, and in the longer term, revenue from technology transfer royalties.*
- *Commercial radioisotope production as a backup to commercial firms and the linac isotope production facility is estimated to be $970,000 annually, based on projected linac downtime and maintenance.*
- *Continuing support by DOE, NIH, NSF, and other federal agencies for operation is expected to be $2,750,000 per year. These funds will be obtained through standard competitive research grants and contracts.*

The business plan presented in Section 9 and Appendix IX shows that expenses begin in year one, but revenue does not begin until year three, when the cyclotron becomes operational. The bottom line of revenues versus expenses shows a deficit through year six, or the fourth year of cyclotron operation. This deficit averages about $1 million and peaks in year four at

$1.2 million. Self sufficiency is achieved in year seven or the fifth year of cyclotron operation.

In the seventh year (or the fifth year of cyclotron operation), the operating revenues go slightly positive as the full operating status is approached. At this point the cash flow begins to accumulate capital for the replacement of equipment, as the equipment reaches the end of its useful life. Thus, self-sufficiency, which is dependent on achieving the estimated market penetration, is achieved in year seven, or the fifth year of cyclotron operation.

2.19 Requirements of the Request for Proposal

The Department of Energy's RFP that solicited proposals for project definition studies of the NBTF contained a requirement for self-sufficiency and payback of construction costs. The goals and objectives of the NBTF set forth in the RFP, however, carry many of the obligations of a public enterprise with neither the support of tax dollars nor the latitude enjoyed by the private sector in choosing its products, markets, and business strategy. Further, the DOE pricing policy for stable isotopes and its own subsidized production of research isotopes presents both a barrier and a competitor to success of the proposed NBTF.

> ***We believe that unqualified support from both DOE and private industry is absolutely necessary for success of the NBTF, whose mission is outlined in the RFP and supplementary information issued by DOE.***

2.20 Request to DOE

The requirement for payback of construction costs by DOE has been built into the proposed business plan that follows in Section 9 and in Appendix IX. We believe that the public mission of the NBTF should be supported by a one-time loan guarantee for construction of a *modest* facility. The NBTF will be supported by *existing* facilities of the Association's collaborating institutions, including medical and general academic institutions and the national laboratories.

> ***We suggest that the mission and goals of the proposed NBTF can best be accomplished through a one-time loan from DOE of $25 million for construction of the NBTF core facilities. We propose repayment of the principle over a 30-year period. Use of the existing Nike site will lower overall construction costs.***

The thirty-year, no-interest loan guarantee will provide for equipment purchases and construction costs, as outlined in the business plan in the *Technical Proposal* that follows in

Section 9 and in Appendix IX. Repayment will start in year four of the plan.

The alternative to a "private sector" NBTF, as suggested in the DOE solicitation, is an NBTF founded on the capabilities of the national laboratory system. However, DOE facilities have historically been an unsatisfactory solution to the supply of isotopes due to mission conflicts. They also suffer from not being able to operate on conventional business principles and practices. The result is that the DOE laboratories have not been able to guarantee delivery, quantity, and performance at the level demanded by industry.

> ***Therefore, we suggest a new paradigm: a businesslike public and private partnership that works like a private corporation acting for the public good, with measured assistance from the state and national governments through both grants and contracts.***

2.21 Industrial Role in Support of the NBTF

In the commercial center's business plan, described in Appendix III, industry will invest approximately $28 million in constructing the commercial production linac, the intense neutron source, and processing facilities located adjacent to the NBTF site. These facilities will provide hot cell facilities for radiochemical processing for the NBTF's high activity level radioisotope products and will provide joint support for some operational areas, such as radiological safety and waste management through standard business contracts between the two entities.

We believe that the larger role of the radiopharmaceutical industry should be to support the program through membership in an industry/university cooperative research center modeled on the exemplary NSF Industry/University Cooperative Research Centers (I/UCRC) program, and through contracts for proprietary research and grants for support of graduate student research on problems of specific interest to industry. The proposed center will administer educational and research programs of this type on behalf of the Association, which will award fellowships and grants.

3.0 FACILITIES AND EQUIPMENT

3.1 Introduction

As discussed earlier in the overview, we propose to construct the National Biomedical Tracer Facility (NBTF), a cyclotron-based research and educational facility, in North Central Texas as part of a center having three contiguous but separate facilities:

- **The NBTF cyclotron-based research and educational facility;**
- **A commercial production facility, including a proton linac and a stable isotope enrichment program; and**
- **An Advanced Medical Imaging Facility.**

The NBTF will be managed by the North Texas Research Institute (NTRI), a not-for-profit corporate affiliate of the University of North Texas (UNT). The other key component of the NBTF Center is a privately funded commercial isotope production facility already underway by Advanced Isotopes Technologies, Inc. (AITI) at the proposed site near Denton, Texas. In the near future, the NBTF will be enhanced by the addition of an Advanced Medical Diagnostic Imaging Facility, also independently funded and operated by the University of Texas Southwestern Medical Center (UTSMC) at Dallas. The synergism of co-locating the production of research radionuclides coupled with research, education, training in the same location as commercial production will promote technology transfer and achieve some economy of scale to assist the NBTF's operating budget.

The University of North Texas at Denton is widely recognized in the accelerator community as the home of the biennial *International Conference on the Application of Accelerators in Research and Industry* (Duggan and Morgan, 1993). The Ion Beam Modification and Analysis Laboratory at UNT and the development of the AITI commercial facilities are further indication of a longstanding interest and practical expertise in the application of accelerator technology to a variety of real world problems.

The DOE request for proposals published in the Federal Register in October 1993, and the recent study by the Institute of Medicine of the National Academy of Sciences, *Isotopes for Medicine and the Life Sciences* (Adelstein and Manning, 1994), both specified that, **"The NBTF should be a large proton accelerator, with supporting facilities, to be utilized for the production, processing, and distribution of radioisotopes used in medical and industrial applications."** The center discussed above, combined with the proposed NBTF Association and business plan, satisfies this specification.

3.2 Nike Site

The *Nike Site*, proposed for the center, is a 20-acre former Nike-Hercules anti-ballistic missile launch site. It is located just outside the city limits of Denton, Texas, approximately five miles north of the UNT campus. The site was decommissioned in 1969 and ceded to the UNT for educational use in 1972. The facilities have since served as research and storage space, and as a location for the university's astronomy teaching laboratories. The site contains three underground vaults. Each is a large open room of about 5,000 sq. ft. (about 70 feet square) with additional rooms on the north side of the large room. All rooms are 18 feet underground with 11 feet clearance to the under surface of the roof's concrete supporting beams. The bunker roof is one foot thick reinforced concrete over the supporting beams, which are approximately three feet high. The approximately three-foot-thick earth overburden is covered at the ground surface with a 6-inch concrete pad.

In the site's operational phase, each vault held three missiles, and each missile was armed with a five-megaton warhead. Nike-Hercules missiles were intended to be launched in salvos of three to intercept incoming ballistic missiles, and the site was hardened to resist the detonation of both incoming and outgoing nuclear ordnance.

The characteristics of these sites were modeled on the "Sugar Bunker" at Nevada's Frenchman's Flat nuclear test site. This was a structure that was tested by nearby nuclear detonations (and passed the test!). The underground vaults at the Denton Nike site are constructed of high-strength, heavily reinforced concrete with over 30 years of cure time. The roof and blast doors are capable of resisting a 100 psi shock wave. The roof is strong enough to support additional radiological shielding over proposed target and cyclotron areas. The site has existing electrical service (13.6 kV), with more than adequate additional electrical service available within a half-mile of the site. The proposed cyclotron, linac, and intense neutron source each will consume about 500 kW of power at full operation.

> ***The adaptive use of these existing structures will materially reduce construction costs of the proposed facilities. The replacement cost of these existing facilities is estimated to be in excess of $5 million.***

The Nike Site is ideal for the proposed center because its inherent shielding and existing configuration will easily accommodate the proposed accelerators and target areas. The 20-acre site is in a rural area surrounded by farmland. This provides opportunities for lease or purchase for future expansion of the center or co-location of compatible industrial and not-for-profit entities at the center.

The site is served by a four-lane divided highway, Loop 288, which joins with I-35 (going north to Oklahoma City), and I-35W (south to Fort Worth) and I-35E (south to Dallas). The site has excellent access via these interstate highways to a variety of transportation centers.

The DFW International Airport is 35 minutes away. It serves numerous airlines and is a hub for both American and Delta Airlines and the UPS package carrier. Alliance Industrial Airport is 25 minutes away. It was recently announced as a hub location for Federal Express. The Dallas Love Field Airport is the hub of Southwest Airlines and is 40 minutes away. With all these travel resources readily available, the Nike Site provides an ideal point in the Central U.S. for radioisotope distribution and human travel. Direct airline flights are available to each of the current Association's members from DFW International or Dallas Love Field.

3.3 Site and Facilities Configuration

The site's potential is illustrated in a number of drawings for the center that depict an approach to be evaluated further in a site-specific, detailed design effort. Each of the facility's components are discussed in detail in the following sections.

Figure 3.3-1, *Site Overview*, is an aerial view of the proposed site development, illustrating the surface facilities. This architect's rendering is meant to convey some sense of the proposed facilities of the National Biomedical Tracer Facility, which we envision as a truly *national* center supporting nuclear medicine and related disciplines.

Figure 3.3-2, is the *Existing Site Plan* showing the three underground vaults at left (one labeled "extent of silo below") on the west side of the 20 acre location. Figure 3.3-3 is the *Phase One Site Plan* showing proposed locations of the various facilities listed on the figure, including proposed locations of the commercial production facility (1. Advanced Isotope Technologies, Inc.) and the proposed NBTF Research and Educational Facility building (2.).

Figure 3.3-4, labeled *Accelerator Plan in Modified Missile Silos*, illustrates proposed usage of the underground vaults to locate the cyclotron (right vault), the linac and target areas (left tunnel and center vault), the intense neutron source (left vault), and linac electronics (also in the left vault but not shown). The ten-foot-wide interconnecting tunnels will house the linac in the west tunnel and a cyclotron beam line in the east tunnel. The strategy is to penetrate the existing vault structures as minimally as possible (only for the beam line) to decrease construction costs. The ten-foot-wide tunnels will be accessible from the surface. In Figure 3.3-4, note the outlines of the facilities at ground surface: from left at top, the control room for the linac adjacent to the western vault, (2) the waste handling and retention facility adjacent to the center vault, and (3) the cyclotron control room adjacent to the eastern vault.

Two cross sections through the underground facilities are illustrated in Figures 3.3-5 and 3.3-6. Figure 3.3-5, labeled *Section #1 Through Modified Missile Silos (View to South)*, shows the cyclotron in the eastern vault (left), the target area in the center vault (middle), the linac tunnel (right, between the center and western vaults) and the western vault (right),

which holds the linac electronics and intense neutron source (not shown in this section). Figure 3.3-6, labeled *Section #2 Through Modified Missile Silos (View to East)*, shows the vault containing the cyclotron (and to the right at the surface) a section through the Research and Educational Facility of the NBTF. At left on the surface is a section through the cyclotron control structure.

Figure 3.3-7, labeled *Modified Missile Silo #1*, holds the linac electronics and the intense neutron source (labeled Pulsed Sealed Neutron Tube™). The room at upper left is a shielded room that served in the Nike Site's operational phase as a location for personnel during missile firing. The linac control room will be on the surface (upper left). The linac injector and RFQ are located in the tunnel to the right. Figure 3.3-8, labeled *Modified Missile Silo #2*, shows the target area, six beam lines terminating in targets, the tune up dump (accessed by both the linac and a cyclotron beam), and a target preparation area. On the surface above the vault is the waste handling and retention facility (top) and the AITI processing building (bottom), both indicated by dashed lines. Figure 3.3-9, labeled *Modified Missile Silo #3*, shows the cyclotron vault and target areas. The cyclotron control room is above on the surface (top). The NBTF Research and Educational Facility is on the surface above (bottom), as indicated by the dashed lines.

Figure 3.3-10, labeled *Klystron Gallery Plan*, shows the surface facility housing linac electronics, power supplies, and klystrons. Figure 3.3-11, labeled *Control Room Plan*, shows a generalized rendering of either the linac or cyclotron control rooms on the surface above their respective vaults.

Figure 3.3-12, labeled *Research and Educational Facility*, shows the surface structure of the National Biomedical Tracer Facility on the south side of the underground cyclotron vault. Figure 3.3-12 illustrates the proposed 20,000 square-foot-space in which research, education, and training will take place. This building includes laboratories, offices, a small lecture hall, limited classroom, and a library/media/distance learning center. A more complete description of this structure and its functions follows later in this section.

Figure 3.3-13, labeled *Commercial Radioisotope Processing Facility*, illustrates the 20,000 square foot radioisotope processing facility of Advanced Isotope Technologies, Inc., which will be used by AITI for processing commercial radioisotopes produced by the linac. The commercial facility includes shielded cell (hot cell) areas with related space, laboratories, and office areas. The commercial facility and its functions are described in Appendix III.

The facilities and equipment of UNT, UTSMC, and the other members of the NBTF Association will be discussed separately later in this section and in the appendices.

Figures 3.3-1 through 3.3-13 follow on the next pages.

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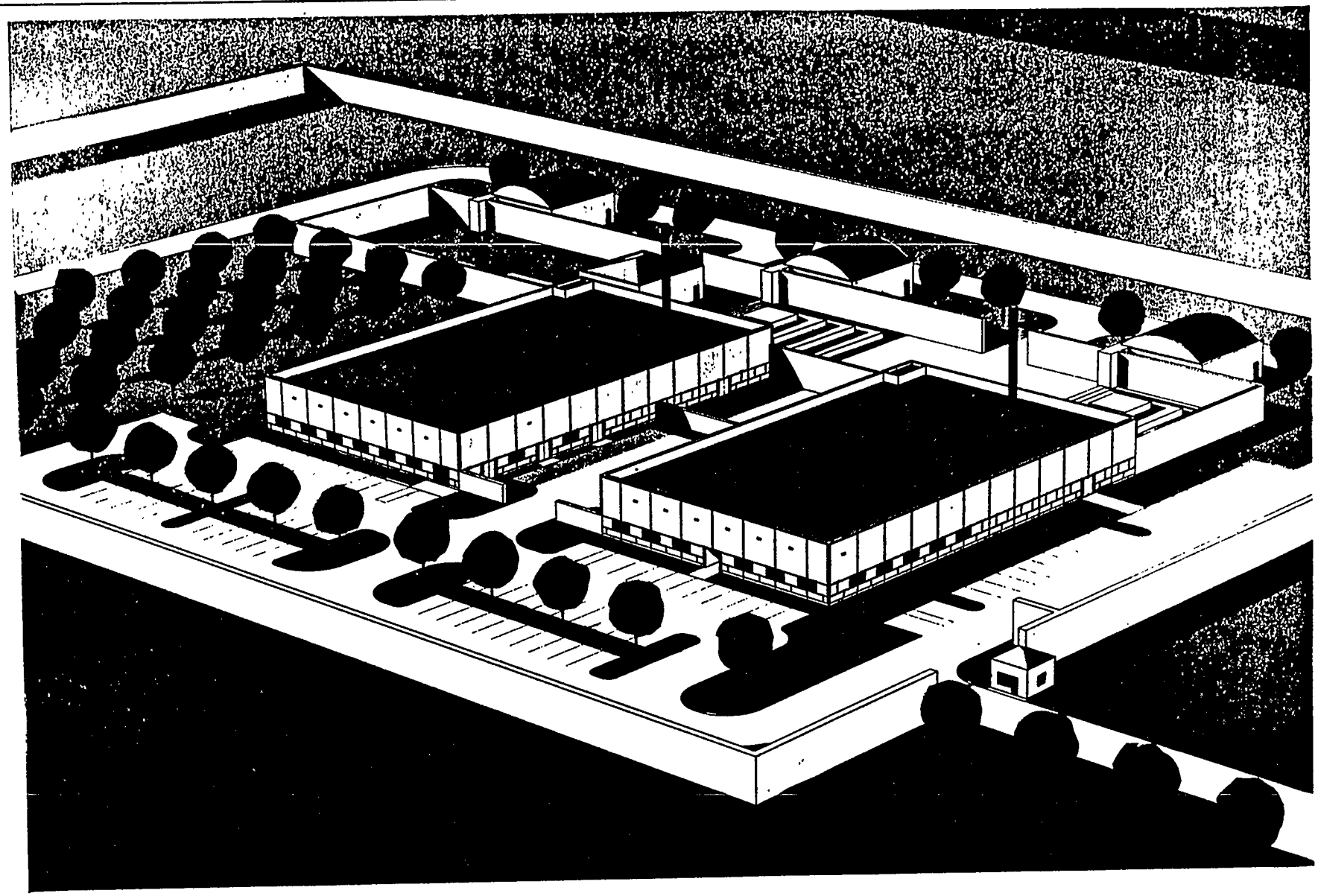

Figure 3.3–1 Site Overview

NATIONAL BIOMEDICAL TRACER FACILITY

James E. Langford, Architect

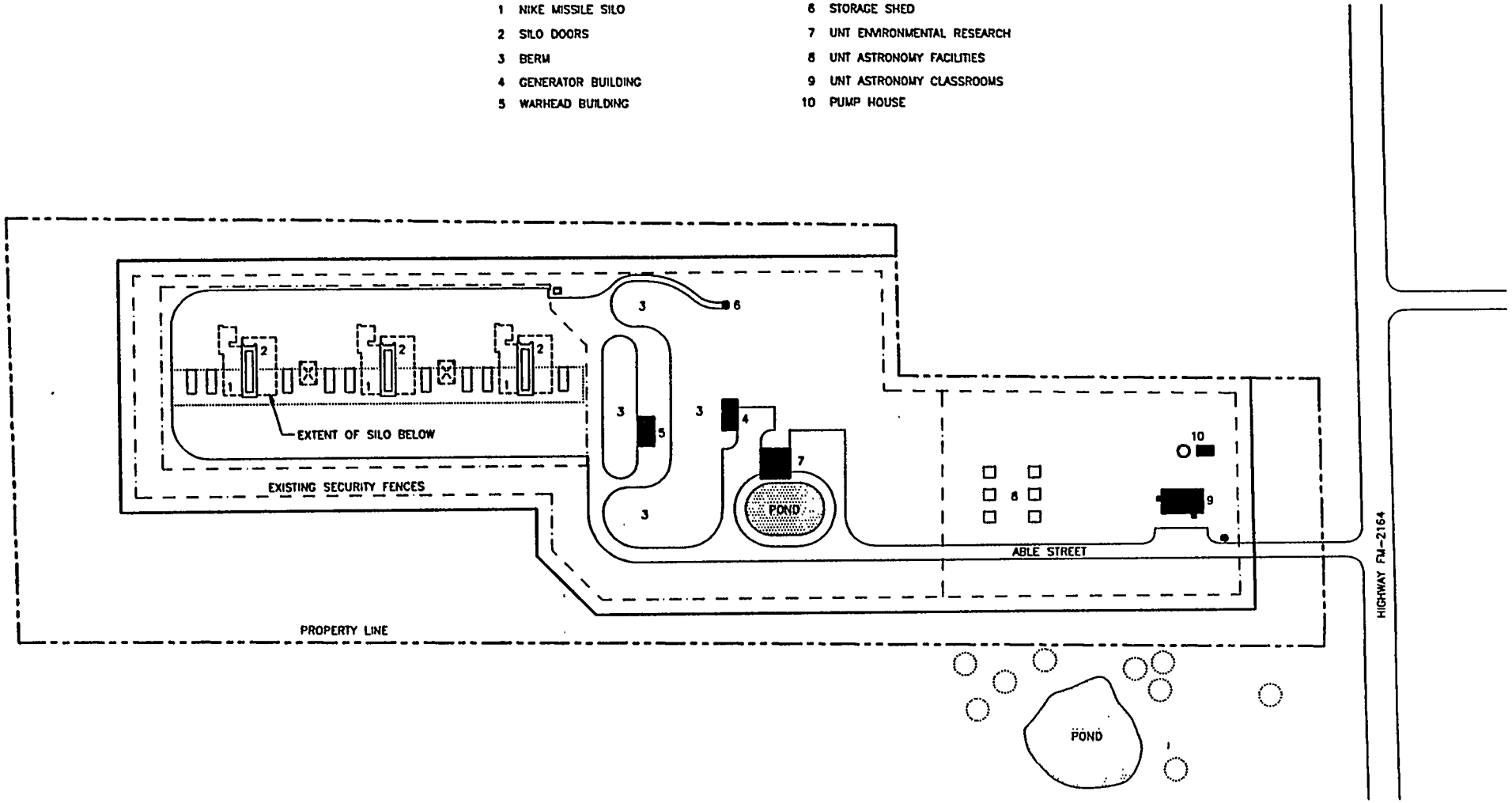

Figure 3.3-2 Existing Site Plan

NATIONAL BIOMEDICAL TRACER FACILITY

James E. Langford, Architect

1 ADVANCED ISOTOPE TECHNOLOGIES, INC.
2 NATIONAL BIOMEDICAL TRACER FACILITY
3 SERVICE COURT (RESTRICTED ACCESS)
4 PARKING
5 NEUTRON SOURCE IN SILO
6 TARGET STATIONS IN SILO
7 CYCLOTRON IN SILO
8 LINAC VAULT BELOW
9 CONTROL ROOM
10 KLYSTRON GALLERY
11 WASTE HANDLING & RETENTION FACILITY
12 ACCESS TO LINAC TUBES
13 EXISTING BERM EXPANDED (15' HIGH)
14 ENTRY GATE WITH GUARD
15 GENERATOR BUILDING
16 UNT ENVIRONMENTAL RESEARCH
17 EXISTING POND ENHANCED
18 UNT ASTRONOMY FACILITIES
19 PUMP HOUSE
20 UNT ASTRONOMY CLASSROOMS

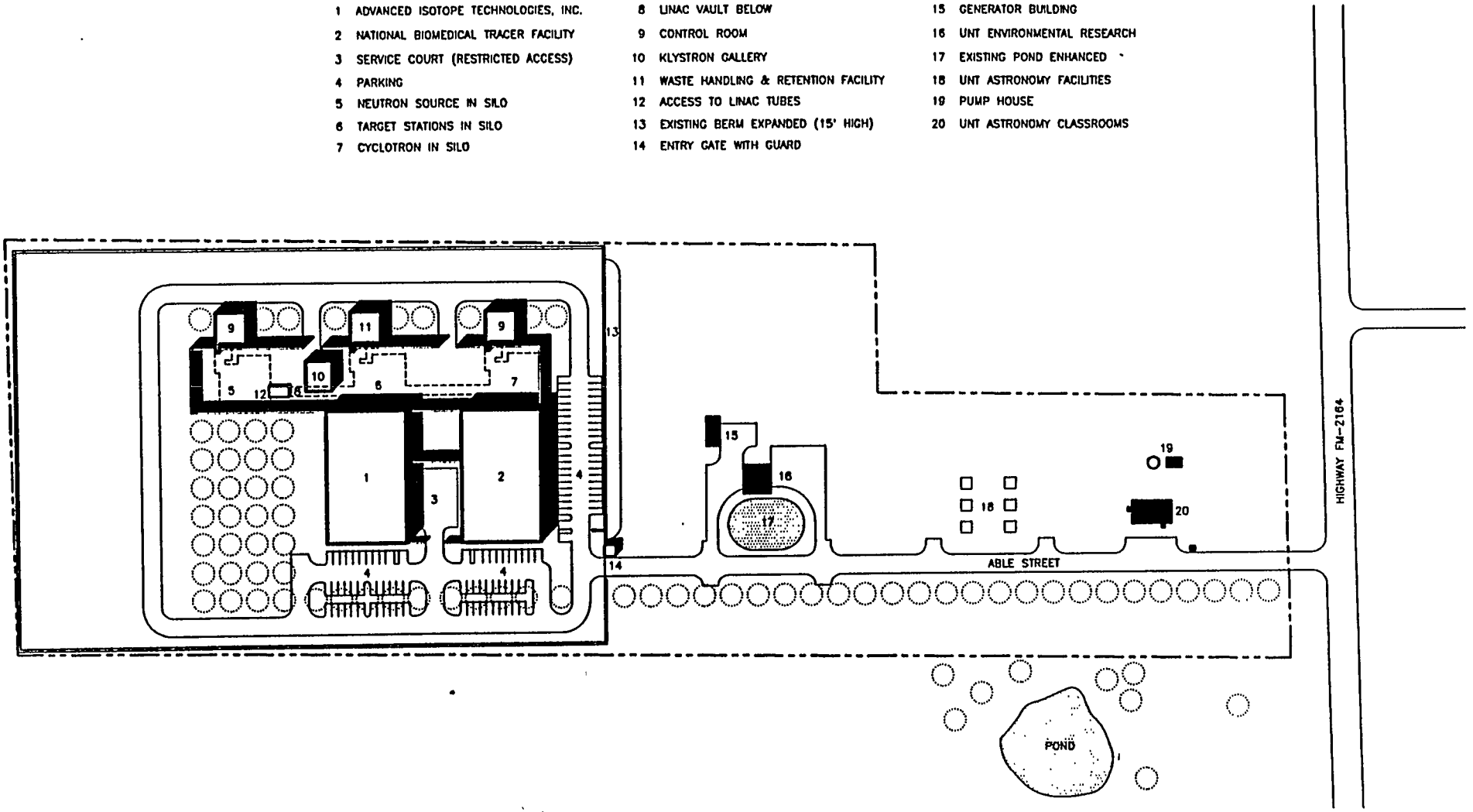

Figure 3.3–3 Phase One Site Plan

NATIONAL BIOMEDICAL TRACER FACILITY

James E. Langford, Architect

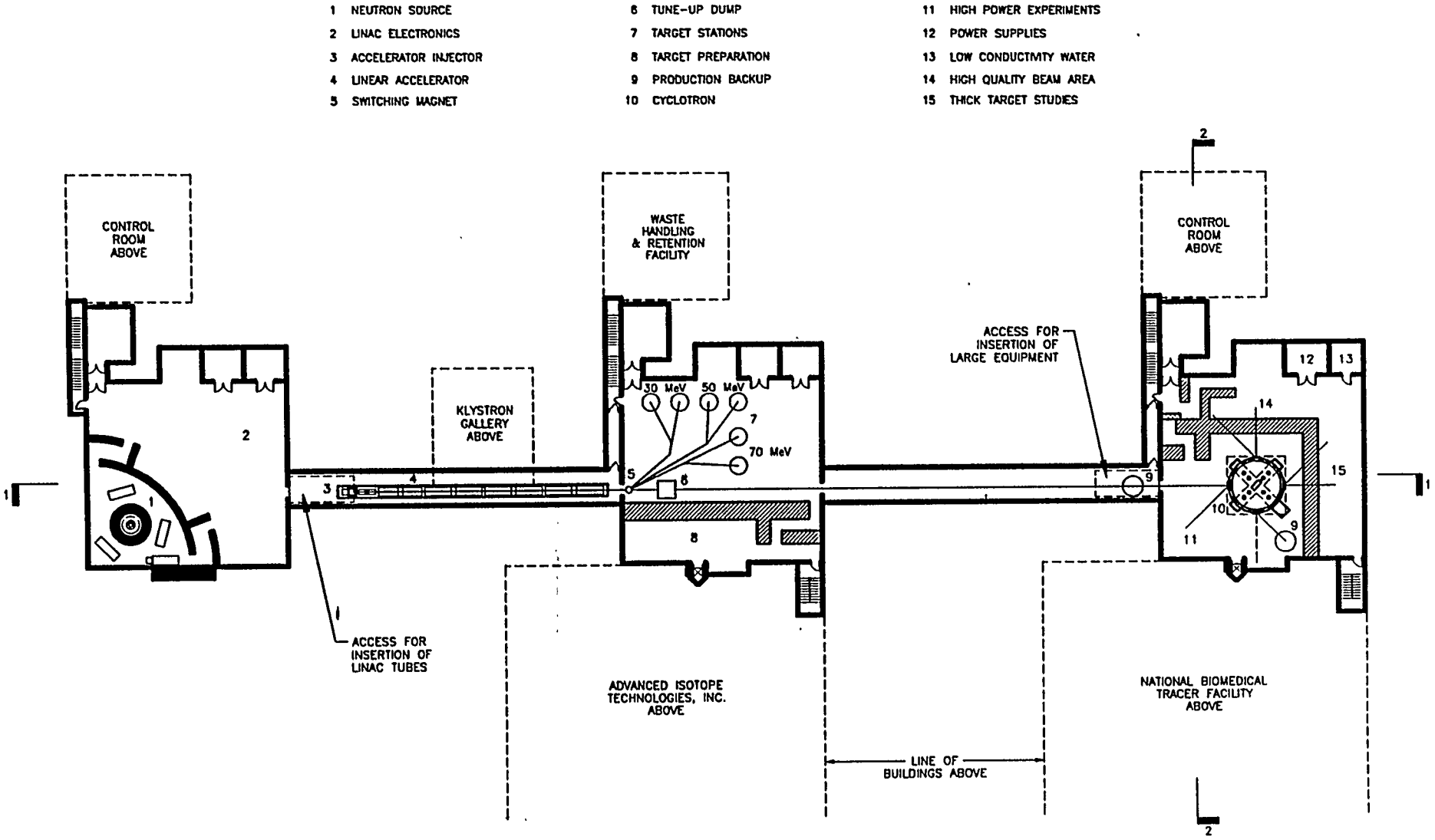

Figure 3.3–4 Accelerator Plan in Modified Missle Silos

NATIONAL BIOMEDICAL TRACER FACILITY

James E. Langford, Architect

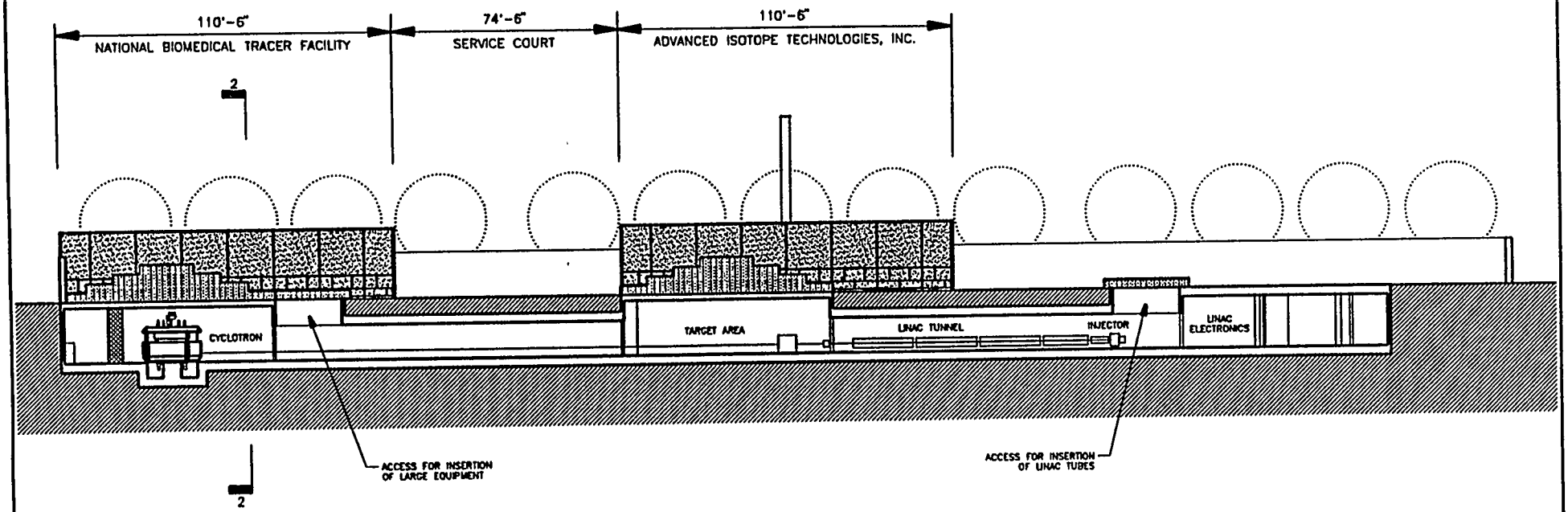

Figure 3.3-5 Section #1 Through Modified Missle Silos (View to South)

NATIONAL BIOMEDICAL TRACER FACILITY

James E. Langford, Architect

0 10 20 30 40

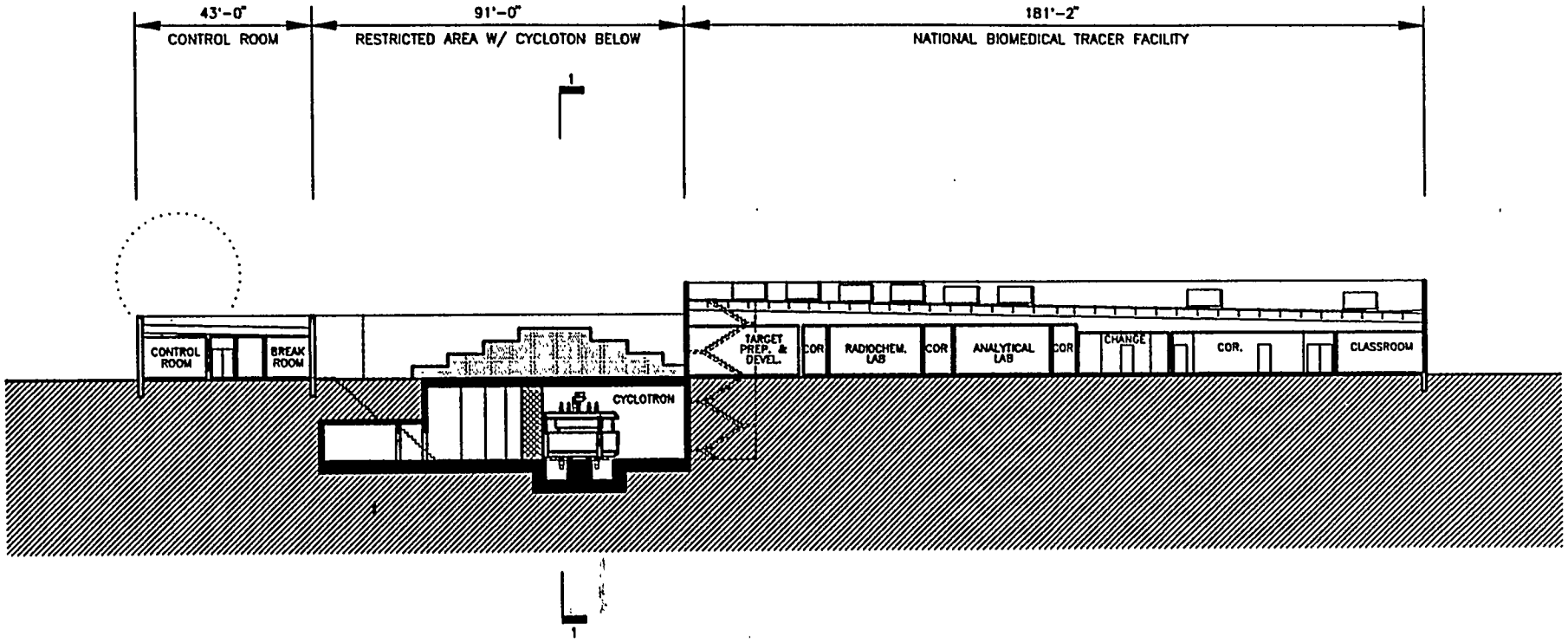

Figure 3.3-6 Section #2 Through Modified Missle Silo (View to East)

N A T I O N A L B I O M E D I C A L T R A C E R F A C I L I T Y

James E. Langford, Architect

0 10 20 30

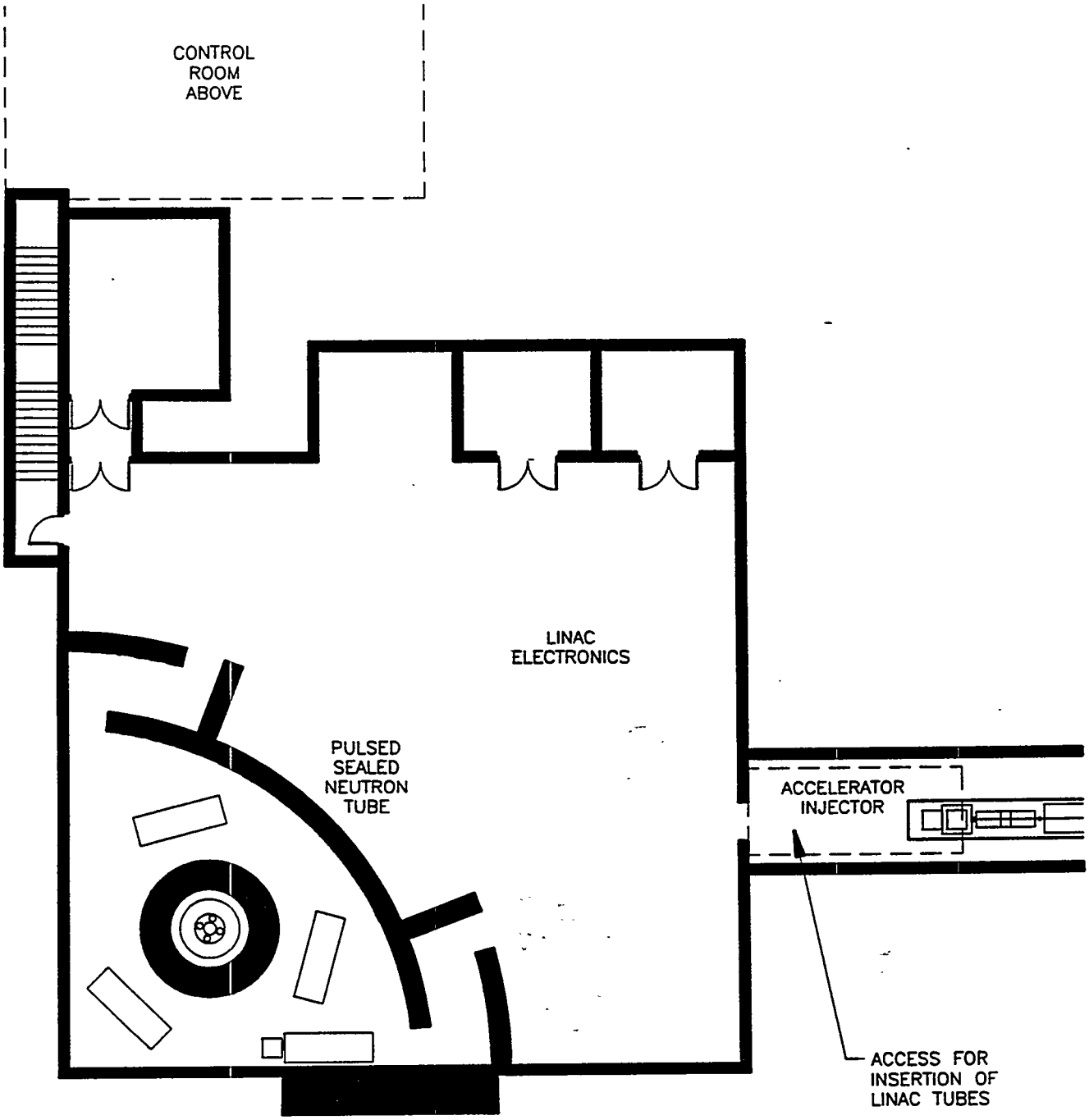

Figure 3.3–7 Modified Missle Silo #1

NATIONAL BIOMEDICAL TRACER FACILITY

0 4 8 12 16

James E. Langford, Architect

North

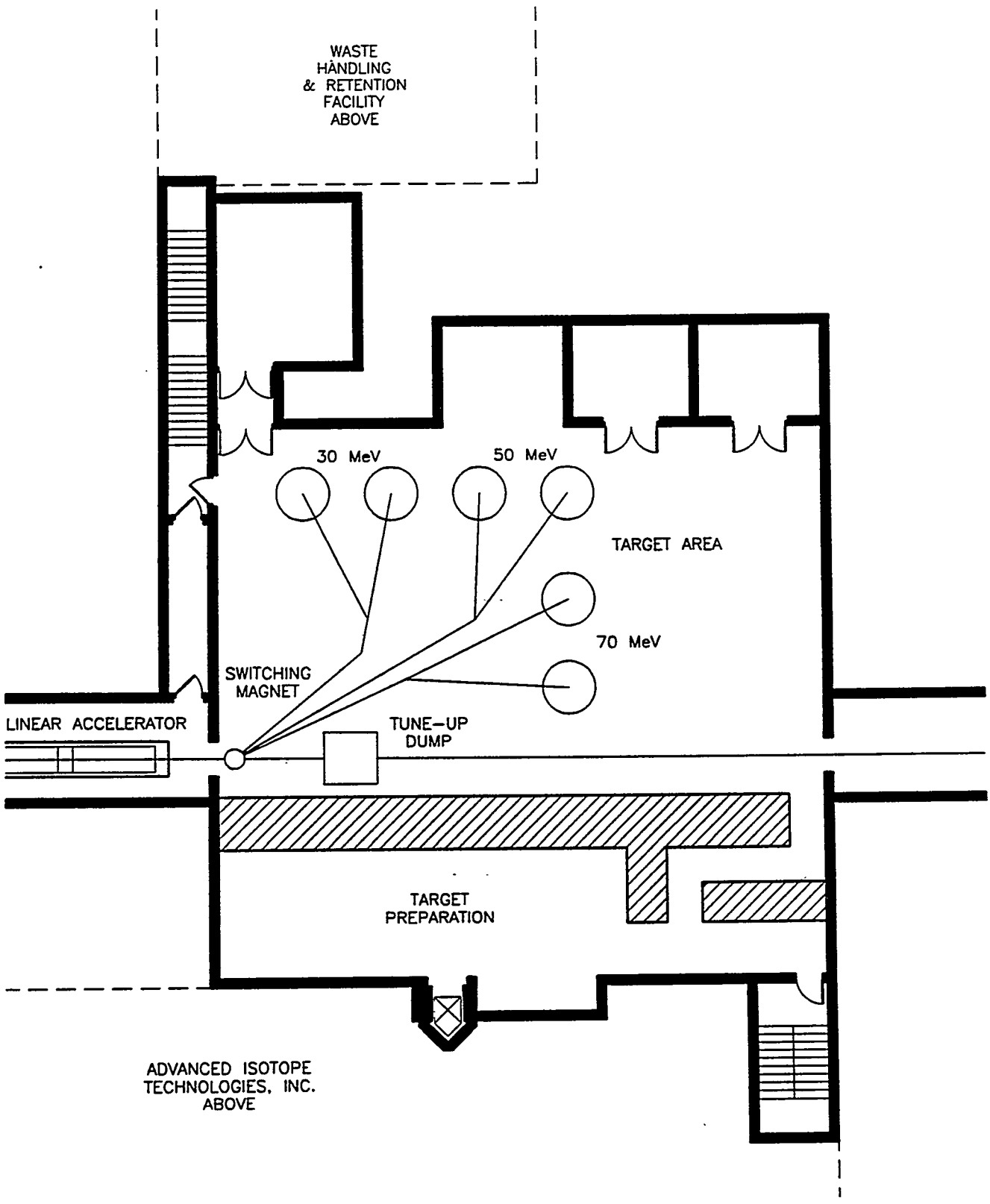

Figure 3.3–8 Modified Missle Silo #2

N A T I O N A L B I O M E D I C A L T R A C E R F A C I L I T Y

0 4 8 12 16

James E. Langford, Architect

North

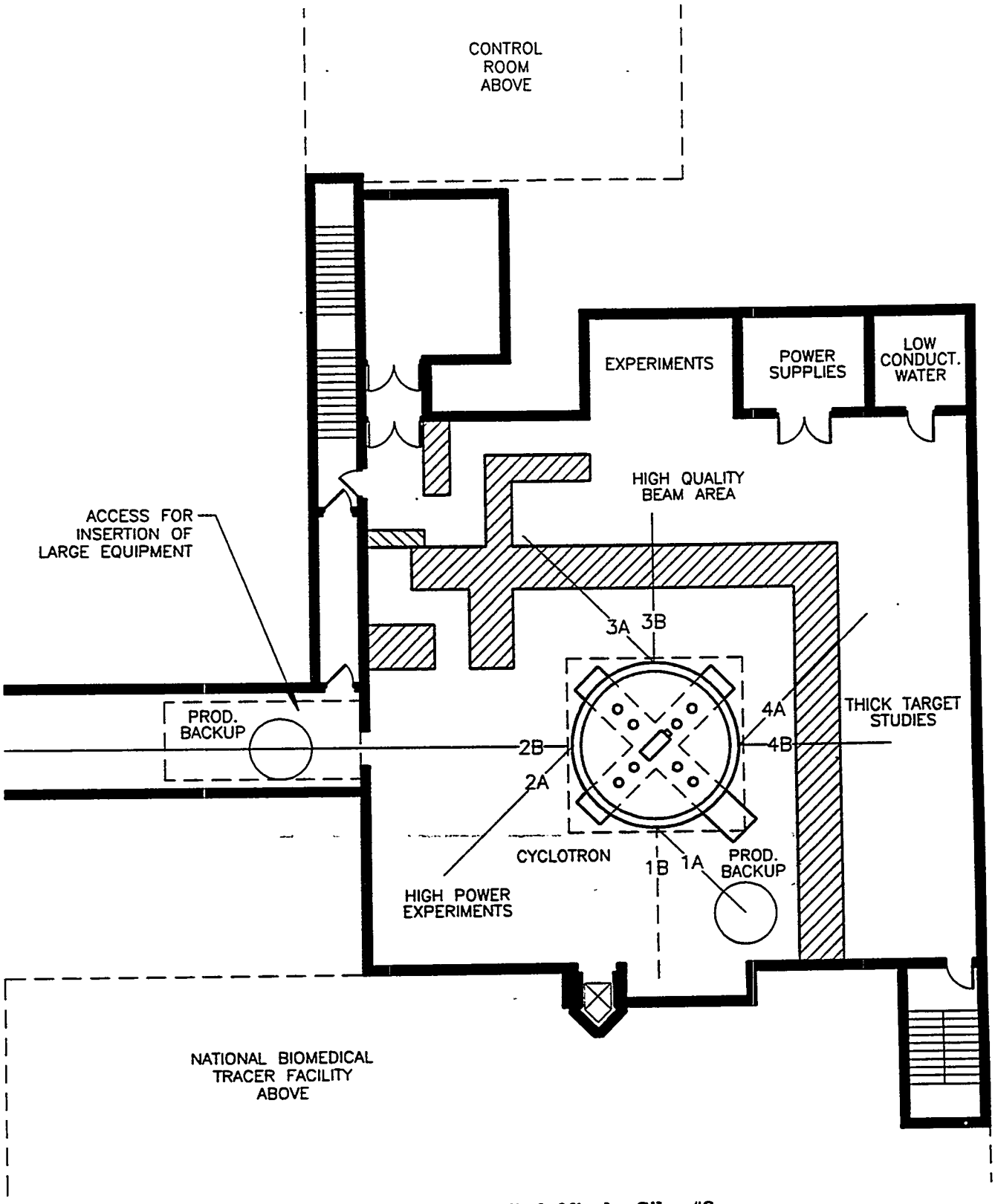

Figure 3.3–9 Modified Missle Silo #3

N A T I O N A L B I O M E D I C A L T R A C E R F A C I L I T Y

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James E. Langford, Architect

North

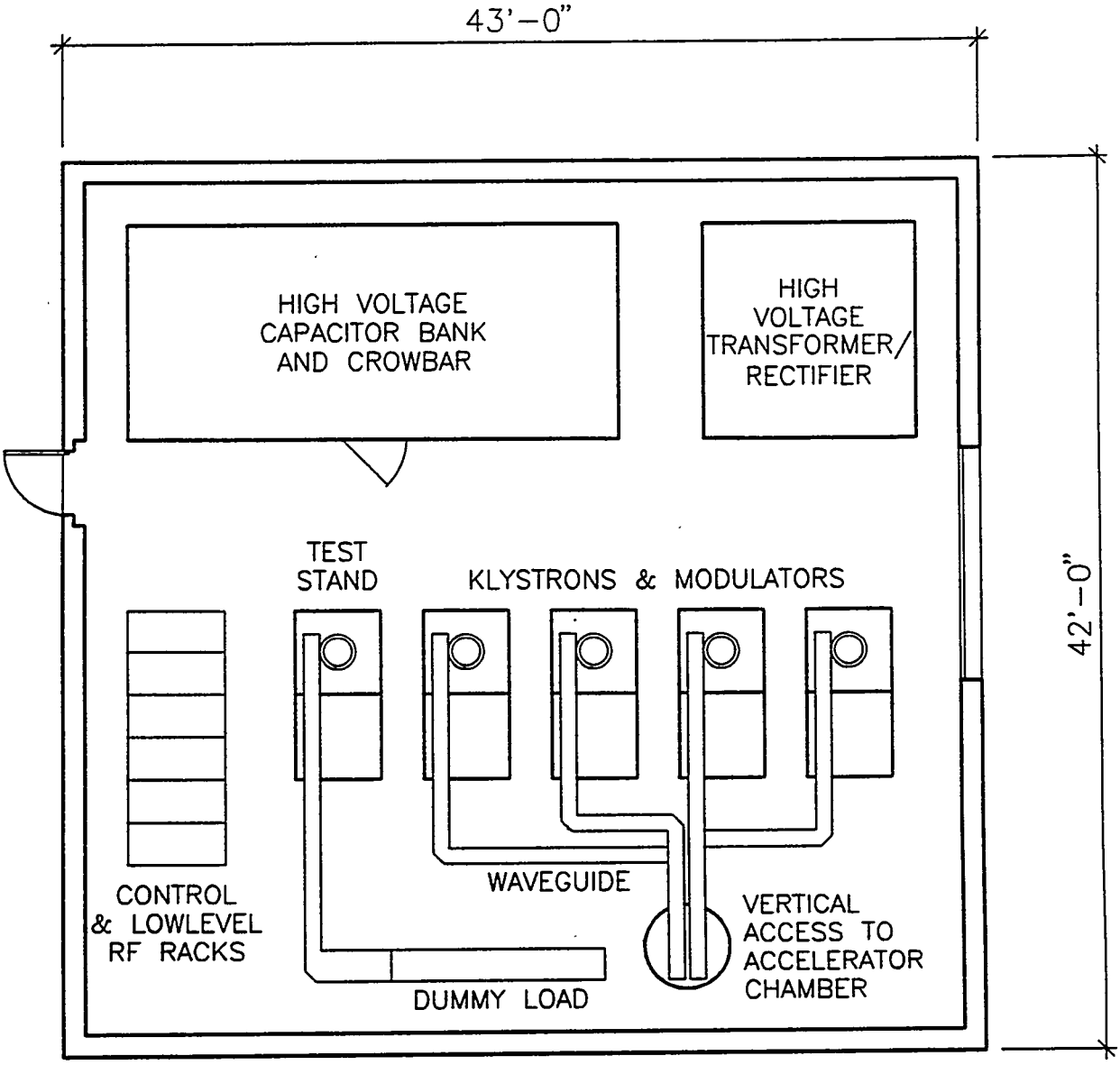


Figure 3.3–10 Klystron Gallery Plan

NATIONAL BIOMEDICAL TRACER FACILITY

0 2 4 6 8

James E. Langford, Architect

North

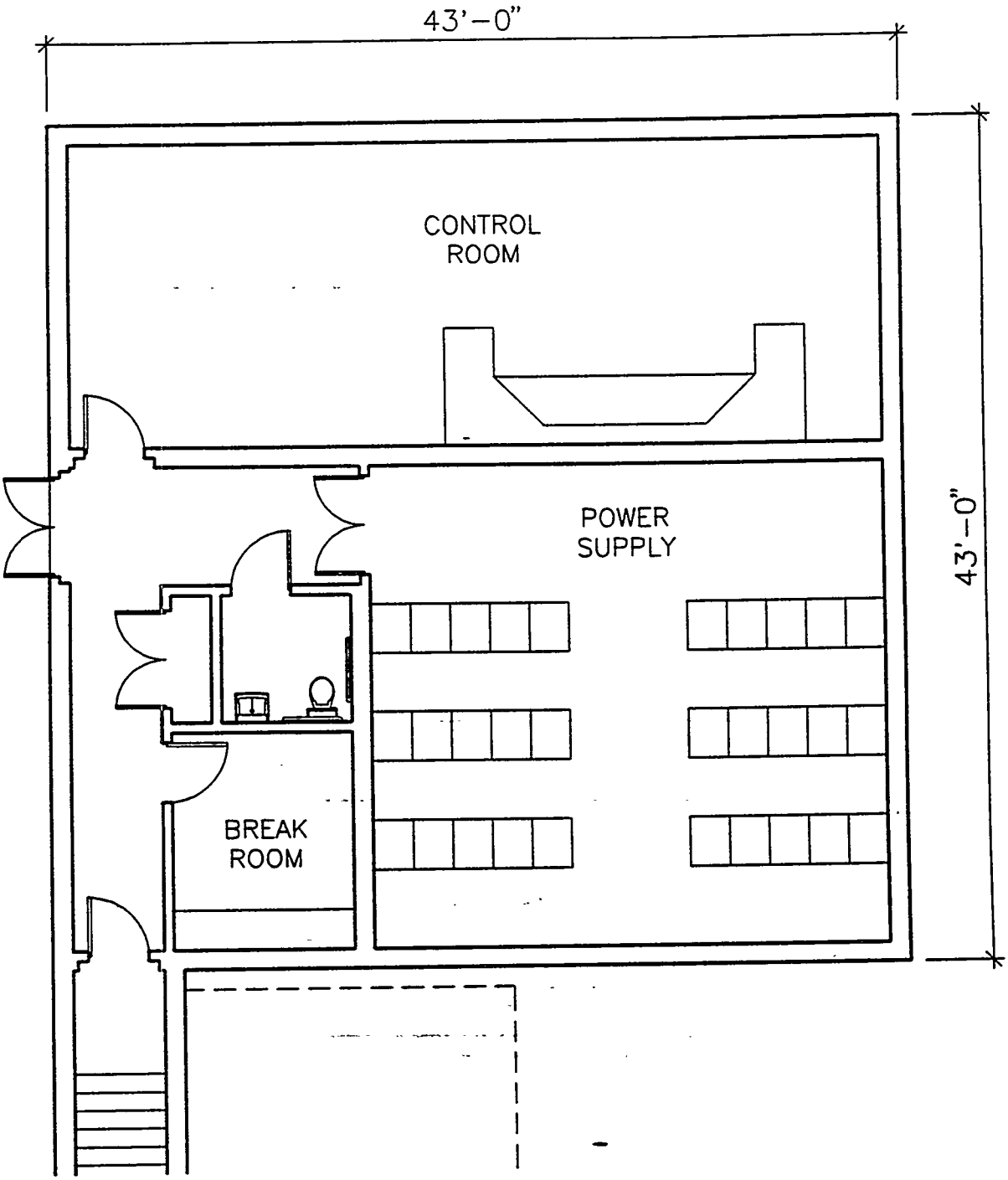


Figure 3.3-11 Control Room Plan

NATIONAL BIOMEDICAL TRACER FACILITY

0 2 4 6 8

James E. Langford, Architect

North

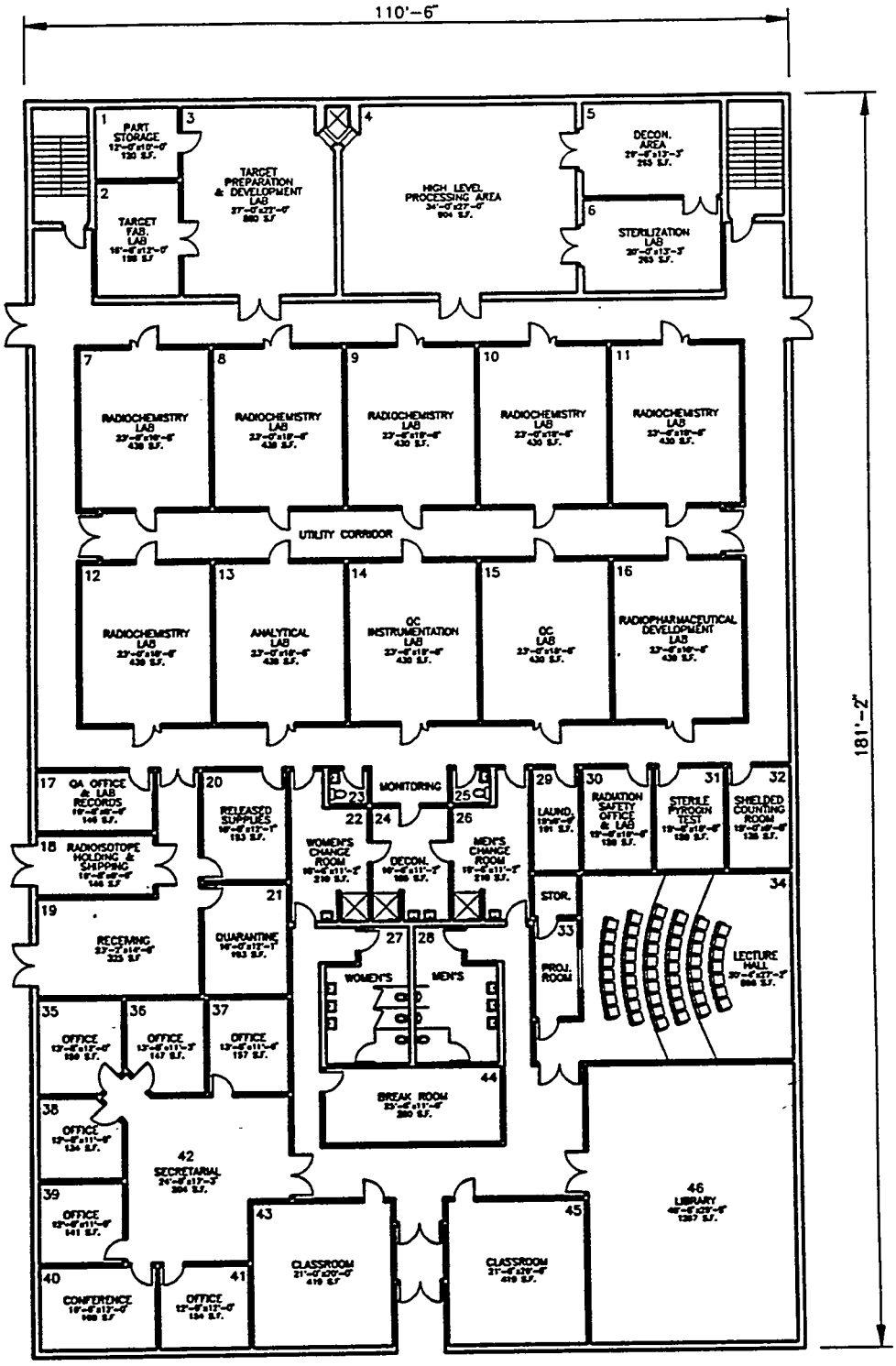


Figure 3.3-12 Research and Educational Facility

NATIONAL BIOMEDICAL TRACER FACILITY

0 5 10 20

James E. Langford, Architect

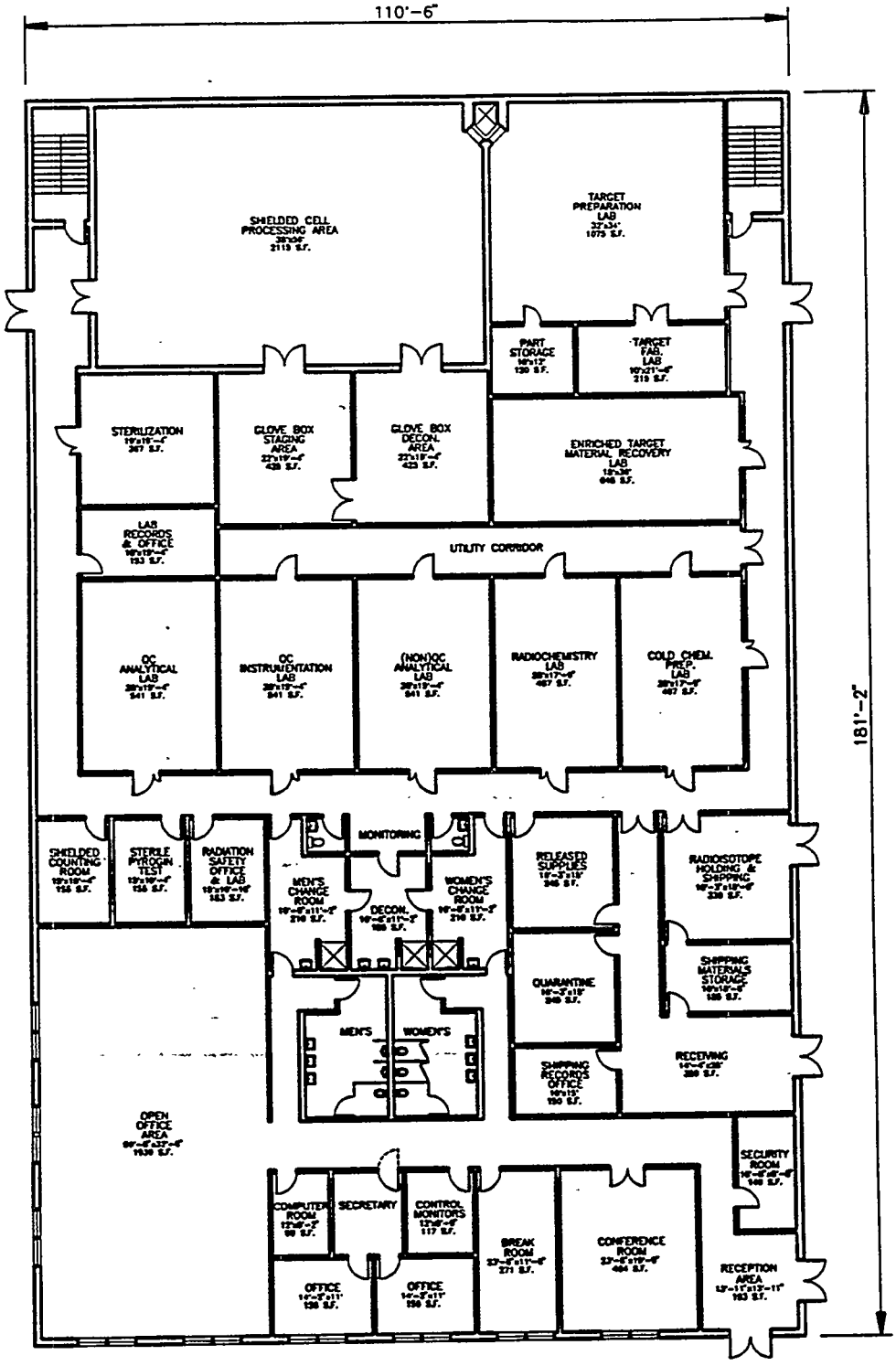


Figure 3.3–13 Commercial Radioisotope Processing Facility

A D V A N C E D I S O T O P E T E C H N O L O G I E S , I N C .

For the National Biomedical Tracer Facility Center

James E. Langford, Architect

0 5 10 20

North

3.4 NBTF Cyclotron

The NBTF's requirements for the production of research radionuclides, research on radionuclide production and applications, and education using accelerator-based technology are best met with a cyclotron. Cyclotrons can produce varying beam energies, and recent advances in cyclotron technology permit a wide range of flexibility in the extracted beam energy and intensity. In terms of training and education, it is significant that cyclotrons are almost exclusively used by industry in commercial radioisotope production. The almost exclusive use of cyclotrons by industry is primarily due to the commercial availability (and guaranteed performance) of cyclotrons and the established, FDA-approved protocols for pharmaceutical production using cyclotrons.

We propose an 80 MeV, 1 mA cyclotron. A higher energy capability would provide a wider research capability, but the capital costs of higher energy are a significant factor in meeting the requirement that the NBTF be self-supporting and reimburse construction costs. The 80 MeV energy is sufficient to support research and the production of research radioisotopes. The 1 mA current will enable the use of multiple beam lines, each capable of being served with a beam current of tens to hundreds of microamperes without disturbing production and research activities on other beam lines.

3.4.1 Choice of Cyclotron Energy

The selection of a variable energy 80 MeV, 1 mA, H^- cyclotron over models with lower (30 to 60 MeV) or higher (100-150 MeV) energy ranges was influenced through a balance of technological considerations, program goals, and practical considerations, including capital cost. While most of the commercial radionuclides can be produced at the lower energies, many other interesting and potentially useful products cannot be made in sufficient quantities in the lower energy range and current.

The proposed 80 MeV cyclotron has the potential to produce most, if not all, of the proton excess radionuclides that have been suggested by the nuclear medicine community. It provides the capability to perform research investigations in target development, nuclear cross reactions, and excitation function measurements, and to provide research quantities of radionuclides for chemical separation studies, generator development, nuclear decay studies, radioanalytical methods development, biochemical labeling research, radiopharmaceutical research, pre-clinical, and clinical research investigations. In addition, the proposed cyclotron can produce bulk quantities of selected radionuclides and serve as a backup to the commercial facility if required.

The NBTF program will depend greatly on the availability of a broad range of enriched stable isotopes as target material to produce products of high radionuclidic purity efficiently.

Even though 90% to 95% of the enriched target material is recovered chemically for reuse, a sizable capital investment is required to initiate the program, adding to the cost of products produced.

Since the spallation reaction threshold is approximately 100 MeV, H^- cyclotron models up to 150 MeV at approximately 0.6 mA beam current were considered for the NBTF program. The higher energy would provide access to an energy region that has been relatively unexplored and, consequently, offers more opportunity for performing basic research. As an example, low energy spallation reactions could be studied and radionuclide yields via these reaction mechanisms could be compared with those of other lower energy reactions. The higher energy would also permit reaching radionuclides farther removed from the beta line of stability, unreachable at lower energies. In these cases, the NBTF accelerator could provide the research community with products that can not be produced by the 70 MeV linac or most of the current commercial machines. The higher energy reactions may open reaction paths that do not require the use of isotopically enriched target materials to obtain an acceptable product.

Experienced cyclotron manufacturers have explored the technology and costs for building high energy (80 to 150 MeV) high beam current (0.5 to 1.5 mA) machines and are convinced that they could be built and operated reliably. These manufacturers include Ion Beam Applications, s.a. (IBA) of Louvain la Neuve, Belgium and Ebco Technologies, Inc. (Ebco) of Vancouver, Canada. For an H^- cyclotron, very high extraction efficiency is necessary to limit the activation of the accelerator components and minimize the radiation exposure to maintenance personnel. To obtain very high extraction efficiency, electromagnetic stripping of H^- ions due to the Lorentz force and interactions with residual gas at the higher energies must be kept low. Therefore, magnetic fields must be reduced and the vacuum in the tank must be improved as the energy is increased. Both requirements increase the initial cost of the accelerator, operating costs and, possibly, facility construction costs.

One important objective of the NBTF proposal request is to demonstrate an ability to reimburse the initial loan and eventually become self-supporting financially. A cyclotron with energies of 100 MeV or more would significantly increase the initial investment and (possibly) the operating costs, and could make the loan reimbursement and self-sufficiency unattainable.

The committee that DOE assembles to review the NBTF proposals could recommend that the research accelerator have an energy in excess of 100 MeV and may drop the reimbursement requirement. In that case, our recommendation for an 80 MeV cyclotron will be reconsidered.

3.4.2 Beam Line Requirements and Cyclotron Specifications

Initially, the cyclotron facility will support up to eight external beam lines and target stations with future expansion capabilities. Each target station and beam line will have specific attributes and flexibility well suited to the NBTF mission. Specifically, the cyclotron will support four simultaneously extracted proton beams at different energies and beam intensities.

The cyclotron specifications that meet the requirements for the NBTF mission have been developed in earlier efforts and have been further refined as part of this project definition study. These requirements are outlined in Table 3.4-1 below and in the following sections.

TABLE 3.4-1 Cyclotron Specifications

Maximum Beam Energy	80 MeV
Minimum Beam Energy	20 MeV
Energy Reproducibility	< 0.1%
Energy Spread	~1%
Energy Variability	Continuous over a factor of two from a single port
Total Extracted Beam Current	1000 μA
Number of Extraction Ports	2 High intensity (~400 μA) 2 Low intensity (~100 μA)
Number of Beam Lines (initially)	6 - 8

The final choice of the maximum cyclotron energy is expected to be 80 MeV, although the additional research capability that would exist with a 100-150 MeV cyclotron is still under consideration. The choice of 80 MeV is based on our research and on the recommendation made by the Institute of Medicine in their recent report on *Isotopes for Medicine and the Life Sciences* (Adelstein and Manning, 1994). It will be necessary to compare the additional cost of the higher energy with the anticipated demand for beam time in this energy range, the ability to be self supporting, and other issues. The minimum extracted beam energy of 20 MeV has been chosen because of the wealth of existing data and machines that are operating at or below 30 MeV and the necessity to provide some overlap between the capabilities of this accelerator and existing facilities.

The machine will be specified for reliable operation at beam currents up to 1 mA (1000 μA) with simultaneous extraction into four beam ports. Two ports will deliver high intensity beams (essentially up to full beam current), and the other two ports will have low intensities, typically 10 - 25 μA with a maximum current of about 50 μA. Each of the extraction ports will be capable of serving up to two target stations initially and may be expanded to three, four, or five beam lines and target stations in the future. Only one target station on a given extraction port will operate at a given time. The extracted beam requirements and operational modes are different for the different extraction ports.

> ***In summary, the proposed NBTF 80 MeV, 1 mA cyclotron will allow four simultaneous proton beams, two at high intensity and two at low intensity, at four different and variable energies for radioisotope production, research, education, and training.***

The eastern vault at the Nike Site has been identified as the location of the cyclotron as depicted in Figure 3.3-4 as item 10. An expanded conceptual layout of the cyclotron and beam lines within the eastern vault is shown in Figure 3.3-9. The beam lines and target stations are labeled 1A, 1B, 2A, 2B, 3A, 3B, 4A and 4B, beginning with the high intensity target on the left side and proceeding in a counter-clockwise direction. Beam lines 1A, 2A and 2B are designed for high intensity operation, and the other four beam lines (3A, 3B, 4A and 4B) for low intensity operation.

The initial configuration will include only three high intensity beam lines with the possibility of adding a fourth (1B) in the future. Target station 2B will also allow the beam to be passed into a beam line for transport to the west into the center vault to a neutron multiplier area so that experimental research and production, utilizing both fast and thermal neutrons, may be performed, as well as for back-up for AITI's commercial production. The AITI commercial production linac will also direct a beam to this multiplier area as shown in Figure 3.3-8 and labeled tuneup dump. The cyclotron beam lines are further distinguished by the operational energy range which is limited by approximately a factor of two between the maximum and minimum extracted beam energies *from a single extraction port*, as described in Table 3.4-1.

The cyclotron and high intensity beam lines are contained within a shielded vault made from stackable cement blocks as depicted in Figure 3.3-9. The low intensity beam lines will pass through the shield wall to the research areas. The shield wall allows access to the low intensity beam line areas for experimental setup while the cyclotron and high intensity beam lines are operating. A thinner stackable shield wall and/or local shielding will be used as appropriate to segregate the low intensity beam lines.

The preliminary beam requirements for each extraction port are identified in Table 3.4-2, which follows on the next page.

TABLE 3.4-2 Extracted Beam Requirements

Beam Line	1A, 1B	2A, 2B	3A, 4A	3B, 4B
Energy Range (MeV)	20-40	40-80	20-80	20-80
Maximum Current μA	0-900	0-900	0-50	0-50
Normalized Emittance Horizontal (π mm mrad)	10	10	<5	10
Normalized Emittance Vertical (π mm mrad)	5	5	<5	5
Energy Spread	~1%	~1%	~0.1%	~1%

The beam emittances and energy spreads presented in Table 3.4-2 represent over 95% of the beam distribution. All of these parameters are readily achievable with commercial cyclotrons with the possible exception of beam lines 3A and 4A, which are dedicated for measurement of cross sections, excitation functions, and other experiments that require high quality beams with low energy spreads. Energy defining slits will be needed for these extraction beam lines after exiting the cyclotron and magnetic analysis in the extraction beam line will be needed to reduce the energy spread to the 0.1% level.

The extracted beam parameters presented in Table 3.4-2 supplement the requirements presented in Table 3.4-1 and define the high level requirements for the extraction systems in the cyclotron. Further requirements related to the reliability, availability, maintainability (RAM), and safety need to be developed to ensure the performance of the cyclotron. The production of radionuclides requires extremely reliable machine operation, minimal unscheduled down time, and reproducible maintenance schedules. These issues will directly impact the cyclotron design with respect to reproducibility and stability of the beam parameters as well as the mean time between failures and scheduled maintenance for the stripper foils, ion source, and other systems.

The conceptual layout shown in Figure 3.3-9 has specific features that will allow for many operational modes. Experimental setup and access to the low intensity experimental areas (Beam lines 3 or 4) can occur while the cyclotron is producing beam in the high intensity area. The choice of whether to include one or two high intensity target stations at each high intensity extraction port is still under consideration. The facility, as shown in Figure 3.3-9, will initially include only these three high power stations with the ability for future upgrades.

The cyclotron beam lines and target systems will be designed to be in strict compliance with all applicable radiation safety regulations as well as the underlying intent of these regulations. These regulations apply to exposures of site personnel, the public, groundwater contamination, and air activation, as well as handling and storage of irradiated components. Specific attention will be given to the choice of materials as well as the design of the cyclotron and beam lines so that component activation is minimized. Standard access protocols such as the *double key interlock system* and the *two-man rule* will be employed.

3.4.3 Cyclotron Procurement

We propose that the NBTF cyclotron be commercially purchased with guaranteed performance specifications to ensure that the required capabilities are achieved. Two international companies, Ebco Technologies, Inc. (Ebco) and Ion Beam Applications, s.a. (IBA), have the capability to design, manufacture, and commission a cyclotron that will meet the NBTF requirements discussed in previous sections. In addition, there are significant existing capabilities and experience in existing commercial organizations (e.g., Bechtel R&D) and at national and international laboratories that will be enlisted. U.S. manufacturers will be used in all areas possible. If a foreign cyclotron manufacturer is used, we would maximize the use of U.S. components to be be built here.

Although Ebco and IBA have produced many lower energy cyclotrons (typically 30 MeV) that meet the beam current requirements of the proposed machine, the requirements presented in the previous section describe a machine that has not been built before. Periodic design reviews will be necessary throughout the procurement to ensure that the performance specifications will be met. We have visited both Ebco in Vancouver, Canada and IBA in Louvain la Neuve, Belgium, as well as the Paul Scherrer Institut in Zurich to discuss design parameters, costs, and construction schedules for the proposed cyclotron for the NBTF.

The contract for the cyclotron will be a competitive procurement. The criteria for selection will include technical and economic considerations, as well as proven capabilities and experience in manufacturing and operating similar systems. The remainder of this section describes many of the specific features that are anticipated in the cyclotron design.

3.4.4 Cyclotron Design and Operation

The cyclotron will likely require a four-fold symmetry in the magnetic yoke to achieve the desired extracted beam specifications from four simultaneous beams. Extraction will

typically be at different energies. A negative ion H^- source with high and low intensity stripper systems is required for this machine. The maximum field will be limited to about 1.5 Tesla at 80 MeV to avoid activation of machine components from electromagnetic stripping of the H^- ions.

Electromagnetic stripping can be reduced to a very small percentage of the beam, which is accelerated above a few MeV by keeping the maximum magnetic field at or below the value cited above. One consequence of this requirement is that the cyclotron becomes significantly larger and heavier (and more expensive) as the energy increases. For example, at 120 MeV the field limitation would be 1.2 Tesla.

The machine diameter is expected to be about four to five meters in diameter for a 70 or 120 MeV machine, respectively, with a total weight of between 100 and 200 tons. The floor slab of the cyclotron vault must be designed for this capability. The RF frequency is expected to be about 50-70 MHz depending on the beam energy, and the dee voltage will be 50-100 kV. IBA and Ebco both use the fourth harmonic mode.

Another important consideration in minimizing the activation of the cyclotron is the neutralization of the H^- ions by the residual gas in the cyclotron. Base pressures of about 10^{-7} torr or less are required to reduce this loss to about 1%. These beam losses will result in activation of the cyclotron, and losses as low as a few percent will result in a few kilowatts of heat load typically along the circumference of the vacuum chamber. A thin water-cooled aluminum chamber can provide heat dissipation and keep long-term activation at low levels. For the proposed cyclotron, the base vacuum will be maintained at 5×10^{-8} torr. Thus, minimum activation of the cyclotron is expected enabling ease of maintenance and reducing radiation exposure to personnel.

The H^- source must produce sufficient beam current to offset injection, bunching, and capture losses in the central region and in the first few turns of the cyclotron. This implies that the source should be capable of producing at least 10 mA for reliable extracted beam currents of 1.0 mA. An external ion source is envisioned to perform routine maintenance with minimal down time. Ion source maintenance periods will be regularly scheduled to allow for replacement and exchange of filaments and other components. There are a variety of different ion sources that could be employed, although the multi-cusp type is probably the best because it is favored by both IBA and Ebco.

The ion source will require a feedback system designed to maintain the total accelerated and extracted beam currents at their programmed intensities based on the different experimental and production needs. The feedback system will be coupled to the extraction system and beam current monitors at each target station so that each target receives the required beam.

Also, this will help minimize the activation of the cyclotron. The beam energy is the other important parameter that must be monitored and regulated on each beam line for simultaneous operation of more than one target station.

We anticipate that each target station will require a different beam energy. Feedback systems that utilize the stripper position, magnetic field of the deflecting dipole magnet, and beam position monitors are under consideration for energy regulation. Adjustable stripper foils mounted on specially designed radial arms are anticipated for the high intensity extraction systems. The foils will be vertically inserted into the beam orbit, with feedback control on the insertion distance to control the intensity. Stripper efficiency is expected to be 99.9%. Each stripper foil is expected to have a lifetime of about 40 mA-hrs. To minimize the downtimes to replace foils, a carousel containing about five foils will be used, giving a total lifetime of about 200 mA-hrs. Since the stripper foils may be inserted through an air lock, the cyclotron chamber will not have to be brought up to atmospheric pressure.

The ability of a single stripper system to cover the full range of extracted beam energies (20-80 MeV) is difficult and requires further evaluation. It may be necessary to limit the range of beam energies from a given beam port to a low or high energy range, as described previously. The challenge is related to positioning the foil at the desired orbit location so that the stripped beam exits the cyclotron return yoke at the same position independent of energy. The angle will necessarily be different for different energies, requiring the use of a bending magnet at each extraction port to steer the beam into the desired target beam line.

Using two carbon foil strippers, it is possible to share the total beam into two high intensity extracted beams of the same energy whose intensity can be varied from 0% to 100% of the total. In addition to the main strippers, the cyclotron will be equipped with two additional secondary strippers made of carbon fibers that will each allow extraction of a small fraction of the total beam (up to 10% maximum) at variable energy into separate beam lines to be used for research and education.

The energy spread of the extracted beam and the dispersive nature of the cyclotron and the steering magnet will require careful design because the energy spread could be as high as a 1-2% for the high intensity beams. This is caused by the overlap between orbits, beam emittance, space charge forces, and the radial or horizontal width of the stripper foil. Each time the energy is changed it will be necessary to re-tune the optics and steering of the transport line. Therefore, the high intensity beam lines must be capable of very low intensities during this tuneup process so that radiation levels, activation, and contamination of beam line components and equipment are minimized.

These low intensity extracted beams may also have restrictions on the extracted energy ranges, and a similar steering dipole magnet will be located just outside the extraction port. The beam current with the low intensity beam lines will be a predetermined fraction of the total current ranging from about 5% down to as low as 0.1% For some research activities, such as precision cross section measurements, the energy spread of the extracted beam must be $<1.0\%$ of beam energy. This performance requirement places some restrictions on the optical design of the cyclotron and beam lines.

It is also desirable, but of less importance, to have relatively small transverse beam emittances for these research beam lines. Some clean-up of the beam can be accomplished in the target transport lines through the use of apertures and energy defining slits. The cyclotron beam to target transport lines are described in greater detail in the next sections.

Loss monitors will be used to detect any significant beam losses in the transport lines. Detection of excessive losses will cause the ion source to be disabled through an interlock system.

3.4.5 Cyclotron Beam Lines

The NBTF cyclotron facility will be initially designed for up to seven target beam lines from the four cyclotron extraction ports. Additional research beam lines can be configured in the low intensity areas as required. Three high intensity production and research beam lines will be supported initially. A schematic floor plan is shown in Figure 3.3-9 as discussed previously. This section will describe the general design of these high and low intensity beam lines beginning with the stripping system.

To extract different beam energies through the same exit port, the stripper must be carefully positioned so that the trajectories for different energy beams intersect at a point just outside the magnet return yoke and approximately at the center of the deflecting magnet at the beginning of the beam line. The circulating beam in the cyclotron will typically be a few millimeters in diameter. There is expected to be some overlap in the beam distribution for nearby orbits, resulting in energy spreads as high as 1.0% of the energy. The beam will be diverging as it exits the cyclotron and the spot size is expected to be 1-2 centimeters in radius.

The function of the cyclotron beam lines is to transport the extracted beam from the cyclotron to the different targets for production and research. The beam line layout must be sufficiently flexible to support a wide variety of user needs. Initially, there will be four

extraction ports with two beam lines on each port, except for one of the high intensity production lines as described above. This section describes the basic configuration of the beam lines based on the requirements of the NBTF mission.

The beam lines must be capable of operation over a wide energy range. The extracted beam emittance (normalized) is expected to be between 5 and 10 π(mm-mrad) with an energy spread of about 1.0%. These beam properties are consistent with most experimental and production needs, with the significant exception of cross section measurements which require a small energy spread and accurate energy definition.

The trajectory of the beam exiting the cyclotron is strongly dependent on the energy and the location of the stripper foils. The stripper foils are carefully positioned so that the trajectories for different beam energies intersect just outside the cyclotron return yoke. A bending magnet, or recombination dipole, will be located at this intersection point so that different beam energies can be deflected into the desired transport channel. The trajectory of the beam for the highest energy (80 MeV) is expected to be about 30 degrees with respect to a tangent to the cyclotron increasing to about 45 degrees at about 30 MeV.

A quadrupole doublet, triplet, or pair of doublets will be located after the bending magnet or recombination dipole. Typically, a quadrupole doublet will be sufficient for production and many experimental needs. The two production beam lines with shielded target stations are expected to include a quadrupole doublet followed by a pair of steering magnets. The steering magnets will also be capable of wobbling the beam to distribute the beam power over the surface of the target. The third high intensity beam line will be designed for experiments and targetry research. The beam optics for this target station will be more flexible, allowing for research into different beam spreading techniques, such as the use of octupole magnets or rotating targets.

Experimental studies of cross sections and associated studies of contaminating reactions require small energy spreads of 100 to 200 keV or less for accurate measurements. The extracted beam from the cyclotron will typically have energy spreads of about 1.0% or about 200 keV at 20 MeV and 800 keV at 80 MeV. A conceptual design of the beam lines required to reduce the energy spread from about 1.0% down to approximately 0.2% has been developed for the study. First order optical studies were performed with both computer codes TRACE3D (Crandell and Rusthoi, 1985) and TRANSPORT (Brown et al., 1980) with similar results. The preliminary nature of the design is largely due to the lack of precise information regarding the trajectories and parameters of the extracted beam and the fact that higher order studies will be required. Final analysis and design of transport beam lines, including the high quality beam line, will be completed during the next phase of the NBTF study.

The beam properties required to reduce the energy spread using slits are a small horizontal waist coupled with a high dispersion. For example, if the horizontal beam spot size for a monoenergetic beam is 0.5 cm (full width) and the dispersion is 5.0 cm/(%dp/p) at the location of a horizontal slit aperture of about 0.5 cm width, the beam which passes through the slit will have a maximum total energy spread of 0.2%, assuming only first order effects. This corresponds to 160 keV at 80 MeV and 40 keV at 20 MeV. These parameters were used in this preliminary conceptual design.

The beam line required to achieve these optics consists of a quadrupole doublet just after the recombination magnet followed by a 90° bend and a drift section of about 2.0 meters. The cyclotron vault shield wall will be located near the 90° bend and subsequent drift section. The distance from the cyclotron to the 90° bend is about 2.25 meters. The gap in the slits will be remotely adjustable. The area where the slits are located will be heavily shielded. The quadrupole doublet following the slits will focus the beam to the desired spot size on target. Target spot sizes of between 0.25 and 3.0 cm radius are easily achieved and the dispersion is also very small at this point. The 90° bending magnet and slits also provide accurate definition of the beam energy. A magnetic field probe (e.g., rotating coil) could be used for an absolute energy calibration.

All beam lines will include suitable diagnostics and safety devices such as toroids, beam profile monitors, beam stops, and radiation monitors. The beam profile monitors will be wire monitors, which detect the secondary emission of electrons and that can be inserted or removed from the beam path. It is expected that the profile monitors at the production target stations will be stationary. The devices in the high intensity lines will require special considerations for high beam power and radiation levels. Frequent access to experimental areas is anticipated which will require redundant and uncoupled safety devices.

The vacuum systems for the beam lines will utilize ion pumps. Turbopumps with cold traps will be used for pump down to the operating range of the ion pumps. Gate valves will be used to isolate the beam line vacuum from the cyclotron during maintenance and setup operations. Fast valves will be included in all high intensity beam lines and other beam lines where gas targets are in use.

The controls for the beam line systems are expected to be fairly routine and will be integrated with the cyclotron control system.

3.4.6 Targetry

The NBTF will feature a wide variety of targets to support the combined missions of research, education, training, and production. While it is beyond the scope of this proposal to discuss all of the targets and target systems that will be employed for the NBTF, the basic features of the target systems are described below.

Target designs for production will require the dissipation of relatively high power levels and will exist in solid, gaseous, and liquid forms. Table 3.4-3 presents some general characteristics of the power level and cooling requirements for typical production targets.

Table 3.4-3 General Target Systems

Target Type	Surface Area (cm^2)	Cooling Area (cm^2)	Cooling	Power Body (W/cm^2)	Power Target (W/cm^2)
Rotating Cone 1-3 Hz Wobbled beam	250	400	1-3 gpm	50-150	20-60
Slanted Target Wobbled Beam	40	30	4-8 gpm	180-450	90-150
Gas-Target Body	250	250	5 gpm	50-150	
Gas 1-2 atm 2cm OD x40 cm L	125 cc	125 cc	Convection	100	60-150/cc
Gas Window Double foil He gas cooled	3.14	3	1.0 l/min @ 2 atm		
Disc - 4 cm OD Wobbled Beam	12.5	3.5	30 gpm	90-200	30-70
Stacked Targets Wobbled Beam	100	300	15 gpm	75-175	25-55

The rms beam spot sizes for the target systems presented in Table 3.4-3 are typically about 3 cm^2 for a beam current of about 250 μA. A discussion of the specific designs of the different target systems and windows is beyond the scope of this proposal. Also, a large

literature exists, which describes many variations on each of these targets. Section 10 cites the excellent series of targetry workshops that have been held since 1984.

The power levels and cooling requirements presented in Table 3.4-3 can be improved on, and many existing systems have much higher power levels. Target systems can be designed to withstand beam currents as high as 1000 μA, although the amount of beam power that a given target can withstand is more dependent on the thermal properties of the stable isotope. Research on the production of any new medical radionuclide at the NBTF will involve a great deal of work on the most appropriate target geometry.

The target design must also accommodate the need to chemically separate the desired radionuclide from the stable isotope and contaminants that are produced by bombardment. Improved cooling technology will be explored, because effective cooling permits the use of higher beam currents and therefore less enriched stable isotopes, which are less expensive than the highly enriched isotopes. Education and training will involve all aspects of targetry, including design, handling techniques, fabrication techniques, preparation methods, materials, and investigations of improved cooling techniques.

The target systems for research beam lines will generally be designed to measure cross sections, and thick target yields, and to optimize the energy range for production so that contaminants from competing reactions and impurities are eliminated or kept to acceptable levels. The targets used for cross section measurements will often be very thin foils so that the energy loss or incident energy and energy range are well defined. Many target materials cannot be produced as thin foils, and these measurements will be more difficult, requiring end point subtractions and very accurate control of the beam energy. In many cases, it will be necessary to accurately measure the stopping power and target thickness for precise cross section measurements. Experimental systems to support all of these research activities will be developed.

A variety of vacuum chambers will be needed for the research beam lines. These chambers will be highly versatile, including many vacuum ports and feedthroughs, allowing for monitoring, in-situ analysis, easy access and recovery of the irradiated targets. Specialized vacuum chambers for hot atom chemistry will also be designed and fabricated as needed.

The production targets will generally utilize self-shielded target chambers because the beam currents are typically one to two orders of magnitude higher. These target chambers include a thick (15-20 cm) tungsten shell around the target body surrounded by about 75 cm of dense polyethylene with appropriate openings for the beam and target handling as shown schematically in Figure 3.4-1. This target chamber is described in greater detail elsewhere in Appendix III.

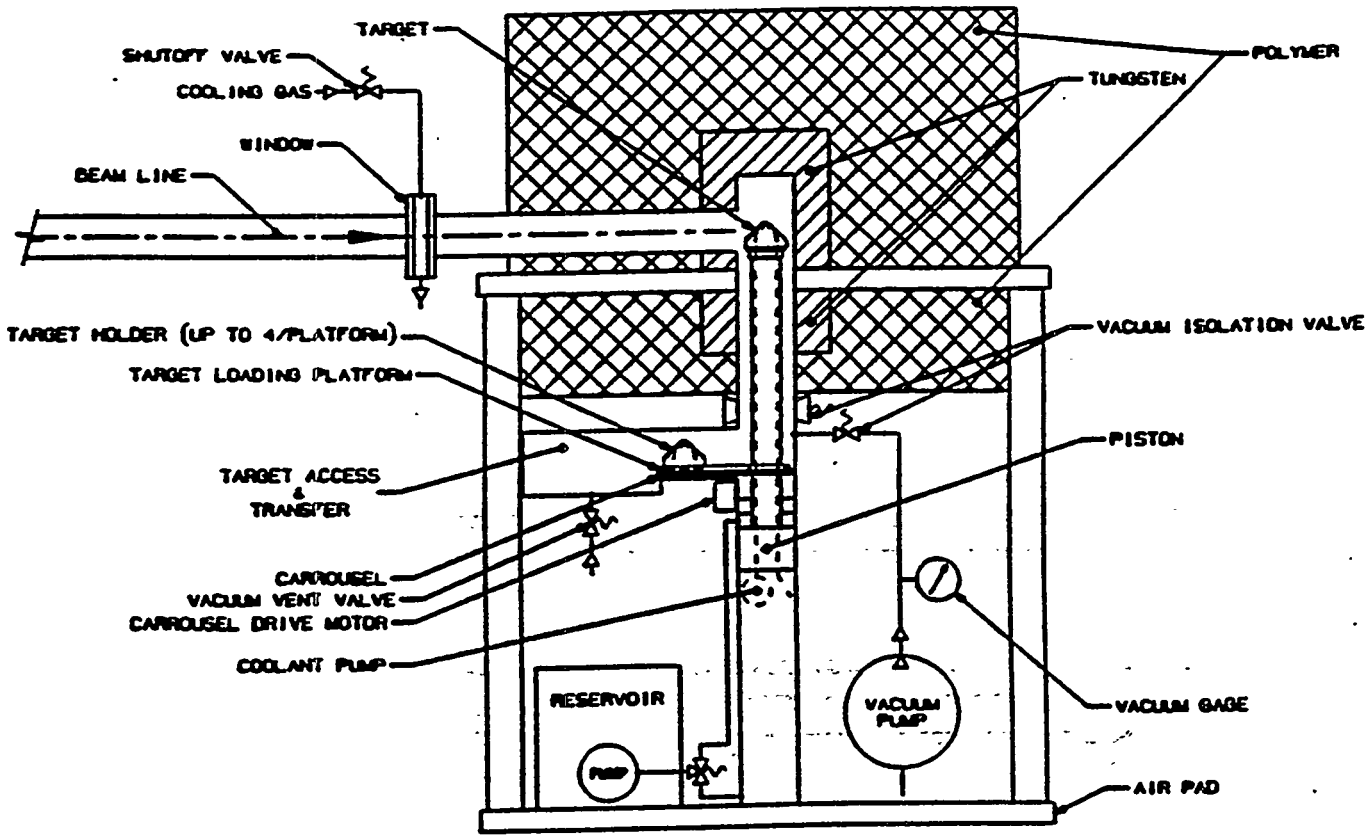


Figure 3.4-1 Target Chamber

Two of the NBTF cyclotron high intensity target areas will have dedicated target chambers of this type, while the third high intensity line will be suitable for different user-provided target chambers to support varying research requirements. This high intensity target area will be optimized for flexibility.

A variety of standard 'tricks-of-the-trade' will be used in the targetry program, including stacked targets and degrader foils to take full advantage of beam intensities and capabilities. Alloyed targets will be used, when appropriate, to raise the melting point of the target material to withstand the intense bombardment necessary in producing some of the product radionuclides.

Numerous support systems are needed for the targets. These systems include the vacuum chamber, water cooling, target handling, target transfer, storage areas for activated target bodies, and target materials. All of these systems will be required for the NBTF facility, and standard, existing techniques and systems will be employed wherever possible to minimize costs. Rigorous protocols and procedures will be developed for handling any activated materials.

The production of the short-lived PET isotopes, ^{11}C, ^{13}N, ^{15}O and ^{18}F, is not part of the NBTF mission, with the possible exception of local distribution of ^{18}F. The cross sections of PET isotopes favor an energy range somewhat below the capabilities of the proposed cyclotron. A dedicated target area on the low energy, low intensity beam line, 3B, for studies with these isotopes is under consideration. However, education and training in the production and uses of these widely used radionuclides will be pursued, to train personnel with knowledge and experience in the production and uses of these radionuclides.

The target systems used to produce PET radionuclides are generally very complex, as they typically involve target materials in the gaseous or liquid state. In addition, the cooling requirements on the target windows can be very demanding, especially considering the trend towards lower energy, higher intensity machines for production of these short-lived isotopes. The syntheses of radiopharmaceuticals from these isotopes is highly automated, and research, education and training in different automation systems and techniques will be pursued.

3.4.7 Target Handling Systems

Target handling techniques will involve a wide spectrum of systems. As described by Link et al. (1992), target handling systems can be categorized in four ways:

a. Manual techniques where the chemists manually perform transfers and additions;

b. Remote techniques where valves or manipulators are used to effect the transfers or additions;

c. Automated systems where a computer is used to control the valves and manipulators which perform the transfers or additions; and

d. Robotic techniques which utilize a mechanical arm to move the reaction vessel or target rather than just moving the chemicals.

All of these systems are expected to eventually be used at the NBTF with a desire to move toward more automation so that the collateral dose received by workers can be minimized, as well as to educate and train personnel on the uses and limitations of each of these techniques. Manual handling of activated materials cannot be avoided in some instances involving unique or highly specialized experiments. Procedures, protocols, and operational rules will be developed prior to approval of any such experiments.

Target handling systems for the production targets are described as part of the commercial production accelerator. Production targets in the cyclotron area will generally employ pneumatic systems for transfer to a centralized high level processing area which is described in Appendix III, which discusses the commercial production facility.

3.4.8 Shielding and Activation

The minimization, regulation, and control of the radiation that is generated at the NBTF is extremely important. Much further study is required. In general, the major concerns fall into five categories:

a. Dose to radiation workers;

b. Dose to public;

c. Air activation;

d. Groundwater activation; and

e. Long term activation of materials.

Each of these concerns has been considered in the conceptual design presented in this proposal. Detailed analysis of the systems and controls required for compliance with all

applicable codes have not been performed. Many such considerations have been incorporated into the proposal in this early design stage.

Preliminary shielding calculations have been performed for all radiation areas, as indicated by the concrete walls shown on the various layouts. The production targets will generally be self-shielded allowing for thinner shield walls surrounding the high intensity beam lines and cyclotron. The cyclotron and beam lines will be designed to minimize beam losses and areas of known beam loss, such as all targets and the energy defining slits which will be shielded locally.

The shielded target stations for radioisotope production are similar to those described by Steyn, et al. (1992). The local shielding around the target reduces the dose by over three orders of magnitude, and the shield wall surrounding the cyclotron vault and production targets reduces the average dose to less than 0.1 mr/hr. The effect of small amounts of beam losses (1-2%) in the beam lines increases the dose outside the shield walls to about 1.0 mr/hr. The target station on beam line 2A will not be self-shielded, but temporary shielding will be used to maintain the maximum dose levels outside the vault shield wall.

Visits to commercial production facilities, as well as experimental sites, were very useful in defining an approach to shielding that will be relatively inexpensive and will protect the permanent structure from activation. In general, stackable, replaceable (and therefore removable) concrete blocks will be used in the high radiation areas surrounding all targets to line the floor and walls to reduce contamination of the facility's poured concrete structure. The type of concrete in the stacked blocks will be carefully chosen for minimal long term contamination wherever possible. The first tenth value thickness in concrete for neutrons produced from 70-80 MeV protons is about 45 cm of concrete, decreasing to about 30 cm as the neutrons are thermalized. The use of borated polymers to line the radiation enclosures and absorb thermal and epithermal neutrons is also under consideration.

The beam areas will all be located in highly shielded underground enclosures. Direct radiation from the beam will not escape these enclosures at levels that affect the public. However, groundwater and air activation are separate concerns, and detailed calculations will be performed to define the shielding and systems required to reduce or eliminate activation of groundwater and air to below the applicable Environmental Protection Agency (EPA) and Texas Regulations for Control of Radiation (TRCR) limits. These systems will be incorporated in the site plan.

All radiation areas will operate with a negative air balance and discharge through a central stack to the outside. The stack will be monitored and alarmed to shut down operations. The facility will use the *contain and decay* approach when an alarm condition exists. The stack

will include the appropriate filters, and its height will be determined from the average wind conditions and the local environment (nearest domicile, land use considerations, etc.) surrounding the site. The modeling code, COMPLY (EPA, 1989), will be used for these calculations.

Preliminary calculations of the beam line activation have been made for both stainless steel and aluminum. Each of these materials will be used in the beam lines. The calculations favor the use of aluminum beam lines wherever possible because the long term activation is about an order of magnitude less. These calculations were based on the induced activity curves presented by Barbier (1969).

3.5 Research and Educational Facility

As pointed out previously, the NBTF research cyclotron will be physically and operationally separate from the production linac and its associated commercial processing facilities. Also, as mentioned previously, the commercial operator will process high activity level irradiated targets from the NBTF cyclotron under contract with the NBTF operating entity.

Figures 3.3-1 through 3.3-13, previously depicted, show the proposed layout of the site and facilities. Figure 3.3-12 specifically illustrates the Research and Educational Facility. The associated commercial processing facility will contain hot cells for manipulating the high activity level irradiated targets from both entities. In the plan presented herein, the research cyclotron will serve in a backup capacity to the linac program, providing highly irradiated targets as needed. Processing of these targets, as well as other very "hot" targets required for the research program, will initially take place in the linac's surface processing facilities.

> ***Consequently, the research facility associated with the cyclotron will not contain hot cells, but will contain space for shielded glove boxes and radiochemical hoods.***

The NBTF research, education, and training facility will consist of a building of approximately 20,000 sq. ft., separated into open and controlled access areas (Figure 3.3-12, shown previously). The open (uncontrolled access) area contains a modest lecture hall, seating about 50 people, two smaller classrooms, a library/distance learning center, secretarial area, six offices for on-site staff professionals, a conference room, eating area, and sanitary facilities. Separate closed areas are provided for receiving, quarantine storage, released supply storage, and a radioisotope holding and shipping area.

Within the controlled access area, space is provided for target preparation and development laboratory, for an associated target fabrication laboratory (machine shop), and a parts storage area. The high level processing area will contain shielded glove boxes and radiochemical hoods. The high level processing area will have a remote transport connection to the target irradiation area below. This remote transport connection will also open into the target preparation and development laboratory. A separate room, adjacent to the high level processing area, is designated as an equipment decontamination area. Separate laboratory areas are also provided for sterilization of equipment, quality control development, analytical chemistry development, and quality control instrumentation. Six radiochemistry laboratories are provided as research space for on-site professionals and student training space.

As students will receive training in Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP), and distributed radiochemical products will be prepared according to these procedures, space is provided for a Quality Assurance and Laboratory Records Documentation Storage. Such records must be available for periodic audits and inspections.

Space is also provided for a Radiation Safety Office and radiation instrument calibration area. A common shielded counting room is included, as well as space for sterility and pyrogen testing. Although not specifically identified in Figure 3.3-12, space will be available for a mock 'hot cell' for student and staff training and for testing components designed for remote manipulation.

Entrance to and egress from the controlled area is provided through men's and women's change rooms, where employees may remove personal clothing and don controlled area personal protective clothing and safety shoes. Note that a common personal decontamination area is located between the change rooms and that a monitoring station is located immediately outside the entrance to the decontamination area. In the event of personal contamination, employees may enter the decontamination area, secure all entrance doors, and proceed with decontamination. After this, the employee may exit to the appropriate change room. Separate sanitary facilities are provided within the controlled area, which eliminates the need to remove controlled area personal protective clothing to reach the sanitary facilities in the open area.

Personnel monitoring is required prior to exiting the controlled area. The procedure described immediately above will be followed in the event of detectable contamination. In the absence of this, the employee will exit through the appropriate change room and remove controlled area protective clothing before entering the open area. All food and liquid consumption is limited to the open area of the facility.

A laundry room is provided to permit the cleaning of re-usable personal protective clothing. The drains from this room will be connected to the below grade radioactive waste storage tanks. The personnel decontamination room drains (floor, shower, and wash basins) will also connect to the radioactive waste storage tanks, while the change room drains connect to the on-site sewerage system.

The initial design for the proposed NBTF research and educational facility does not anticipate a large, on-site group of undergraduate, graduate, and postdoctoral work/study assistants and researchers. In the near term, this space requirement will be addressed by co-locating transportable buildings at the site. Space at the nearby UNT campus will also be available to accommodate some of the graduate student research assistants and postdoctoral fellows. Additional space will be added in the future, as warranted by student enrolment and the volume of research and development activity at the NBTF.

In summary, the NBTF research and education facility will incorporate the requirements for meeting GMP and GLP standards, provide space for maintaining QA files and Laboratory Records, and provide space for radiochemical and radiopharmaceutical research and training, sterility and pyrogen testing, and quality control testing and development.

3.6 Synopsis of Other Center Facilities and Equipment

As discussed earlier in the overview and mentioned again in this section, in addition to the NBTF cyclotron and associated equipment for radioisotope production, research, education, and training, the center will also be co-located with a privately funded commercial isotope production facility. The commercial isotope production facility is already under development by Advanced Isotopes Technologies Inc. (AITI) at the proposed Denton, Texas site. With the commitment to build the NBTF at this site, University of Texas Southwestern Medical Center (UTSMC) at Dallas will move toward establishing an Advanced Medical Imaging Center at the site. The co-location of the three entities provides an ideal environment for technology transfer, training, and education, as well as some economy of scale in certain essential operations such as the processing of high activity targets, radiation safety, etc.

3.7 AITI Facilities and Equipment

The facilities and equipment financed and operated by the private company, Advanced Isotope Technologies, Inc. (AITI), are discussed in more detail in Appendix III. The AITI facilities and equipment will include a 70 MeV, 1 mA linear accelerator for commercial

production of radioisotopes by proton nuclear reactions to produce proton-induced (neutron deficient) nuclides. AITI is presently installing a pulsed dense plasma focus (DPF) device (1.0 MJ) for production of neutron-induced (neutron rich) radioisotope with fast neutron reactions. AITI's proprietary name for the device is the *Pulsed Sealed Neutron Tube*™ The DPF will be used for commercial production of radioisotope by high energy, neutron-induced reactions to produce neutron rich radionuclides, and may be accessed by the NBTF through a contractual agreement with AITI. AITI will also have facilities for stable isotope and enrichment research and production.

3.7.1 Linear Accelerator for Commercial Isotope Production

The requirements for the commercial isotope production accelerator are a 70 MeV energy, 1 mA average proton beam current, with the capability to upgrade to two to three milliamperes in the future. Proton beams of 30, 50, and 70 MeV will be provided for commercial isotope production by the linac. The linac will have a duoplasmatron type H^+ ion source, a radio frequency quadrupole (RFQ), and cascaded drift tube linac (DTL) accelerator tank sections with energies of 30, 50, and 70 MeV. Multiple energy beams are produced by turning on the rf power only to the DTL tanks required to reach the desired energy for a particular beam pulse. Proton beams of the three different energies will bombard up to six target stations. The number of target stations, and energy levels associated with each, will be selected for commercial economic viability, as well as target power density considerations. For commercial isotope production, a linac is preferred over a cyclotron because the linac can deliver beams of 1 mA or greater, which are easily extracted and transported to external targets. The linac is discussed in more detail in Appendix III.

3.7.2 Dense Plasma Focus Neutron Source for Commercial Isotope Production

The dense plasma focus (DPF) is a magnetically driven, deuterium-tritium fusion device that can be fired repetitively to produce a large yield of fast neutrons for many applications. As mentioned above, AITI's proprietary name for the device is the *Pulsed Sealed Neutron Tube*™. AITI is presently constructing a prototype DPF at the Nike Site at Denton, Texas under a CRADA with Los Alamos National Laboratory (LANL). The 1.0 MJ DPF is being developed by AITI to produce 10^{15} D-T neutrons per pulse for commercial radioisotope production. At a 0.1 Hz repetition rate over a four-day activation period, the total D-T neutron yield will be 3.4×10^{19} neutrons. For many radioisotopes of interest, the fast neutron cross sections for (n,p) and (n,α) are quite large, enabling higher yields of carrier-free materials to be produced. The DPF is discussed in greater detail in Appendix III.

3.7.3 Stable Isotopes and Enrichment

The future availability of enriched stable isotopes is a serious concern to the nuclear medicine industry. Commercial production of several radionuclides, such as gallium-67, indium-111, and iodine-123, could not exist without the use of highly enriched stable isotopes to maximize the radionuclidic purity of the final product. Many industry professionals doubt that thallium-201 would never have developed beyond the research stage without enriched thallium-203.

Availability of *new* radionuclides will also depend on a ready supply of enriched stable isotopes at affordable prices. The NBTF radionuclide production and research program must be supported by ongoing research and development on the enrichment/separation of stable isotopes. AITI and affiliated researchers at Association member Missouri University will devote considerable efforts in research on enrichment or depletion of stable isotopes using state-of-the-art laser technology. Customized enrichment/depletion of stable isotopes must be available at reasonable cost if useful quantities of new radionuclides are to enter the research and clinical marketplace. Technologies to pre-enrich some of the low abundance isotopes or to reduce an unwanted isotope prior to enrichment or separation by another technique will be research priorities. For example, the availability of pre-enriched tellurium-123 (to 3% or 4%), accompanied by a similar reduction of tellurium-124, to be used as feed material for subsequent calutron enrichment (at ORNL, for example), would allow any of the 12 MeV (or larger) PET cyclotrons to produce clinical quantities of ultra high purity iodine-123 for regional distribution.

3.8 UNT Facilities and Equipment

Supporting expertise and facilities at the University of North Texas (UNT) are discussed in Section 7 and in Appendix V. UNT is widely recognized for strengths in the physical, life, and computational sciences. Most important are the facilities of UNT's Center for Materials Characterization and the Ion Beam Modification and Analysis Laboratory. The Center for Materials Characterization has a wide array of instrumentation capable of analyses at the single atom level. Facilities include standard and high resolution scanning and transmission electron microscopy (to 1.7 Å), scanning tunneling microscopy, electron spectroscopy (ESCA/Auger and X-ray/ion scattering), FTIR, mass spectroscopy, NMR, and X-ray diffractometry.

3.8.1 Ion Beam Modification and Analysis Laboratory

The University of North Texas has developed an accelerator laboratory for the characterization and modification of materials employing atomic and nuclear physics techniques. The Ion Beam Modification and Analysis Laboratory (IBMAL) (Duggan et al., 1989) employs a variety of accelerator-based techniques for the characterization and modification of materials. Presently available techniques include nuclear reaction analysis (NRA), hydrogen forward scattering (HFS), particle induced x-ray emission (PIXE), Rutherford backscattering spectrometry (RBS), ion channeling (IC), trace element accelerator mass spectrometry (TEAMS) (McDaniel et.al., 1994; Anthony et.al., 1994), and high- and low-energy ion implantation. IBMAL is also used for atomic collision experiments to study ion charge-state dependence of x-ray and Auger electron production.

IBMAL houses five accelerators: a Texas Nuclear Model 9500, 200 kV, 10 mA Cockcroft-Walton; a 200 kV, 3 mA Nova Model NV-200 ion implanter; two 2.5 MV single-ended, High Voltage Engineering Corporation Model AK Van de Graaffs; and a National Electrostatics Corporation Model 9-SDH2 3 MV tandem. The 3 MV tandem accelerator, which is the workhorse of the laboratory, was purchased with an rf charge exchange ion source (alphatross) and a Cs sputter-type ion source (SNICS). A third, ultra-clean, microbeam, raster-scanning, depth-profiling, Cs-sputtering ion source has been constructed for the 3 MV accelerator for Trace Element Accelerator Mass Spectroscopy (TEAMS). TEAMS is used to determine impurities in materials at parts per billion (ppb) by depth profiling techniques. TEAMS has better sensitivities than Secondary Ion Mass Spectrometry (SIMS) for many elements. The TEAMS facility will be used by the NBTF to verify isotopic purity by mass spectrometry.

3.8.2 International Conference on the Application of Accelerators in Research and Industry

Interactions between IBMAL and industry, begun in the late 1970s, have increased dramatically. One of the reasons for the close interactions with industry has been the International Conference on the Application of Accelerators in Research and Industry, which is held biennially at UNT. During the recent conference in November 1994, over 900 people attended from the U.S. and 37 foreign countries. Entire sessions were devoted to atomic and nuclear physics, materials, isotope production for medical applications, biological and medical applications of AMS, accelerator-based neutron sources for boron neutron capture therapy, radiation safety, and other areas. The Denton Conferences are recognized internationally as the largest and most comprehensive conference on accelerator applications.

3.8.3 NSF Industry/University Cooperative Research Center

Based on its facilities and industrial collaborations, UNT was awarded an NSF Industry/University Cooperative Research Center (I/UCRC) grant in 1990 to accelerate the pace of technology transfer to industry. UNT's center, the Industry/University Cooperative Research Center for Nanostructural Materials Research (I/UCRC-NMR), is an interdisciplinary unit that researches the atomic-level structure, or *nanostructure*, of materials used in aerospace, electronics, transportation, metallurgy, and other industries. The I/UCRC-NMR receives support through the NSF grant and from member industries. By supplying much-needed research, technical support, continuing education, and training for industry, I/UCRC-NMR is helping the United States remain competitive in advanced materials — one of five technologies identified by the U.S. Department of Commerce as key to economic growth in the 21st century.

UNT proposes to form a second I/UCRC for Radioisotope Research which will be affiliated with the NBTF. The industrial members of the I/UCRC for Radioisotope Research will be radiopharmaceutical companies and related industries. The mission of the I/UCRC will be radioisotope research and development. UNT staff have already had favorable preliminary discussions with NSF concerning the formation of the I/UCRC for Radioisotope Research.

3.9 UTSMC Facilities and Equipment

The UTSMC Facilities include a vast array of basic science and clinical instrumentation and laboratories. The following describes major facilities or equipment that relate directly to this NBTF study, with emphasis on imaging capabilities and the Department of Radiology, which houses the Radiological Sciences program.

3.9.1 Research Laboratories

Position Sensitive Detector Laboratory. This laboratory includes both anatomic (CT) and functional (PET and SPECT) imaging devices specialized for small animal imaging at high resolution and sensitivity. These specialized devices, currently being constructed and tested, are used to facilitate the translation of new radionuclide agents from the research environment to clinical application.

Radiochemistry Laboratories. Three adjacent Radiochemistry Laboratories (24' X 16') with 3 hoods and sterile box for preparation of radiopharmaceuticals for human use; 24' X

26' with walk-in cold room and freezer room; 24' X 18' with built-in dishwasher, autoclave and oven. Imaging laboratory with 430 sq. ft. of space, SPECT and PET shielded imaging room and electronics/instrumentation shop and fiber optics test facility. The imaging laboratory is connected by secured elevators to the radiochemistry facility.

3.9.2 Clinical Facilities

Nuclear Medicine Facility at Parkland Hospital. This facility is fully equipped with imaging rooms totaling 1870 sq. ft. Two of the rooms have dedicated SPECT cameras. The Medical Imaging Facility is part of the Department of Radiology.

Rogers MR Spectroscopy Center. This facility is devoted exclusively to NMR imaging and spectroscopy research.

Alqurn Meadows Imaging Center. This is a facility dedicated to MR imaging and spectroscopy, including high speed functional imaging with three 1.5T magnets and a fourth bay capable of holding up to 6.0T high field wide bore device.

3.9.3 Laboratory Animal Facilities

Animal Resource Center facility (ARC). This state-of-the-art facility consists of approximately 75,000 sq. ft. of animal housing and support areas located on various floors of seven inter-connected campus buildings. Specialized space includes two cage washing areas, refrigerated food storage, diet kitchen, sterile surgical suites, radiology facilities, intensive care unit, post-operative care room, necroscopy room, and diagnostic laboratory. Animal housing areas are divided into biohazard, barrier, and conventional facilities to insure that spaces suited to specific research needs are available.

3.9.4 Computing Facilities

The medical center's Academic Computer Center allows all departments access to the VAX 8800 mainframe computer. A dedicated SUN SPARstation 330 CX supports the imaging laboratory, as well as a DEC Alpha AXP 3000/300 System Workstation. Personal computers are employed in all facilities.

3.9.5 Major Equipment — Advanced Radiological Sciences

Radiochemistry Laboratory: Capintec CRC 30 dose calibrator, Abbott Labs Gamma Counter, Logic 201 and LPK Gamma Counter, CompuGamma 1282 for 5 radioisotopes with AT&T 6300 computer and LKB-Wallace Printer, Damon International Equipment centrifuge, Mdl Centra-7 and Beckman Microfuge B centrifuge, Beckman 330 HPLC system, Fisher Incubator, Isotemp Mdl 2300, Gibson PC-80K Microfractionator, Yamato RE-46 Rotating Evaporator and Vernitron Verna-Clave sterilizer, imaging laboratory: Small animal PET/SPECT and Gamma Camera Unit, 4096 Channel Pulse Height Analyzer (nucleus), Nal (T1) and HP GE Gamma-Ray Spectrometer, 3 PC compatible computers, MacII Ci with video digitizer card and Sun Workstation.

Waters High Performance Liquid Chromatography (HPLC) System, Waters Differential Refractometer Detector, Milton Roy "Split Pea Accessory" Spectrometer, Galaxy Series, Model 2020 FTIR Spectrometer, PhastSystem Automated Electrophoresis System, Vertis Lyophilizer, pH meters, etc.

3.9.6 Additional Equipment and Facilities

The facilities include a complete 936 sq. ft. prototype machine shop with 2 lathes, welder, 3 milling machines, a Bridgeport (32 Bit DX CNC Control) Milling Machine, as well as components of most any dedicated machine shop, available. The facilities also include a prototype 300 sq. ft. electronics shop with basic assembly, and a variety of instrumentation available.

3.10 Sandia National Laboratories' Reactor-Based Fission and Neutron Irradiation Facilities and Equipment

The Isotope Production and Distribution Program (IPDP) at DOE selected the Reactor Engineering Technology Center at Sandia National Laboratories for production of radioisotopes for nuclear medicine, pending completion of the National Environmental Policy Act (NEPA) process and approval of a detailed resource-loaded schedule. The facilities selected are the Annular Core Research Reactor (ACRR) and the Hot Cell Facility (HCF). The Sandia Pulse Reactor III (SPR III) will also be used without modifications to produce research quantities of radioisotopes.

3.10.1 Sandia/North Texas Agreement

Sandia and the North Texas NBTF Association have agreed, under a Memorandum of Understanding, to cooperate and provide mutual support in research, development, testing, production, and supply of radioactive and stable isotopes and related areas, including detection, imaging, radiopharmaceutical development, automation of separation and manufacturing processes, information technology, hazards analysis, facility operations, and environment, safety, and health issues. Under this agreement the parties will provide to each other such quantities of research and other radioisotopes requested by the other party, consistent with the primary missions of the respective organizations.

3.10.2 Annular Core Research Reactor

Sandia's Annular Core Research Reactor (if conversion approval is received) and SPR III can provide reactor-produced radioisotopes, and the NBTF located in North Texas can provide accelerator-produced radioisotopes, thereby serving the national interest. Other members of the NBTF Association also will be able to access the technologies of Sandia National Laboratories. Sandia can benefit from the experience and capabilities of the NBTF and Association members in identifying and addressing problems in medicine, agriculture, manufacturing, energy, and the environment through the application of the technology of radioactive materials.

3.10.3 SPR III Reactor

The SPR III reactor is operating and does not require modifications to produce radioisotopes. Modifications to the ACRR reactor and Hot Cell Facility, and start up will require approximately 18 months. Production of radioisotopes from the fission process will begin at that time; however, FDA approval may require up to six additional months. Molybdenum-99 suitable for medical use should be available from Sandia by October 1996. It is possible that Sandia will be asked to implement a plan to provide emergency backup to Nordion of Canada for supply of molybdenum-99. In that event, raw molybdenum-99, and possibly iodine-131, and xenon-133, could be available from Sandia as early as October 1995. Implementation of the emergency backup plan would introduce some delays in Sandia's preparations for production of finished molybdenum-99.

3.10.4 Projected Sandia Radioisotope Production

On completion of facility modifications at Sandia, molybdenum-99, xenon-133, and iodine-131 will be harvested from the fission process, and iodine-125 will be produced by activation of xenon-124. Irradiated targets will be transported to the Hot Cell Facility in an adjacent building for processing to extract the desirable fission products. The facility will be capable of exceeding the U.S. demand for molybdenum-99, should this become necessary.

Because the fissioning of uranium-235 produces fission fragment peaks in the mass regions of 90-100 and 135-145, the fission reaction used to generate molybdenum-99 produces a number of other isotopes. A list the radioisotopes and elements with activities greater than 1 curie produced in a 20 kilowatt target after a seven-day irradiation in ACRR are presented in Appendix VI, which describes more fully the Sandia program and the Sandia National Laboratories' reactor-based fission and neutron irradiation facilities and equipment.

3.11 References

Adelstein, S.J. and F.J. Manning (eds.) 1994 *Isotopes for Medicine and the Life Sciences.* Institute of Medicine, National Academy Press, Washington, DC.

Anthony, J.M. et al. 1994 Accelerator based secondary-ion mass spectrometry for impurity analysis. *J. Vac. Sci. Technol.* A12: 1547.

Barbier, M. 1969 *Induced Radioactivity*, North Holland, Amsterdam, p. 340.

Brown, K.L., D.C. Carey, C. Iselin, and F. Rothacker 1980 *TRANSPORT: A Computer Program for Designing Charged Particle Beam Transport Systems.* SLAC-91 (1991), NAL-91 (1991), and CERN 80-04 (1980).

Crandell, K.R. and D.P. Rusthoi 1985 *Documentation for TRACE: An Interactive Beam Transport Code.* LANL Report 85-21.

Duggan, J.L., et al. 1989 The University of North Texas ion beam modification and analysis laboratory. *Nucl. Instrum. and Methods in Physics Research* B40/41: 709.

Duggan, J.L. and I.L. Morgan (eds.) 1993 International conferences on the application of accelerators in research and industry. *Nucl. Instr. Meth.*, B79.

Federal Register, Vol. 58, No. 197, Thursday, October 14, 1993.

Environmental Protection Agency 1989 *User's Guide for the COMPLY Code.* U.S. Environmental Protection Agency, Office of Radiation and Indoor Air, EPA 520/1-89-003, October 1989

Link, J.M., J.C. Clark, and T.J. Ruth 1992 Introduction: State of the art in automated syntheses of short-lived radiopharmaceuticals. *Proceedings of the 4th International Workshop on Targetry and Target Chemistry*, (R. Weinreich, ed.), PSI Villigen, Switzerland, p. 174.

McDaniel, F.D. et al. 1994 Impurity determination in electronic materials by accelerator mass spectrometry. *Nucl. Instr. Meth.* B89: 242.

Parks, B.S. 1991 *Users' Guide for CAP88-PC.* EPA-520/6-91-022 (December 1991).

Steyn, G.F. et al. 1992 *Nucl. Instr. Meth.*, A136: 128-133.

4.0 PRODUCTS AND SERVICES

4.1 Introduction

The National Biomedical Tracer Facility (NBTF) will offer a variety of research radionuclides, specialty radionuclides, irradiation services, and educational/training programs, as well as serving as a back-up supplier to a commercial radionuclide producer (Advanced Isotope Technologies, Inc., AITI), which is a participant in this proposal. Included are tables of *proton-induced* (neutron deficient) research radionuclides produced either directly with a proton beam, or produced indirectly from generator systems. In the generator systems, the mother isotope would be produced with the accelerator.

The proposed cyclotron will be able to routinely produce radioisotope products that are in demand but that have been available to researchers in the past only infrequently from current sources. The NBTF will also be in a position to produce certain commercial products that may be purchased by radiopharmaceutical companies to augment their inventory. Also included in this section are examples of neutron-induced, *neutron excess* radionuclides, which could be developed by the NBTF and made available to researchers and the radiopharmaceutical industry through its commercial affiliate, AITI.

All candidate products identified in this proposal are *carrier free* radionuclides, consisting only of the desired element, because they all are produced from different chemical elements. This permits chemical separation protocols that isolate the element of interest from the target material and provide the researcher with ultrahigh specific activity products. The advantages of carrier-free radionuclides in nuclear medicine applications are well known.

This section also describes various contract services that would be offered to the radiopharmaceutical industry, as well as proposed research, development, education and training programs. A discussion of properties and uses of most of the radionuclides identified as potential NBTF products is presented in Section 7.0 of this proposal.

4.2 Proposed Radionuclide Product List

The following discussion combines both proton-induced (accelerator produced) radionuclides and neutron-induced (reactor or neutron source produced) radionuclides that would be available through the NBTF. We expect that accelerator-produced radionuclides will be the main products of the NBTF, both in the near term and the foreseeable future. However, based on our market study of research isotope needs, neutron-induced radioisotopes have a clearly defined presence that should be addressed by a national facility dedicated to supplying research radionuclides.

4.2.1 Proton-Induced (Neutron Deficient) Radionuclides

The NBTF cyclotron, when used in conjunction with selected enriched stable isotopes as targets, will have the capability to produce more than 98% of accelerator-produced, *proton-induced* (neutron deficient) radionuclides of interest now and in the near term — perhaps a decade, we believe. This opinion is based on interviews with approximately 40 industry leaders, plus our own team's experience and their projections for the future, which are based on their intimate familiarity with the field. In addition, most of the radionuclides discussed here were identified in an extensive literature search and in several prestigious national reports that appeared over the past ten years.

In addition to the NBTF cyclotron, the *intense neutron source* (AITI's Pulsed Sealed Neutron Tube™), will be available to NBTF researchers and production personnel through a contract with AITI. The intense neutron source will have the capability to produce many of the currently unavailable *neutron-induced* radiomuclides for nuclear medicine research and clinical applications.

Examples of radionuclides (of both categories) that could be produced by the NBTF facility are listed in the tables that follow. Since it is impossible to identify the research products that will be of interest in five, ten, or twenty years from now, the individual entries in these compilations are intended as *examples* of the NBTF potential, rather than individually defensible research products that could be argued in a business plan on a product-by-product basis. Nevertheless, the principals who developed this proposal have a wealth of practical experience and theoretical acumen in the business of radionuclide production and applications. They have proved themselves in a demanding marketplace.

The reader should understand that — while demand is important and demand drives the market — the production of specific radionuclides is as dependent on the availability of enriched stable isotopes as it is on the energy of bombarding particles. Hence, the 80 MeV cyclotron, which we propose — coupled with selected enriched isotopes — will be much more productive than a cyclotron with an energy of 100 MeV and beyond but with a limited repertoire of available enriched stable isotopes. For this reason, we propose a research program in stable isotope enrichment/separation, which is mentioned below in this section and more completely described elsewhere (Section 7, and Appendix III).

4.2.1.1 Research Radionuclides

The following research radionuclides are divided into two categories: generator systems and non-generator nuclides.

4.2.1.1.1 Generator Systems

Radionuclide generators provide the researcher and clinician with unique, short-lived products which would otherwise be unavailable without an on-site accelerator or neutron source. Table 4.2-1 lists some generator systems whose mother radionuclides could be produced by the NBTF cyclotron and which have not been routinely available.

4.2.1.1.2 Non-Generator Radionuclides

Table 4.2-2 lists radionuclide candidates that cannot be obtained from generator systems but can be provided directly through nuclear reactions triggered by a proton beam on a stable isotopic target. Such products are distributed directly (typically by overnight air transport) to individual researchers and clinical researchers. Table 4.2-2, which follows, describes suggested product radionuclides and their characteristics.

Tables 4.2-1 and 4.2-2 follow on the next pages.

Please note that all the tables that follow run on for more than one page. We elected this format for readability, rather than reducing the print size to force an entire table onto one page.

Table 4.2-1 Generator Systems

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abundance (%)	Reaction[c]	Beam Energy (MeV)	Comments
Ba-128/Cs-128 (EC/ß+,EC)	2.43 d/3.6 m	Cs-133	100	p,6n	70	a. Need excitation function to 80 MeV b. Target development needed
Fe-52/Mn-52m (ß+,EC/ß+,EC)	8.27 h/21 m	Mn-55	100	p,4n	50	a. Need excitation function to 60 MeV b. Target development needed
Ge-68/Ga-68 (EC/ß+,EC)	288 d/68 m	Ga-69 Ga-71	60 40	p,2n p,4n	30 45	a. Need excitation function to 50 MeV b. Target development needed, alloy with Ni or Ag c. Yield at 45 MeV would benefit from enriched Ga-71.
Hf-172/Lu-172 (EC/EC)	1.87 y/6.7 d	Lu-175	97	p,4n	50	a. Target development needed
Nd-140/Pr-140 (EC/EC,ß+)	3.4 d/3.4 m	Pr-141	100	p,2n	25	a. Target development needed
Se-72/As-72 (EC/ß+,EC)	8.4 d/26.0 h	As-75	100	p,4n	50	a. Need excitation function to 60 MeV b. Target development needed

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abundance (%)	Reaction[c]	Beam Energy (MeV)	Comments
Sn-113/In-113 (EC,IT)	115 d/99.5 m	In-115	96	p,3n	30	a. Need excitation function to 40 MeV b. Target development needed
Rb-81/Kr-81m (EC,β^+/IT)	4.6 h/13 s	Kr-84	57	p,4n	45	a. Need excitation function to 60 MeV b. Target development needed c. Yield would benefit from enriched Kr-84
Sr-82/Rb-82 (EC/β^+,EC)	25 d/1.25 m	Rb-85 Rb-87	72 28	p,4n p,6n	50 70	a. Need excitation function to 80 MeV b. Target development needed c. Yield below 50 MeV would benefit from enriched Rb-85 if used with tandem targets at higher energy
Te-118/Sb-118 (EC/β^+,EC)	6 d/3.5 m	Sb-121 Sb-123	57 43	p,4n p,6n	50 70	a. Need excitation function to 80 MeV b. Target development needed c. Yield below 50 MeV would benefit from enriched Sb-121 if used with tandem target at higher energy

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abund-ance (%)	React-ion[c]	Beam Energy (MeV)	Comments
W-178/Ta-178 (EC/EC,β^+)	21.6 d/9.3 m	Ta-181	99.9	p,4n	50	a. Need excitation function to 60 MeV b. Target development needed
Zn-62/Cu-62 (EC,β^+/β^+,EC)	9.2 h/9.73 m	Cu-63 Cu-65	69 31	p,2n p,4n	25 50	a. Need excitation function to 60 MeV b. Target development needed c. Yield below 25 MeV would benefit from enriched Cu-63
Xe-122/I-122 (EC/β^+,EC)	20.1 h/3.6 m	I-127	100	p,6n	60	a. Need excitation function to 80 MeV b. Target development needed

[a] Decay modes are labeled as alpha decay (α), positron beta decay (β^+), electron capture (EC), gamma ray (γ), internal conversion (e^-), isomeric transition (IT), neutron emission (n), negatron beta decay (β^-).
[b] Half-lives are in time units of year (y), day (d), hour (h), minute (m), second (s).
[c] Proton (p), neutron (n).

Table 4.2-2 Non-Generator Radionuclides

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abund-ance (%)	React-ion[c]	Beam Energy (MeV)	Comments
As-73 (EC)	80.3 d	As-75	100	p,xn	60	a. Reaction goes to Se-72 and Se-73; early processing allows separation of Se-73 (7.1 hr), which decays to As-73 b. Need excitation function to 70 MeV c. Dual product production of Se-72/As-72 with p,4n reaction d. Requires two separations e. Target development needed
As-74 (EC,β^+,β^-)	17.8 d	Ge-74	36.5	p,n	20	a. As-73 also produced b. Need excitation function to 50 MeV to investigate p,3n reaction on Ge-76
Be-7 (EC)	53.3 d	Li-7	92.5	p,n	20	a. Very high yield
Bi-205 (EC)	15.3 d	Pb-206	~86	p,2n	30	a. Need excitation function to 40 MeV b. Reaction uses natural radiogenic lead c. Target development needed
Bi-206 (EC)	6.24 d	Pb-206	~86	p,n	20	a. Reaction uses natural radiogenic lead b. Target development needed
Bi-207 (EC)	38 y	Pb-208	52.3	p,2n	30	a. Target development needed

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abund-ance (%)	React-ion[c]	Beam Energy (MeV)	Comments
Br-77 (EC)	57 h	Se-80	49.8	p,4n	50	a. Br-76 also produced from natural Se target b. Need excitation function to 60 MeV c. Target development needed d. Enriched Se-80 would increase yield and reduce Br-76 e. Production from Kr-82 by p,6n could be useful
Ce-139 (EC)	137 d	La-139	99.9	p,n	20	a. Target development needed
Cr-51 (EC)	27.7 d	V-51	99.8	p,n	20	a. Higher energy could also produce V-48 b. Need excitation function to 60 MeV for evaluation of multiple products c. Target development needed
Cu-61 (β^+,EC)	3.4 h	Ni-62	3.6	p,2n	25	a. Cu-64 also produced b. Need excitation function to 30 MeV c. Enriched Ni-62 (to ~35%) or depleted Ni-64 desirable
Cu-64 (EC,β^-,β^+)	12.7 h	Ni-64	0.91	p,n	20	a. Enriched Ni-64 required
Fe-52 (β^+, EC)	8.27 h	Mn-55	100	p,4n	50	a. Need excitation function b. Fe-55 also produced c. Target development needed

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abund-ance (%)	React-ion[c]	Beam Energy (MeV)	Comments
I-125 (EC)	60.2 d	I-127	100	p,3n	40	a. Reaction goes to Xe-125; early processing allows separation of Xe for subsequent decay with a 16.8 hr half-life to I-125 b. Need excitation function to 80 MeV c. Target development needed
Pb-203 (EC)	52 h	Tl-205	70.5	p,3n	30	a. Enriched Tl-205 available
Re-186 (β^-,EC)	90.6 h	W-186	28.6	p,n	20	a. Low yield expected b. Enriched W-186 would increase yield
Ru-97 (EC)	2.88 d	Tc-99	2.14x 10^5 y	p,3n	40	a. Inexpensive target material b. Target development needed c. Alternative reaction on Rh-103 at 80 MeV by p,7n reaction
Tc-95m (EC,β^+,IT)	61 d	Mo-96	16.7	p,2n	30	a. Need excitation function to 40 MeV b. Target development needed
Tc-96 (EC)	4.3 d	Mo-96	16.7	p,n	20	a. Need excitation function to 30 MeV b. Target development needed

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abund-ance (%)	React-ion[c]	Beam Energy (MeV)	Comments
V-48 (EC,ß$^+$)	16 d	V-51	99.7	p,4n	50	a. Reaction goes to Cr-48; early processing allows for separation of Cr, which decays by EC with a 21.6 h half-life to V-48 b. Need excitation function to 60 MeV c. Double processing required d. Cr-51 will also be produced e. Target development needed
Y-88 (EC,ß$^+$)	107 d	Y-89	100	p,2n	30	a. Reaction goes to Zr-88; processing allows separation of Zr-88, which decays by EC with a 83.4 d half-life to Y-88 b. Need excitation function to 40 MeV c. Double processing required d. Reaction yields two products e. Target development needed

[a] Decay modes are labeled as alpha decay (α), positron beta decay (ß$^+$), electron capture (EC), gamma ray (γ), internal conversion (e$^-$), isomeric transition (IT), neutron emission (n), negatron beta decay (ß$^-$).
[b] Half-lives are in time units of year (y), day (d), hour (h), minute (m), second (s).
[c] Proton (p), neutron (n).

4.2.1.2 Commercial Radionuclides

The principal aim of the NBTF is to supply research radionuclides for the U.S. and North American research community. However, the cyclotron will also be able to supply some commercial radionuclides if there is a need.

4.2.1.2.1 Supplemental Production Products

A top priority of the NBTF will be to supplement production of those high demand, advanced stage research radionuclides that are not routinely available from Los Alamos or Brookhaven National Laboratories or from the commercial sector, as shown below in Table 4.2-3. These are radiochemical grade accelerator products, typically developed and produced at the national laboratories, and are in demand by nuclear medicine researchers and clinicians but whose production is limited by other DOE programmatic demands.

Another high priority of the NBTF will be to develop production technology to insure that successful research products (of the future) will be available for the clinical applications that follow. The NBTF will be in a position to supply new products beyond the R&D stage, if necessary, to insure that they are available for clinical application in usable and affordable quantities until they become commercially available. The NBTF will develop efficient production techniques for the commercialization of the successful research products and transfer that technology to the commercial sector when requested.

Table 4.2-3 Supplemental Products

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abundance (%)	Reaction[c]	Beam Energy (MeV)
Sr-82 (EC)	25 d	Rb-85 Rb-87	70.0 27.8	p,4n p,6n	70
Ge-68 (EC)	288 d	Ga-69 Ga-71	60.1 39.9	p,2n p,4n	45
Cu-67 (β^-)	61.9 h	Zn-70	0.62	p,α	40
Cd-109 (EC)	453 d	Ag-109	48.2	p,n	20

Radionuclide (decay mode)[a]	$t_{1/2}$[b]	Target	Abundance (%)	Reaction[c]	Beam Energy (MeV)
Xe-127 (EC)	36.4 d	Cs-133	100	p,7n	70
F-18 (β^+,EC)	109.8 m	O-18	0.2	p,n	20

[a] Decay modes are labeled as alpha decay (α), positron beta decay (β^+), electron capture (EC), gamma ray (γ), internal conversion (e^-), isomeric transition (IT), neutron emission (n), negatron beta decay (β^-).
[b] Half-lives are in time units of year (y), day (d), hour (h), minute (m), second (s).
[c] Proton (p), neutron (n).

4.2.1.2.2 Commercial Products

The NBTF will perform service irradiations, including production of established commercial products, when requested to supplement production by the commercial sector. These commercial products will be supplied as radiochemical grade products only and will be shipped directly to the requesting pharmaceutical company or industrial user. The NBTF will also provide service irradiations (for non-commercial products) for universities, national laboratories, medical centers, and qualified individual researchers according to conditions outlined in the *custom irradiations* section of this proposal.

Potential Commercial Products

1. ^{57}Co, produced from enriched ^{58}Ni; shipped as processed radiochemical or unprocessed target.

2. ^{67}Ga, produced from enriched ^{68}Zn; shipped as processed radiochemical or unprocessed target.

3. ^{123}I, produced from enriched ^{124}Xe; shipped as processed radiochemical.

4. ^{111}In, produced from enriched ^{112}Cd; shipped as processed radiochemical or unprocessed target.

5. **^{201}Pb**, produced from enriched ^{203}Tl;
shipped as processed ^{201}Pb radiochemical.

6. **^{201}Tl**, produced from enriched ^{203}Tl;
shipped as processed ^{201}Tl radiochemical.

While the NBTF will act as a back-up supplier of ^{201}Tl to the commercial sector and will initially supply the ^{201}Pb precursor produced from the ^{203}Tl(p,3n) reaction, it will undertake at an early stage the development of ^{201}Pb production via the ^{205}Tl(p,5n) reaction (~40 MeV) and later via the ^{206}Pb(p,6n) reaction (~60 MeV) using radiogenic lead. Although the ^{206}Pb yield from the ^{205}Tl reaction is essentially the same as from the ^{203}Tl reaction, this production route has the advantage of utilizing a significantly less expensive and abundant enriched target material. While the calutrons at Oak Ridge National Laboratory have been separating large quantities of thallium isotopes for the past 20, the sales have been limited to ^{203}Tl, leaving tens of kilograms of highly enriched ^{205}Tl isotopes to accumulate in inventory. The use of this enriched isotope by the NBTF would not only provide a market for a surplus ORNL product, but it would reduce future strains on the limited Calutron schedule. The use of radiogenic ^{206}Pb (~86% abundance) and the p,6n reaction as an alternate production mechanism for ^{201}Pb has several advantages: (1) the material is available in large quantities at a very low cost (compared to enriched isotopes) and (2) the production rate of ^{201}Pb would improve by approximately 50%.

4.2.2 Neutron-Induced (Neutron Excess) Radionuclides

The intense neutron source, available to NBTF researchers through a contract with AITI and discussed in Section 7 and in Appendix III, offers production capability for a broad range of neutron-induced (neutron rich) radionuclides. As with proton induced, neutron deficient radionuclides, it is impossible to predict the research products that will be of interest in the long term. However, the following list identifies a few neutron-induced radionuclides that are of current interest and could be produced in research and clinical quantities by fast neutron reactions in the high flux region of the intense neutron source.

Table 4.2-4 Neutron-Induced (Neutron Excess) Radionuclides

Radionuclide	Decay Mode[a]	$t_{1/2}$[b]	Target	Abundance (%)	Reaction[c]
As-77	β^-	38.8 h	Se-77[d]	7.6	n,p
Au-199	β^-	3.14 d	Hg-199[d]	16.8	n,p
Cu-67	β^-	61.9 h	Zn-67[d]	4.1	n,p
Gd-159	β^-	18.6 h	Tb-159	100	n,p
Ho-166	β^-	26.8 h	Er-166[d]	33.4	n,p
P-32	β^-	14.3 d	S-32	95.02	n,p
P-33	β^-	25.3 d	S-33[d]	0.75	n,p
Pm-149	β^-	53.1 h	Sm-149[d]	13.9	n,p
Re-186	β^-,EC	90.6 h	Os-186[d]	1.6	n,p
Re-188	β^-	16.9 h	Os-188[d]	13.3	n,p
Rh-105	β^-	35.4 h	Pd-105[d]	22.2	n,p
Sm-153	β^-	46.8 h	Eu-153[d]	52.1	n,p
Sc-47	β^-	3.42 d	Ti-47[d]	7.4	n,p
Sr-89	β^-	50.5 d	Y-89	100	n,p

[a] Decay modes are labeled as alpha decay (α), positron beta decay (β^+), electron capture (EC), gamma ray (γ), internal conversion (e^-), isomeric transition (IT), neutron emission (n), negatron beta decay (β^-).
[b] Half-lives are in time units of year (y), day (d), hour (h), minute (m), second (s).
[c] Proton (p), neutron (n).
[d] Enriched isotope may be desirable.

4.3 Proposed Research and Development Program

We describe here elements of the proposed research program that relate directly to radionuclide production and would directly involve the personnel and facilities of the NBTF. This discussion is augmented by the discussions in Section 7 and in Appendices III and IV.

4.3.1 Radionuclide Production and Separation Programs

Efficient production of usable quantities of new potentially useful radionuclides, as well as those currently being used, is essential for the continued contribution of Nuclear Medicine to effective health care. A goal of the proposed NBTF and the NBTF Association is to conduct research and development programs geared to researching and evaluating methods for the production of radionuclides with high radiochemical and radionuclidic purity, concurrent with high production efficiency. Bombardment of multiple, high energy targets will lower the unit cost of production. Full development of robotics and other automation procedures for radiochemical separation will lead to products of high purity and reproducibility at lower resource costs.

4.3.1.1 Optimal Production Parameters

When considering production approaches for radionuclides, several nuclear reaction options are often available. A strong research program in measuring excitation functions of appropriate nuclear reactions will help to establish appropriate production parameters. Optimal product yields can be achieved using such data to evaluate and select appropriate nuclear reactions, charged particle energies, target thicknesses, stable isotope enrichment or depletion, and bombardment times.

The NBTF and Association members will institute a program to evaluate the use of higher energy (50 to 80 MeV) protons for radionuclide production. The usefulness of proton-induced fission in high Z materials will be studied.

The availability and cost of isotopically enriched target material is an important consideration in selecting a production method. Experimental excitation functions generated over a wide energy range will be of great value in the selection of target material and purity required for efficient production of the desired radionuclide. Excitation function data will also be useful in designing and implementing innovative target configurations.

4.3.1.2 High Power Target Development

Availability of accelerator targets designed to transfer and remove the heat generated by 15 kW or more of beam power would greatly aid economical production. A program to develop high power targets and target configurations will be established. Other aspects of the target development program will include: laminated and segmented targets for multiple product production; use of alloyed targets to raise melting points and possibly produce multiple products in one irradiation; efficient use of beam dumps for longer lived products; and targets for the production of neutron-induced products.

4.3.1.3 Innovative Radiochemistries

Separation and chemical purification of the radionuclide product from the target material and its holder is often labor intensive and leads to variations over time in the specifications of the final product as operating personnel change. We propose to initiate a program to develop the use of robotics and other automation techniques for radiochemical separations and purifications to improve reproducibility, decrease manpower requirements, and maintain low personnel radiation exposures. This program will focus on developing separation processes and equipment designed to be compatible with robotics. Special emphasis will be placed on selecting reagents which have low biotoxicity and which are environmentally safe.

The development program will also emphasize the development of radiochemical procedures that result in radiochemical products of very high chemical purity, which is necessary for efficient labeling of proteins, peptides, and other biomolecules. Of necessity, the program will require the development and use of highly selective and sensitive tests of purity.

Another important part of the NBTF R&D program will be to establish highly efficient and reliable chemical processes to recover isotopically enriched materials in a form suitable for reuse. This will also be a consideration when selecting the most efficient nuclear reaction for the production of a specific radionuclide.

4.3.1.4 Proprietary Support and Technology Transfer

The NBTF and NBTF Association will establish a program to offer contract proprietary research and development support to the radiopharmaceutical industry. The NBTF will contract to perform specifically requested work, such as the measurement of excitation functions, comparison of yields from different nuclear reactions, development of innovative chemical separation procedures, and process validations.

An integral part of the program will include technology transfer of non-proprietary radionuclide production methods and related procedures developed by the NBTF and the NBTF Association for experimental work in the biomedical sciences. In this manner, production of radionuclides demonstrating early stage clinical usefulness may be transferred to industry and made available on a larger scale for expanded clinical evaluations.

4.3.2 Enriched Stable Isotopes

The future availability of enriched stable isotopes is a matter of serious concern to the nuclear medicine community, especially since the beginning of this decade when funding shortfalls limited the federal enrichment program. As mentioned previously, the production of radionuclides is vitally dependent on affordable enriched stable isotopes for both established clinical applications and for research investigations. Both areas of radionuclide

production are in jeopardy as the U.S. supply of enriched feed stocks continues to decline and be supplanted in the marketplace by foreign products. The calutrons at ORNL have been placed on standby for extended periods at least twice since the mid 1980s, with the most recent period being from mid 1991 through early 1995.

Commercial production of several radionuclides, such as ^{67}Ga, ^{111}In, and ^{123}I, cannot continue in the absence of enriched targets that are required to maximize the radionuclidic purity of the final product. For example, without enriched ^{203}Tl target material, production of ^{201}Tl today would require an additional 24 commercial cyclotrons to meet the clinical demand in the U.S. alone. Despite an estimated expenditure of $20 million for enriched ^{203}Tl feed stock over the past 20 years, the commercial sector has realized a savings in excess of $200 million in production costs. In fact, the current ^{201}Tl market would most likely not exist, had not enriched ^{203}Tl been available in the beginning.

Likewise, the availability of *new* radionuclides in the 21st Century is vitally dependent on an abundant supply of economically priced enriched stable isotopes. The NBTF Association will contribute to this effort by exploring new enrichment technologies. We also hope for continued federal funding for the ORNL calutron program. Facilities and expertise of Association members will be marshalled to explore advanced enrichment techniques (as well as examining depletion methods for isotope enrichment).

An integral part of the R&D program will be development of technology to pre-enrich one or more of the low abundance isotopes (or to reduce the abundance of an unwanted isotope of an element) prior to enrichment or separation by another process. For example, if a method could be developed for enriching ^{123}Te by a few percent, while at the same time achieving a reduction of ^{124}Te by a like amount, the isotopic mixture subsequently passed through the calutron would yield a target that would allow any of the 12 MeV (or higher energy) PET cyclotrons to produce clinically useful quantities of ultra high purity ^{123}I for regional distribution.

More extensive discussion of specific separations research is found in Section 7 and Appendix III. Currently, two active programs exist among the proposed Association members: at the University of Missouri where the CRISLA process is being developed and at AITI/NTRI where the AVLIS process is being investigated.

4.3.3 Radiolabeling

Radionuclides produced in an accelerator may not be in a suitable chemical form for biological evaluations. After the production of a desired radionuclide with appropriate radionuclidic purity, it will be converted into a suitable salt and formulated in a medium suitable for biological evaluations. In other cases, the radionuclide has to be complexed/chelated with an appropriate ligand such that the radiolabeled product has affinity

and selectivity for the desired organ or lesion, plus the appropriate pharmacokinetic characteristics. The participation of nearby UTSMC at Dallas will permit research and development of new ligands, radiolabeling techniques, and formulations suitable for biological evaluations. Analytical methods will be developed to test these new agents for radiochemical purity, stability, and pharmaceutical quality. Such new tracers will be evaluated in appropriate animal models at UTSMC. Such biological evaluations will involve the generation of pharmacokinetic and biodistribution data with appropriate animal imaging studies. In selected cases, animal imaging studies will be performed with new experimental imaging devices currently under development at UTSMC. These devices promise better performance characteristics than conventional gamma cameras.

The Association, including OU, UNM and UTSMC, will offer research and development programs to explore radiolabeling techniques for proteins, peptides, oligo-nucleotides, and other receptor binding ligands, on-site labeling kits, robotics, analytical methods, pre-clinical studies, and radionuclide generators. Additionally, opportunities for practical experience in nuclear pharmacy and the development of radiopharmaceuticals will be offered.

4.3.4 Nuclear Medicine

The future of clinical nuclear medicine is promising on several fronts. Clinical nuclear medicine, like other imaging modalities, compete with each other for the best technique in diagnosing a specific patient problem. Nuclear medicine always has had the greatest target to background (contrast) of any of the imaging modalities. This is not surprising since one can pick the radioisotope and pharmaceutical product to fit a specific need. However, a disadvantage is the lack of resolution in the detecting systems. Presently, nuclear medicine has a typical resolution of approximately 5-6 mm while CT/ultrasound/MR has approximately 1-2 mm of resolution. New instrumentation designs should allow the resolution for nuclear medicine to drop to 1-2 mm, which ought to lead to a shift of many patient examinations back to nuclear medicine as a preferred primary diagnostic method.

UTSMC is in the forefront of the development of new imaging technologies and will use a variety of new radionuclides from the NBTF in this research and development. The proposed, on-site Advanced Medical Imaging Center has been mentioned earlier.

Nuclear medicine is relatively inexpensive, compared to CT or MR and has widespread availability in most hospitals. Nuclear medicine always has been one of the preferred methods in understanding physiology because it allows you to view tracers passing through the body or binding to specific tissues. This should become a very exciting area of clinical medicine as new imaging technologies with better resolution are developed, along with the ability to label subsets of receptors in the central nervous system, heart, and in cancer cells. The ability to examine phenomena with short temporal resolution in *real time* should open up many new areas of research in biochemistry and physiology in human health and disease.

The new camera designs also will also permit use of a far wider variety of isotopes and radiopharmaceuticals. Currently, most gamma cameras work best within a range of 100-200 keV. The new cameras image in this range but actually become even more efficient at higher energies, up to 1 MeV. The ability of the NBTF to produce such new radioisotopes will be a great aid in creating new radiopharmaceuticals in a broad area of new diagnostic and therapeutic agents. New camera designs and new radioisotopes and radiopharmaceuticals can create a renaissance in nuclear medicine. But unlike the original explosion in the 1960s, current nuclear medicine physicians are more knowledgeable about potential applications.

In summary, the creation of the NBTF project, coupled with the development of new nuclear medicine imaging technology, should lead to an explosion of new tests to better understand the biochemistry and physiology of disease states. This will lead to better and earlier diagnosis, better targeted therapy, and patient management that should be cost effective for both the patient and society.

The University of Texas Southwest Medical Center at Dallas has extensive experience and facilities for pre-clinical, clinical, and research and development studies. (Section 7.3.3 and Appendix III). As an NBTF Association member located on the NBTF's doorstep, the UTSMC's nuclear medicine professional staff will stimulate the development of new products and direct pre-clinical evaluations, Phase I/II clinical evaluations, innovative imaging studies, and computer-assisted dynamic studies.

4.3.5 Contract Specialty Development

The NBTF will be positioned to provide a variety of specialty R&D on a contractual basis with industry and other institutional users of radionuclide-based technologies.

4.3.5.1 Specialty Radionuclide Development

The NBTF and the NBTF Association will have the expertise, staff, and facilities to offer the development of specialty radionuclides to the radiopharmaceutical industry. Candidates in this category include radionuclides of interest that have not been produced in quantity previously and could be used for biomedical research (e.g., ^{95m}Tc, ^{48}V) or very early stage clinical use candidates, such as ^{67}Cu and ^{97}Ru. Private communication with radiopharmaceutical industry leaders has indicated that scheduling time and other resource limitations at the radiopharmaceutical companies will make this NBTF service valuable to the industry.

Developmental work on new products and procedures for industry will be performed under specific contract with either commercial or research institutions. Services available will be target development, high purity separations chemistry, product yield optimization, enriched

target recovery procedures, excitation function measurements for product yield optimization, and custom formulation development for radiopharmaceutical products. The NBTF Association members have many years of expertise in these areas of development.

4.3.5.2 Analytical Methods Development

The NBTF staff and NBTF Association members also will offer analytical methods development on a contract basis. This service will develop analytical methods for new products and may investigate methods to improve the efficiency, ruggedness, precision, and accuracy of existing assays, particularly those that are currently problematical. Radio-HPLC, ion chromatography, gel electrophoresis, and gamma spectrometry techniques will be available, along with more traditional techniques.

4.3.5.3 Analytical Methods Validation

Validation of analytical methods is an integral part of GMP and GLP, and is currently receiving much attention by regulatory agencies. The NBTF and NBTF Association members will develop protocols and generate data to validate analytical procedures under specific contracts with the radiopharmaceutical industry. Typical validation characteristics which will be considered are accuracy, precision, specificity, detection limits, quantitation limits, linearity, and range. Since many analytical validations are time consuming and manpower-specific, it is expected that the pharmaceutical industry will be interested in contracting for this service.

4.3.6 Custom Irradiations

The NBTF will offer custom cyclotron irradiations to all qualified users of radioactive materials. Custom irradiations offered as a user service will be done on a contract basis, with confidentiality and proprietary rights reserved to the user, when requested. Charges for custom irradiation services will be based on one or more of the following criteria: units of activity shipped; hours of cyclotron time used; total integrated cyclotron beam current; radiochemistry manpower and facilities required; and the degree to which existing technology can be used. This service is intended to stimulate research and development, as well as training and education at other locations, by providing facilities and expertise not ordinarily available. We expect many institutions and commercial companies will use this service to help develop new products, new production techniques, and investigate higher energy reactions to improve the overall efficiency of radionuclide availability.

4.3.7 Customer Supplied Targets

The NBTF will contract to back-up radionuclide production for the commercial sector using targets and enriched target materials supplied by the customer. The product will be shipped either as unprocessed targets or as processed radiochemical grade product. The customer will be charged a competitive price based on a combination of beam time, integrated beam current, and required processing.

The NBTF will also provide (customer supplied) target irradiation services to universities, hospitals, government agencies and their contractors, and commercial organizations for development of new products and more efficient production techniques. When requested, the NBTF will provide technical assistance to the customer for target and radiochemistry improvements. The customer will be charged a combination of beam time, integrated beam current, and technical service assistance.

4.3.8 NBTF Supplied Targets

The NBTF will furnish standard or customized targets for production of specialty radionuclides (i.e., those products not under NBTF development or promotion) for those institutions involved in research and development on new radionuclides or improvements to existing products. The NBTF will assist any customer in the design, fabrication, and development of targets and technology leading to more productive nuclear reactions, improved thermal dissipation, and more efficient processing techniques. The customer will be charged according to the services they receive and the assistance they provide in the work. If the customer's objective is a proprietary investigation of a new radionuclide, the charge will be based on beam time and technical services. If, however, the customer's objective is a joint investigation of a new or improved product, then the actual expenses of the project will be shared.

4.4 Priorities Among Production of Research Radionuclides and Proprietary Work

The principal function of the NBTF is the production of research radioisotopes for North American research institutions. A corollary function is research on radionuclide production and applications. At some point, such activities become product development.

> ***The NBTF will not undertake product development. However, as indicated above and elsewhere, the NBTF will accommodate proprietary research for industry under appropriate contractual arrangements.***

It is a truism that commercial operations push out research. Therefore, to avoid abrogating

the principal mission of the NBTF — production of research isotopes — we will develop a set of rules to guide the acceptance of proprietary research. A clear option is to submit all proposals for proprietary research to the Scientific Advisory Committee of the NBTF and NBTF Association for approval within the context of the mission and goals of the institution.

4.5 Education, Training, and Technology Transfer

Education, training, and technology transfer are discussed fully in Section 8.0, and additional information is provided in several of the Appendices (IV, VI, VII, VIII). These, too, are products and services of the proposed NBTF, and particularly the NBTF Association's universities and medical centers.

5.0 ENVIRONMENTAL, WASTE, SECURITY, REGULATORY LICENSING, AND LIABILITY ISSUES

5.1 Environmental Compatibility of the Nike Site with its Neighbors

The research and development, production, and educational activities foreseen for the Nike Site are fully compatible with present and future agricultural, residential, business, and recreational activities located nearby. The accelerator-based technology and related activities of the NBTF and the adjacent commercial facility will not pose any unusual hazards to nearby residents, visitors, or employees. The anticipated activities have no qualitative difference from commercial facilities located in other parts of the country and R&D activities that are routinely conducted on major university campuses and health science centers.

Currently, the 20-acre Nike Site is surrounded by farm and ranch land. One private residence is located approximately 500 yards east of the site, with another three or four residences within a half mile. All nearby residences are on the east side state highway FM 2164. The Nike Site is located on the west side of FM 2164. By comparison, the Du Pont Merck radiopharmaceutical plant, located in North Billerica, Massachusetts north of Boston, is surrounded by suburban residential areas.

5.2 Air Pollution

We anticipate no significant generation of air pollutants by the NBTF, the commercial facility, or the Advanced Medical Imaging Center. NTRI will place one or more air monitoring stations at the site and use meteorological data from the Denton Municipal Airport, located approximately six miles southwest of the Nike Site, to establish a baseline pre-construction and pre-operation database. Acquired data will include standard meteorological measurements, including airborne particulates, visibility measurements, and radiological air monitoring. Because the site will not generate a high amount of traffic, and electrical energy to the site will be supplied by municipal utilities, it is expected that ozone, sulfur oxides (Sox), nitrogen oxides (Nox) will not be generated and therefore will not be measured.

5.3 Environmental Impact

Upon approval of funds for further study, and if required, NTRI will initiate an environmental impact assessment study by a third party, consistent with existing local, state, and federal laws. State law requires environmental assessment in the case of highway

modifications, and in this case none are planned. However, federal law requires an environmental assessment at a site which is subject to "any major federal action," such as a construction loan and initial operating assistance for the NBTF. Federal grants and contracts also will support some of the research performed at the NBTF. We are confident that the third party's, study, if required, will result in a "finding of no significant impact" (FONSI).

5.4 Security

No special security measures other than controlled access to the site will be required. Currently, a double security fence surrounds that portion of the Nike Site proposed for the NBTF and the commercial facility. The proposed Advanced Medical Imaging Center would be located apart from this higher security area but within an existing single security fence.

Moderate security practices consistent with those used in industry will be applied for the commercial facility, the cyclotron vault, and radiological safety areas of the NBTF facility. Hospital level security will typify the Advanced Medical Imaging Center. Collectively, the proposed activities at the Nike Site will pose no unusual security demands beyond that typical of industrial R&D operations (commercial facility and NBTF) and a university medical center (imaging center).

The astronomy teaching activities currently housed at the Nike Site would be moved to another site, approximately eight miles southwest of the Nike Site on an entirely different tract of land.

5.5 Hazardous Waste Generation, Storage, and Disposal

Virtually all scientific research, product development, technical refinement, services, and manufacturing activities create some form of hazardous waste in liquid or solid form. However, the R&D activities envisioned for the NBTF will produce relatively small amounts of hazardous waste materials, just as current R&D activities on the University of North Texas campus in Denton and most other major university campuses do not produce large amounts of hazardous waste. The commercial operation will create hazardous waste materials as well, but no more so than similar licensed industrial facilities currently located in suburbs of Boston, Chicago, and St. Louis.

Regulatory issues stemming from the handling, retention, and eventual disposal of solid and liquid radioactive waste are governed by the *Texas Regulations for the Control of Radiation (TRCR): Volumes G, L, and R.* All radioactive wastes produced by the NBTF, the commercial facility, and the Advanced Medical Imaging Center will fall into the *low-level radioactive waste* category. Producing and processing radioisotopes at the commercial

facility and the NBTF will generate a certain amount of *low-level*, solid radioactive waste. Most of this waste will be in the form of used laboratory expendables, such as latex gloves and absorbent paper used to protect laboratory counter tops from direct exposure to spilled materials. These materials will be compacted and disposed of through the usual commercial channels used by universities, medical institutions, and industrial users of radioactive materials.

Between scheduled waste pickups, compacted materials containing longer-lived radioisotopes will be temporarily retained on-site in a specially designed, low-level waste facility. The low-level radioactive waste holding facility on-site will serve in a waste reduction capacity and will greatly reduce the amount of radioactive waste to be removed to a permanent radioactive waste disposal facility.

The *Texas Regulations for the Control of Radiation Part 21, Appendix H* permit a limited amount of certain radionuclides to be disposed of by transport to a Type I municipal waste facility. Generally, these radionuclides have half-lives of less than 300 days. TRCR Part 21.1304 contains a list of those radioisotopes that are either exempt or allowed to be transported to a Type I municipal solid waste site for disposal as defined in Section 3(15) of the Solid Waste Disposal, Health and Safety Code Chapter 361. This enlightened Texas regulation gives the NBTF and the commercial facility a distinct advantage compared to locations in many other states where landfill burial of radioactive waste exhibiting *any* detectable level of radioactivity is forbidden.

The operation of the NBTF and the commercial facility will include the chemical separation of radioisotopes. This may lead to the production of some *mixed hazardous waste*; i.e., a mixture of low-level radioactive materials, water, organic solvents, and inorganic salts. Common practice is to hold such materials for a period of time on-site until the radioactive isotopes decay to stable isotopes, whence the materials can then be moved off-site for disposal by commercial waste handlers.

The technology also exists to greatly concentrate the volume of liquid waste materials by evaporating the non-radioactive liquid portion of waste and incinerating the non-radioactive volatile organics. The NBTF and its commercial affiliate will have access to this technology and other waste reduction and disposal technologies through the Los Alamos and Sandia National Laboratories' industrial applications offices, which assist industry with technology transfer, licensing, and contracting services.

A fully instrumented, continuously monitored mixed waste treatment and holding facility will be constructed on-site. This facility will be adequately bermed or contained to ensure complete containment in the event of a catastrophic failure of the holding tanks, thereby preventing inadvertent release to the environment.

5.6 Other Hazardous Materials

For hazardous materials other than waste, a small chemical storage facility will also be constructed to hold organic solvents and bottled gasses prior to their use in the facility, similar to existing facilities on the UNT campus in Denton and other such R&D, teaching, and hospital facilities.

5.7 Waste Minimization Program

The combined facilities will establish a state-of-the-art *Waste Minimization Program.* Waste minimization (Wmin) is the reduction, to the extent feasible, of hazardous waste that is generated prior to treatment, storage, and disposal of the waste. Waste minimization includes any source reduction or recycling activity that results in either (1) reduction of the total volume of hazardous waste, (2) reduction of toxicity of hazardous waste, or (3) a combination of both.

The goal of both the commercial facility and the NBTF will be to reduce non-hazardous and hazardous solid and liquid waste and the by-production of radioisotopic and chemical waste to the absolute minimum technically achievable. This approach is both environmentally sound and economically attractive. The less waste produced, the less the amount and cost of commercial disposal, particularly with respect to hazardous waste.

NTRI and AITI have initiated preliminary discussions concerning waste minimization technology transfer with the national laboratories, including LANL and SNL. The DOE is currently establishing state-of-the-art waste minimization demonstration projects at two reactor sites in Washington (FFTF) and Idaho (NPR). AITI's commercial facility could become the first commercial demonstration project for industrial waste minimization, approaching zero net waste production. We would hope to make the NBTF the leader in this technology in the public sector.

5.8 Federal and State Regulatory Requirements for Radiation

The Nuclear Regulatory Commission (NRC) regulates facilities that handle "special nuclear materials;" i.e., nuclear fuels and weapons grade uranium, thorium, and plutonium. The NBTF and the commercial facility will have no such materials, and thus are not a *fixed nuclear facility*, which is defined by the NRC as an installation that handles special nuclear materials.

Particle accelerators, such as those to be installed in the NBTF and the commercial facility are specifically exempted from NRC regulation, but such facilities *are* subject to state

licensure. Likewise DOE regulations do not apply to non-DOE accelerator operation, even though DOE funding may support part of the activity (DOE Accelerator Safety Order, 1991; Appendix D).

Production, use, handling, retention, and disposal of radioisotopic materials, such as those that will be produced by the commercial facility and the NBTF, are regulated through state agencies. The activities of NTRI's accelerator center will be licensed through the Texas Department of Health's Bureau of Radiation Control and the previously mentioned TRCR regulations. Both UNT/NTRI and AITI have considerable experience with the licensing of accelerators. Conversations with the leadership of the state agency have indicated that there will be no special obstacles in licensing the proposed activities.

The procedures outlined in *TRCR Regulatory Guide 3.13*, titled *Guide for the Preparation of License Applications for the Use of Accelerators to Produce Radioactive Material* will be observed in the preparation of applications for accelerator licensing and accelerator registration by the NBTF and the commercial facility. Both facilities will also be licensed for waste handling by the same state agency. These facilities, which will produce radioisotopes destined for incorporation into commercial radiopharmaceutical products or experimental materials used with human subjects, will also be licensed by the U.S. Food and Drug Administration (FDA).

UNT/NTRI, UTSMC, and AITI have years of experience in handling radioisotopes and cooperating with the appropriate regulatory agencies. For example, at UNT and UTSMC the universities' Radiation Safety Committees oversee the procurement, use, and disposal of radioactive materials.

The NBTF, the commercial facility, and the Advanced Medical Imaging Center will jointly establish a comprehensive oversight structure, based on contractual arrangements between the three entities. Each will employ a senior radiation safety officer and technical staff to monitor and enforce radiation safety practices and regulations. The radiation safety committees of the three entities will have the ultimate responsibility for the safe operation of the center. The committees shall consist of the following persons:

Radiation Safety Officer (all entities)
Health Physicist (all entities)
Accelerator Operations Supervisor (NBTF and commercial facility)
Radiochemistry Operations Supervisor (all entities)
Facility Director of Design (all entities)

The three committees (for the NBTF, Advanced Medical Imaging Center, and the commercial facility) will meet both individually and jointly at least four times per year and will review any reports on hazardous conditions. Any changes or additions to the guidelines

set forth in the *Radiation Safety Manual* of each entity will first be reviewed and approved by the appropriate committee.

The radiation safety program will also include organized courses in radiation safety and continuous in-service training for all personnel. In addition, employment requirements and incentives also will be used to promote the safety program.

5.9 Radiological Water and Air Monitoring Systems

Guidelines for water and air effluent monitoring of radioactivity are established by the EPA and OSHA, requiring monitoring of water and air discharges to certify that the radioactive content is within the range of admissible amount for discharge. In the event the levels rise above allowable limits at any time in a given space, that operational unit must be isolated such that no discharge occurs until the radiation levels have decayed to a permissible level.

Air flow ionization chambers will be used to monitor the radiation level of air discharge. Both sewer and groundwater liquid samples will be periodically taken for assay using sensitive, low-level scintillation counter systems. A stack emissions sampling and monitoring program will be established to meet regulatory standards.

5.10 Regulatory Environment and Compliance Measures for Radiological Safety

Each of the proposed entities — the NBTF, commercial facility and Advanced Medical Imaging Center — will be separately licensed and accountable.

All regulatory controls and guidance originate in the following federal and state documents:

Federal:

1. *National Emission Standards for Hazardous Air Pollutants (NESHAP): Code of Federal Regulations Title 40 Part 61, Subpart I.*
2. *A Guide for Determining Compliance with the Clean Air Act Standards for Radionuclide Emissions from NRC-Licensed and non-DOE Federal Facilities: REV 2 EPA 520/1-89-002 (October 1989).*
3. *Water Pollution Control Act* (WPCA).
4. *Pollution Prevention Act of 1990.*
5. *Occupational Safety and Health Act* (OSHA).

State:

1. *Texas Radiation Control Act; Article 4590f, Vernon's Texas Civil Statutes.*
2. *Texas Regulations for the Control of Radiation* (TRCR); *Vols. G, L, and R .*
3. *Texas Clean Air Act.*
4. *Texas Water Code.*
5. *Texas Medical Waste Management Regulations.*

The design and operational protocols of the proposed NBTF and associated facilities will be developed to assure a safe working environment, as well as to assure the safety of the public at all facilities. The efficacy of the design and operational protocols will be evaluated on a continuing basis through air and water monitoring, both internal and external to the facility and in the effluents resulting from operations.

Guidelines have been established by OSHA for protection in the workplace, and guidelines for the protection of the general public have been developed by the EPA. These guidelines are reflected in Texas regulatory documents which require the monitoring of water and air discharges to certify that the radioactive content is below the permissible amount for discharge or occupational protection.

Compliance with EPA regulations requires the use of stack monitoring, site meteorological data, and the EPA-developed COMPLY code to demonstrate conformity with the permissible radioactive emissions. During the pre-construction and construction phases of the proposed project, site specific meteorological and demographic data will be collected to permit demonstration of compliance during facilities commissioning and eventual operation.

In addition to occupational radiation exposure monitoring of the NBTF staff, monitoring of the workplace environment is provided to ensure that access to radiation areas may be controlled. The fixed radiation monitoring systems will include measurement of neutron, beta, and gamma radiation in the target areas and beta and gamma radiation in the processing facilities. Fixed instrumentation, air monitoring devices and filtration equipment will be capable of:

a. Detecting environmental radiation levels that would result in exposures of ten percent of the annual limits in unrestricted areas of the facility;

b. Accurately measuring instantaneous releases of airborne activity in the target and processing areas; and

c. Integration of instantaneous releases of airborne activity to determine total activity released in accident situations in the target and processing areas.

Detection sensitivities and efficiencies will be determined using standard calibration techniques and appropriate sources. Each area monitor will also be equipped with visual/audible alarms indicating radiation levels in excess of compliance limits.

The processing facilities will be designed to provide single point release of all facility air through ducting to a single stack. HEPA filtration will be used to remove particulates from this effluent stream and stack gases will be monitored using EPA Method 114. It is anticipated that air flow ionization chambers for particulate matter and scintillation detectors for gaseous emissions will provide appropriate selectivity, sensitivity and dynamic range for this task. Any detection of excessive airborne radiation will activate controls to isolate and close-in the room with the release to minimize releases to the environment. Facility air discharge data will be logged electronically to provide the required documentation of the radiation levels.

The radiation detection systems will also be interfaced with the facility annunciator and control systems. The annunciator system will operate in a surveillance mode and provide both a visual and audible indication if dangerous or potentially dangerous conditions occur. Interfacing with the accelerator control system provides a means of terminating accelerator operation in the event of an accident condition in the target area that may result in the release of airborne radiation or produce excess radiation levels exceeding compliance limits.

Monitoring strategies for both air and water emissions will be developed and included as part of the facility licensing process. These plans will be developed and submitted along with the necessary documentation required by the Texas Department of Health's Bureau of Radiation Control.

5.11 Regulatory Environment and Compliance Measures for Waste Handling and Disposal

5.11.1 General Requirements for Waste Handling and Disposal

Unless otherwise exempted, a licensee shall transfer waste for disposal, discharge, or decay only in accordance with any the following procedures:

1. By transfer to an authorized recipient as provided in TRCR Parts 21 and 44 of these rules, or to the U.S. Department of Energy; or
2. By decay in storage; or
3. By release to the environment within the limits given in TRCR Parts 21.301/302 and NESHAP 40 CFR Part 61 Subpart I; or
4. As authorized pursuant to TRCR 21.1003 or 21.1004.

Further, in accordance with TRCR Part 21.1304, a listing is given of those radioisotopes which are either exempt or allowed to be transported to a Type I municipal solid waste site for disposal as defined in Section 3(15) of the Solid Waste Disposal Act, Health and Safety Code Chapter 361.

5.11.2 Discharge by Release into Sanitary Sewerage (TRCR Part 21.1003)

A licensee may discharge licensed material into sanitary sewerage if each of the following conditions is satisfied:

1. The material is readily soluble, or is readily dispersed biological material in water; and
2. The quantity of licensed radioactive material that the licensee releases into the sewer in one month divided by the average monthly volume of water released into the sewer by the licensee does not exceed the concentration listed in Table III of Appendix 21-B; and
3. If more than one radionuclide is released, the following conditions must also be satisfied:
   i. The licensee shall determine the fraction of the limit in Table III of Appendix 21-B represented by discharges into sanitary sewerage by dividing the actual monthly average concentration of each radionuclide released by the licensee into the sewer by the concentration of the radionuclide listed in Table III of Appendix 21-B in TRCR; and
   ii. The sum of the fractions for each radionuclide required by 21.1003 (a)(3)(i) does not exceed unity; and
4. The total quantity of licensed radioactive material that the licensee releases into the sanitary sewerage in a year does not exceed 5 curies (185 gigabecquerels) of hydrogen-3, 1 curie (37 gigabecquerels) of carbon-14, and 1 curie (37 gigabecquerels) of all other radioactive materials combined.

   Note: Excreta from individuals undergoing medical diagnosis or therapy with radioactive material are not subject to the limitations contained in 21.1003(a).

5.11.3 Commercial Facility Liquid Wastes

Liquid radioactive waste resulting from the processing of accelerator products or from the washing down of hot cells or other decontamination procedures will be contained in storage tanks outside the commercial radioisotope facility. Three storage tanks with a combined capacity of 15,000 gallons will be installed for the purpose of liquid radioactive waste retention. It will be possible to route the liquid waste to any one of the three tanks and also

to pump from one tank to another. This allows different levels of activity and/or different isotopes to be retained separately. The outlet from the tanks feeds into the sanitary waste system via a locking valve, the key to which will be held by the facility's radiation safety and security departments. Samples from each tank will be continuously assayed by the Radiation Safety Office to ensure activity levels do not exceed allowable limits. Results of all assays will be kept on file. The radioactive content of the effluent will be assayed using a sensitive low level scintillation counting system.

The purpose of such holding tanks is to provide for on-site decay and dilution of the effluent stream to levels of activity where it is permissible to dispose of the waste through discharge into the sewage system. It is intended that this series of tanks will be used to contain successively lower concentrations of radioactive elements. It will be possible to further reduce the concentration of the radioactivity in the effluent through dilution, and this approach will be used if possible. It is anticipated that the capacity of the storage tanks will be sufficient to permit the holding of radioactive wastes until decay to negligible levels has taken place and that it will not be necessary to discharge the tanks more than once every three or four months. The tanks will be housed in a containment facility to prevent release to the environment in the event of a total liquid release accident.

5.11.4 NBTF Liquid Wastes

A liquid waste handling facility essentially identical to that described above, will be constructed and operated to serve the NBTF. Identical procedures will be used as mandated by the appropriate regulations.

5.11.5 NBTF and Commercial Facility Solid Wastes

The solid wastes from NBTF and operation of the commercial facility are anticipated to be from two sources. The first is from the activation of target system components. These components are designed to be reusable after suitable decay while in retention. Components that are not reusable will be allowed to decay during retention to a level where disposal through transfer to a low-level burial site or to a normal landfill operation is possible. The second source of solid waste is the disposable protection clothing worn in the processing facility. These items will be assayed, bundled and/or compacted, and disposed of by methods appropriate to the level of contamination.

5.11.6 Mixed Waste

It is anticipated that some mixed waste will result from the processing of both production and

R&D targets. Specific waste handling protocols for this waste will be developed as part of the efforts to develop efficient and effective processing methods. In general the approach will be to minimize the production of mixed waste and to allow on-site decay of the radioactive component prior to disposal of the hazardous chemical component. This strategy will require identification and assay of the radioactive components using commercially available analysis equipment.

5.11.7 Disposal Costs

Waste disposal costs are a component of the production costs of the radiochemicals and thus must be controlled. The proposed approach to waste minimization and handling will be evaluated both for its efficacy and its economic impact on the operations of the facilities as part of a continuous process improvement plan to be developed.

5.11.8 Treatment by Incineration (TRCR Part 21.1004(a))

A licensee may treat licensed material by incineration only in the amounts and forms specified in 21.1304(a) or as authorized by the Agency. Disposal by incineration is not expected to be a part of either the NBTF or the commercial facility's radioactive waste disposal program.

5.12 Radiological Licensing Costs

The Texas Department of Health's Bureau of Radiation Control Licensing/Registration Fee Schedule (TRCR Part 12), dated January 1, 1995, lists the following fees that would be required separately by the NBTF and the commercial production facility:

Facility/Operation	Annual Fee
1. Accelerator Registration	$3625.00
2. Broad License	$4900.00
3. Calibration/Reference (exempt) Sources	$ 300.00
4. Demonstration/Sales	$ 905.00
5. In-vitro Use of RAM	$ 335.00
6. Manufacturing/Commercial Distribution	
i. Processing of Loose (dispensable) RAM	$11540.00
7. Medical Therapy (unsealed sources)	$ 535.00
8. Radiopharmaceutical Manufacturing	$4965.00
9. Research and/or Development	$ 705.00
10. Tracer Studies(non-well)	$ 1545.00
TOTAL:	$29,355.00

Stipulations in the licensing procedures include the following:

A. Payment for annual fees must accompany the application for the germane license or registration, which fees are non-refundable.

B. Subsequent annual fees must be submitted prior to the license or registration expiration date.

C. "The annual fee of a Certificate of Registration for radiation machines and services shall not exceed $4000.00 per year" [12.11(b)(3)].

5.13 Liabilities, Insurance, and Taxes

The NBTF will be operated as a not-for-profit entity but will carry appropriate forms of insurance, including liability insurance, casualty insurance, and errors and omissions insurance. Standard employee insurance, plus commercial coverage will be provided through NTRI if NTRI manages the NBTF. NTRI currently carries directors and officers liability insurance. Because the commercial facility will process and distribute research radioisotopes

produced by the NBTF cyclotron under contract, AITI's insurance coverage will figure into moderating the liability by the NBTF. Both the NBTF and AITI will adjust the protection limits of their policies and add additional coverage as the amount and types of activities change.

The commercial production facility, managed by AITI, will carry all necessary forms of liability insurance appropriate to its various activities. Currently, AITI is covered through standard commercial insurance and carries product liability insurance in the amount of $2 million. Directors and officers liability insurance, errors and omissions, business interruption, casualty insurance, and accident insurance are also carried. The levels of coverage and premiums will be adjusted in relation to gross revenues and gross salaries. Operational insurance regarding accidents, shipping of radioactive materials and accidental loss of products is covered under a separate policy and is directly related to gross revenues.

Because the NBTF will be managed as a not-for-profit, 501(c)(3) corporation, its research and educational activities will be tax-exempt. However, production research radioisotopes at the NBTF will be pursued to provide a revenue stream to help sustain the facility. These products will be taxable and will generate tax revenues.

AITI will operate as a for-profit, commercial venture, which will generate tax revenue as would any other corporation in the private sector. Any development catalyzed by the RPF and the NBTF will increase the tax base.

The proposed Advanced Medical Imaging Center will be operated by the University of Texas Southwestern Medical Center at Dallas and as such will be a not-for-profit, tax-exempt entity.

5.14 Radiation Safety and ES&H Training Program

The University of North Texas currently operates a radiation safety training program for faculty, students, and employees. In addition, students in the natural sciences and engineering technology may enroll in an organized course in radiation safety and receive academic credit for the course. The radiation safety course is cross-listed among the science departments, so that a student may enroll in his own department, yet get credit for a highly interdisciplinary course of study that applies directly to his or her graduate degree plan requirements. The radiation safety course and other courses in nuclear engineering technology are also offered currently via distance learning technology to a remote site.

This base, plus the considerable personal experience of the principals involved in this study, will form the foundation of a an Environmental Safety and Health (ES&H) training program. The intent of this program is to ensure that all permanent employees, students, postdoctoral

fellows, visiting scientists and technical personnel, plus visiting industry professionals possess adequate knowledge to work and learn at this facility safely and efficiently. Below are the chief components of such a training program:

General employee orientation
Hazardous material communication (e.g., MSDS sheets)
Waste minimization/reduction
OSHA safety guidelines/procedures
Emergency evacuation procedures
Fire safety/response
Radiation safety/exposure effects
Chemical inventory procedures/program
Accelerator safety
Air and water monitoring programs
Hazard and accident reporting/prevention

We previously studied the feasibility of using assets of the Superconducting Super Collider (SSC) to construct a commercial radioisotope production facility based on the DTL linac section of the SSC linac. A draft radiation safety and procedures manual was prepared in that study and is available as a starting point for the NBTF manual. In addition, extensive training programs and instructional materials have been developed at the DOE national laboratories. These will be valuable assets in the development of training programs appropriate for the NBTF.

6.0 MANAGEMENT OF THE NBTF AND ASSOCIATED FACILITIES

6.1 Model Management Structures

We have considered a number of alternative management structures, ranging from state ownership and operation (such as the Missouri University Research Reactor center) to not-for-profit corporate ownership and operation (such as SRI International), to for-profit corporate ownership and operation (such as Bell Laboratories). A variety of models of public/private partnerships exist. These include for-profit consortia, such as the Microelectronics and Computer Technology Corporation (MCC) and the Semiconductor Manufacturing Technology initiative (SEMATECH). Examples of not-for-profit consortia are NSF's Industry/University Cooperative Research Centers (I/UCRC) at the national level and the Houston Advanced Research Center (HARC) at a regional level.

Still other organizational models are those related to large, multi-partner university consortia, such as the Universities Research Association (URA), which oversees Fermilab, and the Southern Universities Research Association (SURA), which oversees CEBAF (Continuous Electron Beam Accelerator Facility). The Oak Ridge Associated Universities (ORAU) is yet another multi-university organization tied to a specific facility, but with initiatives that reach beyond that facility. However, none of these organizations quite fits the mix of products and services we foresee for the NBTF and its not-for-profit academic associates and its for-profit corporate affiliates.

Perhaps the most relevant model organizations are MURR and HARC. The Missouri University Research Reactor (MURR) is probably the most successful state-owned nuclear reactor center. It has operated successfully for nearly 30 years with only a partial subvention in its yearly budget by the State of Missouri. MURR is a university facility, as opposed to a departmental facility, that reports to MU's central administration. Its operation, oversight functions, facilities enhancement, and programs are reviewed and approved by a Reactor Advisory Committee consisting of members of MU departments, MURR itself, other University of Missouri System campuses, and outside members. This committee is advisory to the MURR director. MURR's operational structure provides for a wide range of activities, including research isotope production, similar to that envisioned for the NBTF. MURR is functionally organized into a reactor operations group, a series of technical support groups, and four programs (biomedical, neutron materials, nuclear analysis, reactor engineering — each with several sub-groups).

HARC is a not-for-profit 501(c)(3) consortium of Texas universities and other collaborating entities with separate facilities located in Houston, Texas. It has survived and grown in scope through the entrepreneurship of its leaders and the continuing generosity of a Houston-

area developer who donated the land and construction funds for its first buildings. HARC's R&D mission and its inter-institutional network has similarities to the mission and membership of the structure we propose. HARC's governance includes a prestigious board of directors that includes the presidents of each of the four original founding universities. The President of HARC is assisted by a President's Advisory Council that also includes well-connected people. The functional organization consists of a series of centers and laboratories, each headed by a director. In addition to the president, the administration includes a vice president for business affairs, a vice president for research, a chief scientific officer, a chief technical officer, and other directors or managers for development, communications, contract administration, personnel, and finance.

6.2 Fiscal Realities of the Proposed NBTF and Rationale for Associated Facilities

Our financial and market analyses indicate that a **stand-alone** National Biomedical Tracer Facility (NBTF) could not be self-sustaining as required by the conditions of the DOE solicitation for proposals and supplementary information issued by DOE.

Our analyses also suggest that a **stand-alone** NBTF could not fully address the current and future needs of the nuclear medicine community as addressed in previous studies and in the recently-released report of the Institute of Medicine (IOM) on *Isotopes for Medicine and the Life Sciences*. However, our studies also indicate the following:

> ***If the NBTF core facility is structured as part of a center that also contains a state-of-the-art commercial production facility and an isotope user facility (the proposed Advanced Medical Imaging Center), the NBTF can be both self supporting and meet the needs defined in the IOM report.***

Thus, the management structure we propose for the NBTF is based on fiscal realities that require a mix of mutually supporting facilities that achieve some economy of scale in certain areas such as radiochemical processing and that leverage more support from the private sector.

6.3 Proposed Management Structure

We propose that the NBTF operate as a key component of the ***NBTF Core Facilities***, located in North Central Texas. The other key component of the proposed Core Facilities is a privately-funded, state-of-the-art commercial production facility already in the initial stage of development by Advanced Isotope Technologies, Inc. (AITI). The Core Facilities would be further enhanced by the addition of an Advanced Medical Imaging Center, also independently funded and operated by the University of Texas Southwestern Medical Center.

We also propose the formation of an National Biomedical Tracer Facility Association (NBTF Association), which would tie together the NBTF located in Texas and affiliated centers of excellence elsewhere in North America.

The new NBTF Association, open to both the public and the private sector, would address all isotope related issues raised in the IOM report. The Association would be both a forum for the discussion of such issues and an instrument for solving problems through the proposed NBTF Core Facilities in North Texas and the collaborative efforts of its individual members. The IOM report suggested the formulation of a *national isotope policy*. The NBTF Association we propose could be a step toward this goal. We foresee the charter membership of the NBTF Association as including the members of this consortium, but the Association would be open to all other responsible entities who wish to join.

As shown in Figure 6.3-1, the NBTF Association, would unite the NBTF Core Facilities located in North Central Texas with multiple centers of excellence elsewhere. Figure 6.3-2 details the facilities proposed for NBTF Core Facilities. These include the NBTF, the commercial production facility, and the proposed Advanced Medical Imaging Center. The North Texas center could also encompass other for-profit or not-for-profit facilities, such as a regional radiopharmacy or a training center operated by a community college or state technical college.

The NBTF would be a division of NTRI, the not-for-profit corporate affiliate and technology transfer arm of the University of North Texas. The director of the NBTF would be appointed by the executive director of NTRI and ratified by the NBTF Association and NTRI's boards of directors. NTRI is suggested as the NBTF manager because it is an existing, corporate entity set up to facilitate R&D and bridge the gap between the not-for-profit sector and technology-based industries. Alternatively, a new, not-for-profit corporation could be founded, or the NBTF Association could be incorporated to manage the NBTF.

We are not in favor of state management without a state appropriation to assist in supporting the center. A variety of state-mandated regulations would likely hamper operations; e.g., unwieldy purchasing and sales requirements would retard production and timely delivery of research isotopes to users.

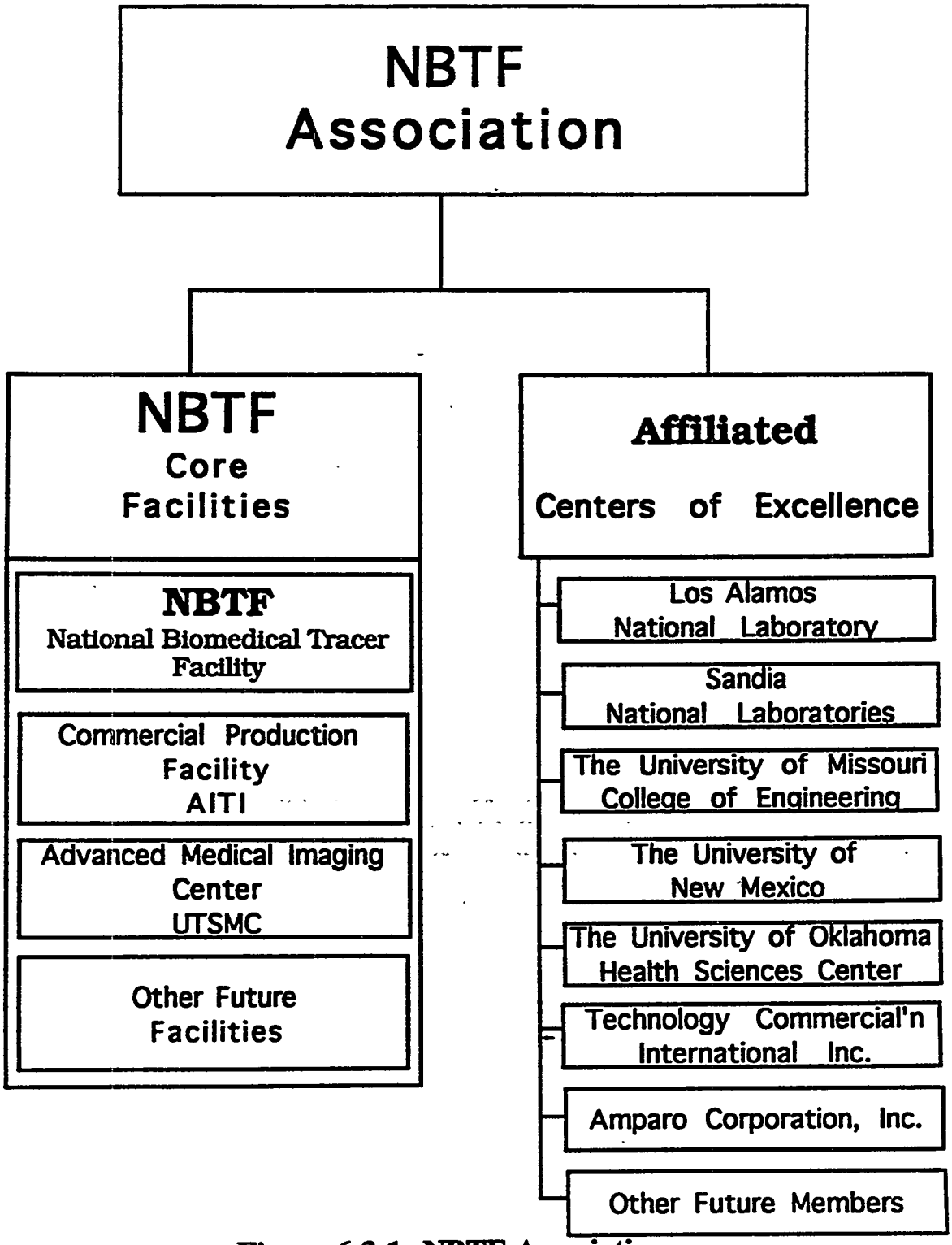


Figure 6.3-1 NBTF Association

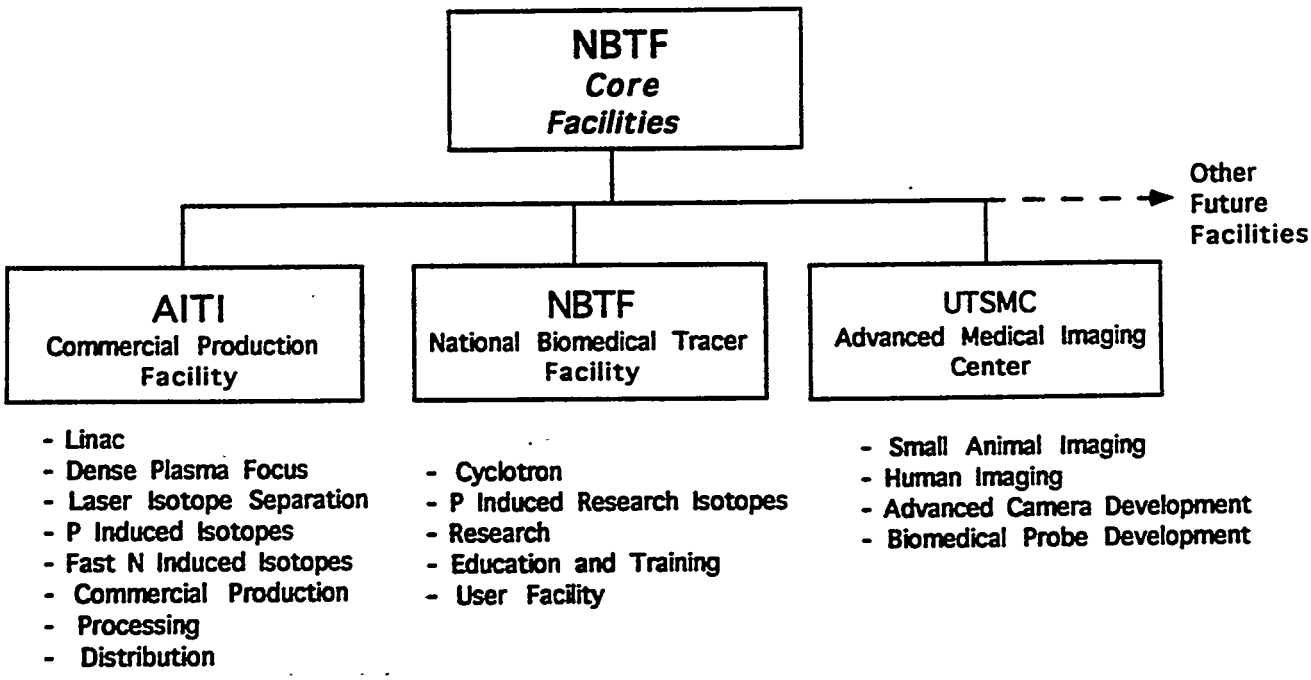


Figure 6.3-2 NBTF Core Facilities

6.4 Operational Management of the NBTF and its Affiliates

As noted elsewhere, the NBTF and the proposed commercial production facility would share some operational functions through mutually supporting *contractual* arrangements. For example, the cyclotron would provide a high intensity beam to back up the linac, a businesslike contractual arrangement that would provide an additional revenue stream to help sustain the operations of the cyclotron-based research and educational unit. As recommended in the IOM report, *Isotopes for Medicine and the Life Sciences*, high activity research isotopes produced by the cyclotron would be processed by the commercial operator under contract with the NBTF. Other functions, such as radiological safety, waste management/handling, QA/QC, product shipping, etc., also could be shared under specific contractual arrangements between the for-profit commercial company and the NBTF. Quality assurance to guarantee Good Manufacturing Practice (GMP) in the production of commercial radioisotopes and Good Laboratory Practice (GLP) and/or GMP in the production of research isotopes also could be shared through reciprocal contracts to serve both the NBTF and the commercial operator.

> **All interactions between the NBTF, the commercial facility, the imaging center, and other affiliates at the North Texas site comprising the NBTF Core Facilities would be through standard business contracts with appropriate insurance protection and performance guarantees.**

The administration and fiscal support of each facility would be entirely separate, since the sources of revenue would be generated through different channels. NTRI would provide fiscal, legal, and other administrative assistance to the NBTF through its existing infrastructure and that of the University of North Texas.

Figure 6.4-1 provides a sketch of how the relationship of the commercial operation and the NBTF might be structured. We emphasize that this is *merely* a sketch that is subject to extensive further development. Such an organization will have to be clearly defined through strict contractual arrangements; otherwise, the commercial side might tend to push out the production of research isotopes and the other public services for which the NBTF is intended. Further study is also necessary to identify legal questions and federal regulations that would affect the NBTF and the NBTF Association. Nevertheless, if the NBTF must generate sufficient revenues to be self supporting, its operations must be integrated with the commercial production center and other on-site affiliates to meet the requirement for self-sufficiency.

FUNCTIONAL RELATIONSHIPS BETWEEN NBTF AND AITI
(Substantive Interactions are through Standard Business Contracts)

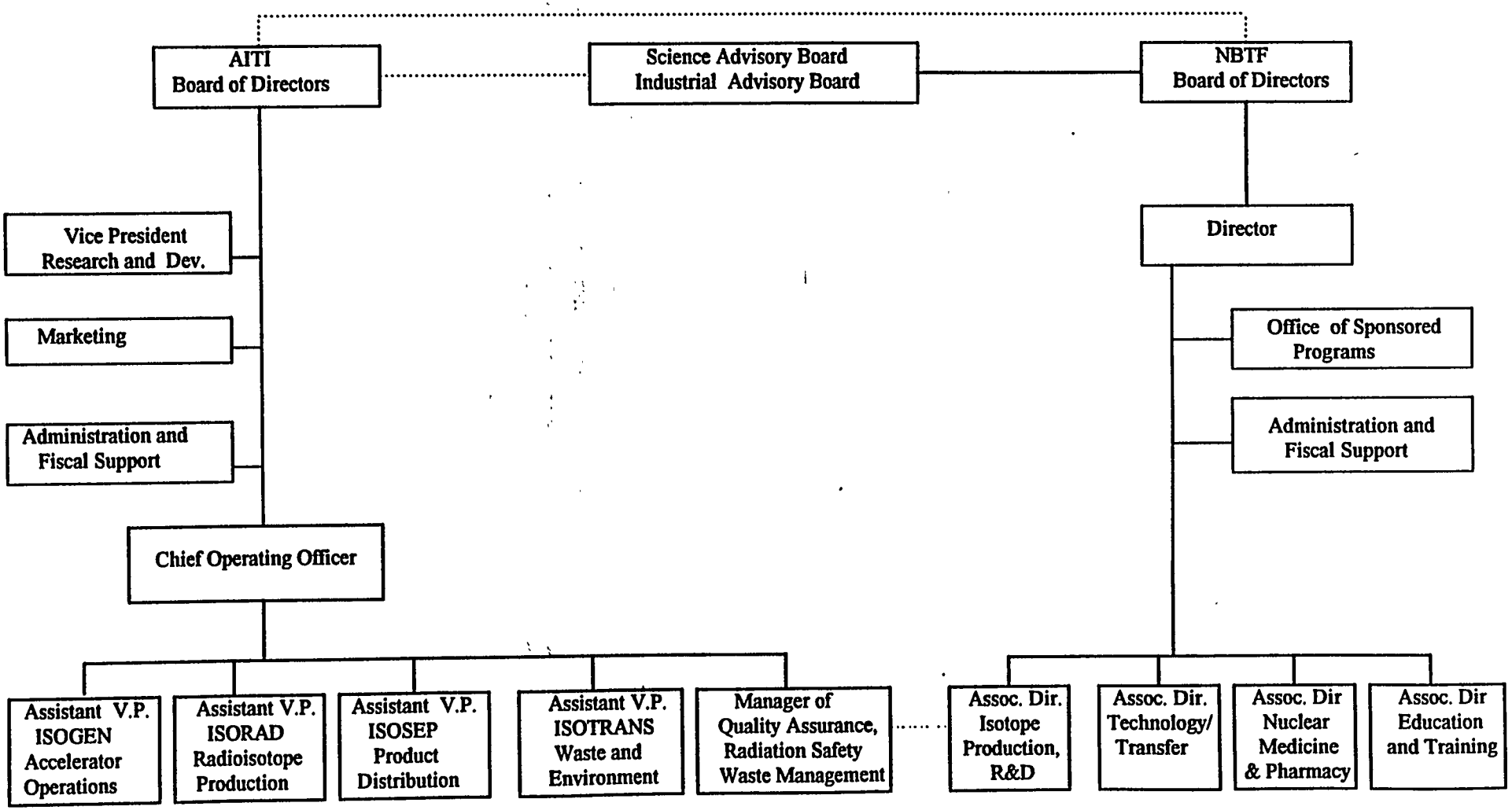


Figure 6.4-1 Operational Structure

Operational management of the NBTF would be directed by an executive director, assisted by specialists that provide operational support in the areas of accelerator operations, targetry, radiochemistry, etc. The director and scientific staff members would be full-time employees of the NBTF, but those holding the appropriate terminal degrees would be eligible for joint faculty appointments to the graduate faculties of UNT, UTSMC, and other universities of the Association, as appropriate.

6.5 Oversight and Advisement

The boards of directors of both the NBTF and the commercial operation would be advised by a **Science Advisory Committee** appointed by the NBTF Association. The Science Advisory Committee's membership would be drawn from the nuclear medicine community and related interest groups, including appropriate federal agencies. The Science Advisory Committee would play a strong role in determining the direction of research performed at the NBTF and the type of research isotopes produced. In parallel, the boards of directors would also be guided by an **Industrial Advisory Committee** appointed by the NBTF Association and made up of members of the radiopharmaceutical industry, radiopharmaceutical distributors, and health organizations.

6.6 Technology Transfer

A strong Technology Transfer Division in the NBTF will ensure timely transfer of technology from the R&D stage to commercial product development and manufacture by industry. The most relevant, existing technology transfer program is that of the Tri University Meson Facility (TRIUMF), Canada's national research center for sub-atomic physics. TRIUMF, a consortium of Canadian universities, funded principally by federal dollars, operates a 500 MeV cyclotron and currently produces commercial and research radioisotopes in partnership with Nordion of Canada, which also operates other cyclotrons at the site. Although most research done at TRIUMF is basic in nature, a number of commercial spin-offs have made TRIUMF's technology transfer program a sound success, with at least 25% of its patent disclosures generating some level of commercial activity since the program was formally initiated in 1990 (Gardner, 1994). TRIUMF's first commercial venture was the partnership with Nordion to produce radioisotopes.

The proposed NBTF would model its technology transfer program on that of TRIUMF, albeit on a smaller scale. Importantly, royalties and licenses of TRIUMF technology have become a significant revenue stream that helps to support the institution's fundamental efforts in basic research (Gardner, 1994; Verma and Gardner, 1994).

The proposed NBTF technology transfer program would likely favor industries of the North American Free Trade Agreement (NAFTA) group. However, non-NAFTA industries would not be excluded; in fact, a totally exclusive policy would be difficult to maintain in an era of multi-national companies and an increasingly global market.

Like TRIUMF, the NBTF technology transfer program would have two objectives:

- Dissemination of technology transfer opportunities to industry in support of economic development, and
- Provide additional revenues through royalties and technology licensing to support the research and educational missions of the center and the Association.

Finally, TRIUMF and other research centers have amply demonstrated the importance of international participation in research. Hence, both North American and all international users and user groups would have access to the NBTF's research facilities, with priority determined through peer review involving the NBTF Association. Proprietary research under contract with industry would be individually considered and approved by the NBTF's Science Advisory Committee. Proprietary research would be accommodated on a time-available basis, not to disrupt or displace basic research nor the production of research isotopes.

6.7 Educational and Research Opportunities Program Management

The section on education and technical training in this report describes a program that includes a system of competitive scholarships and grants to fund undergraduate and graduate training, postdoctoral fellowships, and faculty/staff exchanges. We propose that the NBTF manage this educational program and that a standing committee of the NBTF Association be established to review and award the scholarships and grants. The scholarships and grants would support work at any of the Association's member sites, not just the NBTF Core Facilities in North Texas.

7.0 PROPOSED NBTF RESEARCH PROGRAM AND RESEARCH CAPABILITIES OF KEY AFFILIATES

7.1 NBTF-Based Research Program

The Research Program utilizing the 80 MeV, 1 mA cyclotron of the National Biomedical Tracer Facility will concentrate on three national needs:

1. **Production of research radioisotopes for researchers in the life sciences, medicine, and industry;**
2. **Research on the production of radioisotopes with potential uses in the life sciences, medicine, and industry; and**
3. **Research on the applications of radioisotopes in the life sciences, medicine, and industry.**

Emphasis will be placed on the first two needs. The third area will be pursued on a time-available basis. The research done by outside users and user groups will fall into the second and third categories. Such research might also include proprietary research and development under contract with industry. Proprietary research would only be done on a time-available basis and would be approved by the Scientific Advisory Committee of the NBTF Association.

7.2 Candidate Research Radionuclides

The following candidate research radionuclides were chosen both by the personnel who developed this report and through interviews with approximately 50 professionals through our market studies. The comments included with each entry are intended to provide a frame of reference for the reader. The radioisotopes below are listed in alphabetical order, not in the order of expected demand, if any. Appearance of a radioisotope on this list indicates sufficient interest among those interviewed to indicate that there may be some level of interest, or even a market for the radioisotope, as a research radioisotope. In some cases, a current market exists (e.g., ^{18}F, ^{68}Ga, ^{82}Sr) or might develop if an assured supply of the isotope was available (e.g., ^{73}As, ^{97}Ru, and ^{127}Xe).

The research radionuclide list summarized on the following pages can be characterized in six generalized groups:

1. Radionuclides that facilitate new applications, especially in the fast growing area of oncology diagnosis and therapy. Examples: ^{72}As, ^{166}Ho, ^{186}Re, ^{97}Ru.

2. Radionuclides that have characteristics that enable them to replace and improve existing commercial products. Examples: ^{52}Fe, ^{203}Pb, ^{127}Xe.

3. Existing commercial products where research and development of targetry or production methods could result in lower production cost or higher purity. Examples: ^{201}Pb, ^{123}I, ^{82}Sr. These radionuclides are not discussed below since they are used to produce radiopharmaceuticals that are already approved for human use by the FDA.

4. Radionuclides that could become important when high resolution imaging equipment of higher energy gamma photons becomes available. Examples: ^{113m}In, ^{52}Mn, ^{77}Br, ^{124}I.

5. Generator-based radionuclides that bring cost and/or convenience benefits. Examples: ^{128}Cs, ^{62}Cu, ^{122}I, ^{68}Ga, ^{82}Rb.

6. Radionuclides for life sciences research, analytical standards, or industrial applications. Examples: ^{73}As, ^{7}Be, ^{139}Ce, ^{51}Cr.

Candidate Research Radionuclides and Other Potential Radioisotopic Products

ANTIMONY, ^{118}Sb via a ^{118}Te/^{118}Sb generator. The parent has a 6.0-day half-life and the daughter has a 3.5 minute half-life. The parent is made by proton irradiation of natural antimony by a combination of (p,4n) and (p,6n) reactions using 50 and 70 MeV protons, respectively. Excitation function measurements are needed to determine: (1) the need for enriched stable target material; and (2) amounts of $^{121\,m\&g}$Te (154 d & 16.8 d $T_{1/2}$) and ^{119m}Te (4.68 d $T_{1/2}$) co-produced under varying conditions. In a proposed use, the ^{118}Te parent would be chemically tagged onto a monoclonal antibody or peptide and injected as a tumor marker. Since the ^{118}Te parent has no gamma emission, imaging would be accomplished through the 3.5 min ^{118}Sb daughter, always in equilibrium with its parent.

ARSENIC, ^{72}As via a ^{72}Se/^{72}As generator. The parent has an 8.4-day half-life, while the daughter half-life is 26 hours. The parent is made by proton irradiation of natural arsenic by the (p,4n) reaction using 50 MeV protons. Research on a suitable target material and reaction excitation function measurements are needed. Separations chemistry investigations on the Se/As generator have been performed at LANL. Arsenic-72 has been proposed as a

radioimmuno imaging agent.

ARSENIC, ^{73}As ($T_{1/2}$ = 80.3 days). According to the 1991 *National Biomedical Tracer Facility Planning and Feasibility Study* (R. A. Holmes, ed.), the U.S. Geological Survey had earlier expressed interest in ^{73}As as an environmental tracer for investigating arsenic contamination by mining operations. At that time, the radioisotope was being recovered for research purposes from the RbBr target solutions processed at LANL for ^{68}Ge. Some interest continues in this nuclide, since 1993 sales from LANL amounted to $10,000. Contamination with ^{74}As ($T_{1/2}$ = 17.78 days) is a problem with the LANL product. Assuming highly enriched ^{73}Ge target material was available, ^{73}As could be produced essentially free from ^{74}As by the (p,n) reaction.

ARSENIC, ^{74}As ($T_{1/2}$ = 17.78 days). In the past this nuclide has been used for *in vivo* studies of the brain. This nuclide could be produced relatively free from other radioactive impurities by the (p,n) reaction using a highly enriched ^{74}Ge target. Target development, excitation function measurements, and chemical processing R&D will be necessary before a product is ready for exploring biomedical applications.

BERYLLIUM, ^{7}Be ($T_{1/2}$ = 53.26 days). This nuclide has been used in human berylliosis investigations in the past and has some applications in the physical sciences as well. It can be readily made by the (p,n) reaction on natural lithium targets. Research is needed to develop a suitable target that is able to withstand high intensity proton beam irradiation.

BROMINE, ^{77}Br ($T_{1/2}$ = 2.376 days). This nuclide was developed at LANL via spallation reactions (P. M. Grant, R. E. Whipple, J. W. Barnes, G. E. Bentley, P. M. Wanek and H. A. O'Brien, Jr. 1981 The Production of ^{77}Br at Los Alamos for Nuclear Medicine Studies, *J. Inorg. Chem.* 43: 2217-2222.) and was provided in specific activities approaching the theoretical limit. This product was used in labeling estradiol derivatives for measuring estrogen receptors in humans (D. S. Wilbur, G. E. Bentley and H. A. O'Brien, Jr. 1981 A Rapid Synthesis of A-Ring Bromine-77 Labeled Estrogens with High Specific Activity. *J. Labl. Cmpd. Radiopharm.* XVIII: 1693-1702.). Quantitative measurements in humans using a gamma camera proved difficult due to the poor resolution of the higher energy gamma photons. However, a product with a similar specific activity from the NBTF is expected to be used extensively in radio-halogenation labeling studies with monoclonal antibodies and peptides. Bromine-77 is made by (p,n), (p,2n), and (p,4n) reactions on ^{77}Se, ^{78}Se and ^{80}Se, respectively. The only potential contaminant of consequence is ^{80m}Br ($T_{1/2}$ = 4.42 hours).

CERIUM, ^{139}Ce ($T_{1/2}$ = 137.2 days). Cerium-139 is produced using naturally occurring lanthanum target by the $^{139}La(p,n)^{139}Ce$ reaction. Cerium-139 is used as an industrial standard.

CESIUM, ^{128}Cs ($T_{1/2}$ = 3.62 minutes). Cesium-128 is produced from the decay of ^{128}Ba ($T_{1/2}$ = 2.43 days) via a barium/cesium generator. Cesium-128 is a positron emitter and may be taken up from the blood stream by muscle tissue in a manner similar to potassium and rubidium ions. If so, this nuclide could be useful in heart damage measurements, stroke studies, brain tumor studies, and renal blood flow measurements. Its parent, ^{128}Ba, can be produced by the (p,6n) reaction on natural cesium targets using the 80 MeV protons available from the NBTF cyclotron. Alternatively, the (p,3n) reaction on highly enriched ^{130}Ba could be investigated. Major drawbacks to this approach are: (1) very low natural abundance of ^{130}Ba (0.106%); (2) the short half-life of ^{128}La (4.6 minutes); and (3) the amount of time required to remove the target and chemically isolate the lanthanum fraction.

CHROMIUM, ^{51}Cr ($T_{1/2}$ = 27.7 days). Chromium-51 can be produced by the $^{51}V(p,n)^{51}Cr$ reaction on naturally occurring vanadium targets at about 20 MeV. At higher energies, the same target may be used to produce ^{48}Cr, a precursor of ^{48}V. This is an example how two useful products may be produced during the same irradiation. Chromium-51 is used to assess red blood cell survival.

COPPER, ^{61}Cu ($T_{1/2}$ = 3.41 hours). This short-lived positron emitter has been identified as having potential applications in PET imaging. On the negative side, the short half-life will limit distribution to a small geographic area. A nickel target enriched in ^{61}Ni and ^{62}Ni will be required to produce ^{61}Cu by a combination of (p,n) and (p,2n) reactions.

COPPER, ^{62}Cu ($T_{1/2}$ = 9.74 minutes). This nuclide is produced from the decay of ^{62}Zn ($T_{1/2}$ = 9.22 hours) by positron emission and electron capture. It also emits a high energy photon (1173 keV). An enriched ^{63}Cu target would be required to eliminate the co-production of ^{65}Zn ($T_{1/2}$ = 244.1 days). A possible limiting factor is the relatively short half-life of ^{62}Zn, which is comparable to that of ^{99m}Tc. ($T_{1/2}$ = 6.01 hours). Copper-62 has been proposed as a generator produced positron emission imaging agent for dynamic studies using PET or an appropriately collimated SPECT camera.

COPPER, ^{64}Cu ($T_{1/2}$ = 12.7 hours). This nuclide has a complex decay scheme, including electron capture, positron emission, and beta decay. It also has a high energy gamma photon (1344 keV). Production in the NBTF cyclotron would require a highly enriched ^{64}Ni target. Note that ^{64}Cu can and has been made by the (n,p) reaction on ^{64}Zn using the fast component of a nuclear reactor spectrum. The (n,p) reaction cross section for 14 MeV neutrons from a dense plasma focus neutron generator is about 160 mb.

COPPER, ^{67}Cu ($T^{1/2}$ = 2.58 days). Copper-67 decays by beta emission and has an associated gamma photon from ^{67}Zn (185 keV) that is readily imaged with a conventional gamma camera. This nuclide is widely believed to hold great potential as a radioimmunotherapy agent for tumor treatment when coupled to monoclonal antibody or peptide vectors. Neutron-induced (neutron rich) nuclides are difficult to produce with low

energy accelerators. Copper-67 has been produced in a reactor via the $^{67}Zn(n,p)$ reaction (H. A. O'Brien, Jr. 1969 The Preparation of ^{67}Cu from ^{67}Zn in a Nuclear Reactor. *Int. J. Appl. Radiat. Isotop.* 20: 121-124.) and at LAMPF from spallation reactions using a ZnO target (J. W. Barnes, K. E. Thomas, G. E. Bentley, F. J. Steinkruger and H. A. O'Brien, Jr. 1982 Copper-67 Production and Recovery from ZnO Targets. *J. Nucl. Med.* 23: P102.). For the NBTF cyclotron, the $^{70}Zn(p,\alpha)^{67}Cu$ will be investigated. The 1991 *National Biomedical Tracer Facility Planning and Feasibility Study* (R. A. Holmes, ed.) projected a $1.4 M market for this nuclide.

FLUORINE, ^{18}F ($T_{1/2}$ = 1.83 hours). This nuclide is a widely used labeling agent for fluorodeoxyglucose studies in conjunction with PET imaging. The short half-life limits this nuclide to a regional distribution area. Even so, this nuclide is expected to produce a significant source of revenue for the NBTF.

GALLIUM, ^{68}Ga ($T_{1/2}$ = 1.13 hours). This nuclide is available as a generator product from the decay of ^{68}Ge ($T_{1/2}$ = 270.8 days), which decays by electron capture without the emission of a gamma photon. Germanium-68 is produced by a combination of (p,2n) and (p,4n) reactions using a natural gallium target. Research is required to develop an appropriate target to withstand high intensity proton beam irradiations. The present major use of the parent/daughter product is as a transmission calibration source for PET cameras. In 1993, the LANL market for this product amounted to $406,000. Gallium-68 has been used for PET studies when labeled to a variety of compounds.

GERMANIUM, ^{71}Ge ($T_{1/2}$ = 11.2 days). Germanium-71 would be of use as a calibration source and a tracer for measuring extraction efficiencies for solar neutrino experiments in Russia (the SAGE collaboration) and in Italy (the GALLEX experiment). Both these experiments are expected to have long lifetimes, but the revenue for NBTF is anticipated to be small. The product is made by a (p,n) reaction on enriched ^{71}Ga.

HOLMIUM, ^{166}Ho ($T_{1/2}$ = 26.8 hours). Holmium-166 decays by beta decay giving rise to numerous gammas of low abundance. The average energy of the beta decays is 665 keV with an equilibrium dose constant of 1.4 gm-rad/μCi-hr making it an ideal candidate for in-vivo radiotherapy. Holmium-166 is best produced carrier-free by the $^{166}Er(n,p)^{166}Ho$ reaction. Considerable development effort for target development, separation chemistry and labeling techniques is needed and could be provided by the NBTF effort.

INDIUM, ^{113m}In ($T_{1/2}$ = 1.66 hours). Indium-113m is produced from the decay of ^{113}Sn ($T_{1/2}$ = 115.1 days). The parent is made by a combination of (p,n) and (p,3n) reactions using a natural indium target. The daughter nuclide was used as an imaging agent in nuclear medicine before ^{99m}Tc and the Anger camera became the industry standards. Indium-113m decay produces a 393 keV gamma photon that may produce good spatial resolution with the new generation of cameras.

IODINE, ^{122}I ($T_{1/2}$ = 3.6 minutes). Iodine-122 is available from the decay of ^{122}Xe ($T_{1/2}$ = 20.1 hours) via a generator system. The parent could be produced by the $^{124}Xe(p,3n)^{122}Cs$ ($T_{1/2}$ = 21 seconds) reaction. Currently the $^{124}Xe(p,2n)^{123}Cs$ reaction is employed to produce 13.0-hour ^{123}I, which has enjoyed some popularity as a radio-halogenating agent in nuclear medicine. Thus the same target could yield two separate products, ^{122}Xe and ^{123}I. Although some interest has been expressed in using positrons from the decay of ^{122}I in conjunction with PET imaging, this application requires rapid radio-halogenation chemistries and *in vivo* localizations.

IODINE, ^{124}I($T_{1/2}$ = 100.3 hours). Iodine-124 decays by electron capture and positron emission, giving rise to a 59% abundant 603 keV gamma and numerous other gammas at low abundances. It is produced by the (p,xn) reaction on several stable isotopes of tellurium. Iodine-124 can be used to label numerous biologically active radioimmunotherapy agents. Imaging may be accomplished currently with a PET camera, and probably with the next generation of planar cameras under development.

IODINE, ^{125}I ($T_{1/2}$ = 60.1 days). This nuclide has wide applications for *in vitro* radioimmunoassays. Although it has been made by accelerator irradiation, the most economical method of production is neutron capture on ^{124}Xe to form ^{125}Xe ($T_{1/2}$ = 17.1 hours), which subsequently decays to ^{125}I. Development of accelerator production technology is important to provide a backup supply of ^{125}I during periods of shortage from the reactor source.

IRON, ^{52}Fe ($T_{1/2}$ = 8.28 hours). This nuclide decays by positron emission and electron capture and has a 169 keV gamma photon from ^{52}Mn, which is readily imaged with existing gamma cameras. Hence, this product has potential as both a PET and conventional gamma camera imaging agent. It can be produced by two separate reaction routes: $^{55}Mn(p,4n)$ and $^{54}Fe(p,3n)^{52}Co$ --> ^{52}Fe. The latter reaction path requires an enriched target material, while the former does not, and thus would be the preferred production method.

KRYPTON, ^{81m}Kr ($T_{1/2}$ = 13 seconds). Krypton-81m is the daughter radionuclide of 4.6 hour ^{81}Rb and can be eluted from its parent with a flow of carrier gas such as air or oxygen. The ^{81}Rb parent has been produced in limited quantities at various cyclotron facilities by a proton nuclear reaction on naturally occurring krypton and the generator pair used for investigational lung ventilation studies. The short-lived daughter decays before redistribution can occur in the alveolar sacs, permitting multiple view imaging with the patient's normal breathing of air or oxygen carrier through a mask attached to the generator.

LEAD, ^{203}Pb ($T_{1/2}$ = 52 hours). Lead-203 is a low-level byproduct of the $^{203}Tl(p,3n)^{201}Pb$ reaction used to obtain the medically important heart agent, ^{201}Tl. Lead-203 is produced directly by the (p,n) reaction on ^{203}Tl or by the (p,3n) reaction on ^{205}Tl. An abundant supply of highly enriched ^{205}Tl is available from the tailings of the isotopic enrichment process for

^{203}Tl. Lead-203 decays by electron capture giving rise to 95% abundant 279 keV gamma. The gamma energy is not optimum for imaging with current gamma cameras but will be well suited for the newer imaging devices under development. Lead-203 has been suggested for radioimmuno imaging and for abscess localization when labeled to oxine. It holds promise as a less expensive substitute for ^{111}In, currently used for imaging.

LUTETIUM, ^{172}Lu ($T_{1/2}$ = 6.7 days). Lutetium-172 is available from the decay of 1.87-year ^{172}Hf, which can be produced by a (p,4n) on ^{175}Lu. Hafnium-172 was produced at LANL via spallation reactions (R. J. Daniels, P. M. Grant and H. A. O'Brien, Jr. 1978 The production, recovery and purification of ^{172}Hf for utilization in nuclear medicine as the generator of ^{172}Lu. *Int. J. Nucl. Med. Biol.* 5: 11-17.) and a Hf/Lu generator system was developed (P. M. Grant, R. J. Daniels, W. J. Daniels, G. E. Bentley and H. A. O'Brien, Jr. 1983 The generator production of ^{172}Lu from ^{172}Hf for limited nuclear medicine research. *J. Radioanal. Chem.* 76: 319-323.). Although one application of ^{172}Lu has been published (P.M. Grant, G. E. Montero, A, M. Newman and H. A. O'Brien, Jr. 1985 First Use of Millicurie Levels of ^{172}Hf/^{172}Lu in the Industrial Sector. *Radioanal. Nucl. Chem. Lett.* 96(6): 629-634.), the lack of interest demonstrated to date indicates this would be a very low priority for the NBTF program.

MANGANESE, ^{52m}Mn ($T_{1/2}$ = 21.1 minutes). Manganese-52m is the radioactive daughter of ^{52}Fe and decays by positron (92%) and electron capture (8%), giving rise to a 1.43 MeV gamma photon from ^{52}Cr. Production of the ^{52}Fe parent is discussed above. Manganese-52m may be useful when used in conjunction with PET systems and with the developing new generation of high energy, high resolution cameras.

RHENIUM, ^{186}Re ($T_{1/2}$ = 91 hours). Rhenium-186 decays by B giving rise to a 137 keV gamma photon. It is produced directly with neutrons by the ^{185}Re(n,γ)^{186}Re reaction, or carrier-free in an accelerator by the ^{186}W(p,n)^{186}Re reaction. Rhenium has been used investigationally labeled to monoclonal antibodies for radioimmunotherapy and as a palliative agent for pain in bone cancer. The gamma emission facilitates imaging the biodistribution and any specific tissue uptake following its administration.

RUBIDIUM, ^{82}Rb ($T_{1/2}$ = 1.251 minutes). Rubidium-82 is available from the decay of its parent ^{82}Sr ($T_{1/2}$ = 25 days). The generator system was studied by LANL scientists in the mid-1970's (P. M. Grant, B. R. Erdal and H. A. O'Brien, Jr. 1975 A ^{82}Sr/^{82}Rb Isotope Generator for Use in Nuclear Medicine. *J. Nucl. Med.* 16: 300-304) and a commercial generator was subsequently developed by E. R. Squibb & Sons in collaboration with LANL (R. D. Neirinckx, J. F. Kronauge, G. P. Gennaro, M. D. Loberg and the Los Alamos Medical Radioisotope Group 1982 Evaluation of Inorganic Adsorbents for the Rubidium-82 Generator. I. Hydrous SnO_2. *J. Nucl. Med.* 23: 245-249 & 500.). Rubidium-82 is useful, in conjunction with PET imaging, in heart and stroke studies, renal function measurements, and brain tumor investigations. The major advantage of this generator system is that it allows a

PET center to perform a number of significant studies without the necessity of having an on-site cyclotron to generate the imaging radioisotope. Squibb (now Bracco Diagnostics) has fourteen customers for its generator, but the growth of the market has been impeded by the lack of approval for third party payment for PET studies. Strontium-82 can be produced on the NBTF cyclotron by a combination of (p,4n) and (p,6n) reactions on natural rubidium targets. In 1993, the LANL market for this product was $391,000. Because of the limited operations of the LAMPF accelerator at LANL, a facility operating the entire year could anticipate significant revenues from a ^{82}Sr product.

RUTHENIUM, ^{97}Ru ($T_{1/2}$ = 2.89 days). Ruthenium-97 decays by electron capture and has two gamma photons (216 and 324 keV) that can be imaged with a gamma camera. Some researchers are promoting this nuclide as a labeling agent for monoclonal antibodies and peptides for diagnostic studies. Should these investigations prove fruitful, ^{103}Ru ($T_{1/2}$ = 39.4 days) could be substituted for radioimmunotherapy of tumors. Ruthenium-97 can be produced by the ^{99}Tc(p,3n) reaction without co-production of radiocontaminants. No-carrier-added ^{103}Ru could be produced on the NBTF cyclotron using the ^{105}Pd(p,3p) reaction and an enriched ^{105}Pd target.

TANTALUM, ^{179}Ta ($T_{1/2}$ = 1.7 years). Tantalum-179 decays by electron capture without an accompanying gamma photon. It is proposed as a replacement for ^{241}Am, an alpha emitter, in X-ray fluorescence and thickness gauging. Definite interest in this nuclide has been expressed by members of the nuclear community. It can be produced by a combination of (p,n) and (p,2n) reactions on natural hafnium targets. The extent of the potential market is unknown at this time.

TECHNETIUM, ^{95m}Tc ($T_{1/2}$ = 61 days) and ^{96}Tc ($T_{1/2}$ = 4.3 days). Technetium-95m and -96 are being sought as tracers for technetium chemistry research, where longer lived isotopes are needed in elucidating chemistry associated with ^{99m}Tc labeling and related radiopharmaceutical metabolism. No-carrier-added products are required in order that these products will exhibit the same behavior as generator produced ^{99m}Tc. Both products are expected to achieve more than a minor market, since extensive technetium compound development research is being conducted worldwide. In 1993, the LANL market for these products amounted to $7,500, but the extent of radionuclidic purity of each of these is not known. If the products were obtained from spallogenic reactions, there was, in all likelihood, a mixture of technetium isotopes in the products. Using appropriate enriched molybdenum target materials as targets, each of these products can be made by (p,n) reactions.

VANADIUM, ^{48}V ($T_{1/2}$ = 15.98 days). Vanadium-48 is a positron emitting nuclide that currently has applications in nutrition and environmental chemistry research. The market is expected to be small, for example in 1993 the LANL market was $3,000. This nuclide can be made by the (p,n) reaction using an enriched ^{48}Ti target.

XENON, ^{127}Xe ($T_{1/2}$ = 36.4 days). Xenon-127 decays to ^{127}I, which emits gamma photons of higher energy and thus is less subject to attenuation corrections in lung imaging than the existing ^{133}Xe ($T_{1/2}$ = 5.25 days) product. Also, ^{127}Xe has a longer shelf life (due to its greater half-life) that many medical institutions consider a distinct advantage. Although ^{127}Xe can be produced in a reactor, an expensive enriched ^{126}Xe target is required, and the target is shipped with the product. At one point, ^{127}Xe was available as a spallogenic product from LANL at a modest cost. However, the limited operations at LAMPF restricted distributions throughout the year and the market subsequently declined. There is a real possibility that the market would return with a continuous product availability from the NBTF. Pure ^{127}Xe can by produced by the (p,n) reaction on a natural iodine target.

> ***This product may typify the role of NBTF in finding a market niche. A major radiochemical firm has decided not to produce ^{127}Xe, but at least one major radiopharmaceutical company believes there may be a market for the product. Because of the recent approval of Technegas (labeled with ^{99m}Tc), some believe the xenon product has no chance. Although lung studies are performed infrequently, the product must be available when they are required. The longer shelf life is a distinct advantage.***

YTTRIUM, ^{88}Y ($T_{1/2}$ = 106.6 days). Yttrium-88 decays by electron capture, but also has a weak positron branch. It has two prominent gamma photons of 898 and 1836 keV. In the past it has been extensively used as a gamma photon standard for calibrating counting systems and as a radiotracer in the development and biodistribution measurements of yttrium labeled monoclonal antibodies and peptides. Yttrium-88 can be made by two methods: directly from the (p,n) reaction on ^{88}Sr, and indirectly from the decay of ^{88}Zr, which is produced by the (p,2n) reaction on ^{89}Y. In 1993, the LANL market for ^{88}Y was $15,000.

ZIRCONIUM, ^{89}Zr ($T_{1/2}$ = 3.27 days). Zirconium-89 decays by electron capture and positron emission. This is an example of a potential future product that does not, at this time, have a known biomedical application. The product can be readily made by the (p,n) reaction on natural yttrium targets.

7.3 Use of Existing Research Facilities at Other Locations

We envision that the NBTF and the NBTF Association member institutions will be involved in a broad scope of collaborative research that relates to radioisotope applications in the life sciences, medicine, and industry.

> ***We propose to use existing research facilities and expertise at the collaborating academic institutions, medical centers, and the national laboratories.***

7.3.1 Reactor Facilities at Sandia National Laboratories

The contributions of the reactor facilities at Sandia National Laboratories (Albuquerque, NM) to radioisotope production were mentioned earlier and are discussed more fully in Appendix VI. Sandia's reactor and the Reactor Engineering and Technology Center's processing facilities provide ample opportunities for research as well as accommodating the current DOE plan for commercial production of molybdenum-99 using the Sandia reactor. The Sandia Annular Core Research Reactor was, in fact, designed as a *research* reactor whose annular core is ideally suited to research. Sandia, MU, UNM, and UNT would also contribute expertise in nuclear technology, nuclear engineering, nuclear engineering technology, health physics, and related areas.

7.3.2 Reactor Facilities at the University of Missouri

The University of Missouri Research Reactor (MURR) currently operates an extensive production facility for research radioisotopes, making approximately 2,000 shipments annually to various industrial, government, and university-based laboratories. MURR is willing to cooperate with the NBTF on potential radioisotope applications and related research. However, because of its long-established business and service activities to industry and government, MURR will continue to produce and market its radioisotopes through its established marketing chains. The cooperative tie with the NBTF will be established through the MU College of Engineering and its Department of Nuclear Engineering, which are participants in this proposal.

7.3.3 Stable Isotope Separations Research at the University of Missouri

The College of Engineering at the University of Missouri (MU) will make its principal research contributions in three areas: (1) research on laser-based separation of stable isotopes, (2) as an entré to collaboration with the research program at the Missouri University Research Reactor (MURR), and (3) in the proposed distance learning program where Missouri would contribute considerable expertise.

Recently, the Department of Nuclear Engineering at MU received a gift of the patents on a laser isotope separation process, Chemical Reaction Isotopic Separation by Laser Activation (CRISLA), plus approximately $500,000 in CRISLA equipment. This gift from an alumnus of the department, was also accompanied by a gift of money for development of the process. The donor's company had been working in Canada to develop CRISLA for uranium separation, but the end of the Cold War caused the market for the product to plummet. The company elected to close out this section of its R&D program; hence the donation to MU.

Although previous investigators claimed that they demonstrated milligram to gram quantities of uranium enrichment, MU intends to demonstrate adequately, under peer review, the separation of an appropriate *medical* isotope. However, the concept is well beyond the basic research phase.

Separation of ^{98}Mo has been chosen for this demonstration project. Molybdenum-98 is the target material for (n,gamma) production of ^{99}Mo in a high flux nuclear reactor. Although, this method cannot achieve the very high specific activity of the fission product ^{99}Mo, it does result in a production method with very low by-product waste. The method is also attractive in that any high flux research reactor could produce ^{99}Mo by the (n,gamma) method without costly modification of the reactor or undue disruption of ongoing research.

The proposed method also fits in with a joint program between MURR and Mallinckrodt Chemical Corporation to use ^{98}Mo in the new gel method for production of ^{99}Mo that would achieve the patient carry-over, purity requirements.

A five-year research plan has been developed, based on the previous experience of the private company that was developing the CRISLA method. Currently, the principal investigator of this research program, Dr. Jay A. Kunze, is seeking funding for the project beyond that available from the gift to the university. NTRI and its affiliates intend to assist in the CRISLA research effort and in attracting funding. Both public sector and private industrial funding is being sought. Ultimately, if successful, the process would be licensed for industrial application.

Once the proof of principle is accomplished, MU would set up a pilot production unit at the NBTF. The focus here would be to widen the scope of enrichment efforts to stable isotopes other than molybdenum isotopes, to those stable isotopes germane to medical isotope production at the NBTF. Ultimately, the use of the method for production of stable isotopes would either (1) be expanded, with industry participation and operation, at NBTF, or (2) licensed for industry to establish a production facility elsewhere.

Beyond this plan, CRISLA might be applied to radioisotopes at a facility equipped to handle such elements. This could be at the NBTF or possibly at MURR if current plans for expansion come to fruition. These plans include a building expansion and new hot labs.

In a related development, AITI in cooperation with Los Alamos National Laboratory, is seeking patent rights, technology, and know-how in relation to the Molecular Laser Isotope Separation (MLIS) process for stable isotope separation. Assuming fruition of these efforts, AITI plans to construct a prototype commercial system based on this technology and begin pilot operations in late 1996. Both research and development teams (AITI/NTRI and MU) will work together through non-disclosure agreements toward a mutual development of the respective laser-based technologies.

7.3.4 Nuclear Medicine Facilities at UTSMC

The University of Texas Southwestern Medical Center at Dallas (UTSMC) has existing, excellent facilities for radiochemistry, radiolabelling, medical imaging (both anatomical and functional), animal studies, and human clinical research. This facility is located approximately 40 minutes by car from the proposed NBTF site and the University of North Texas. The research program in Nuclear Medicine would be centered in the facilities of UTSMC at Dallas, within the departments of Radiology and Radiation Oncology, both involving the graduate program in Radiological Sciences. The educational and research program in Radiochemistry would be centered in the NBTF facilities, the facilities of UTSMC in Radiological Sciences, and UNT's graduate program in Chemistry. UTSMC would staff and manage the proposed Advanced Medical Imaging Center (Appendix IV) adjacent to the NBTF in Denton.

7.3.5 Radiopharmaceutical and Waste Research at UNM

The University of New Mexico has established a unique cross-disciplinary alliance that unites three colleges and schools in research and education in the radiopharmaceutical sciences. The alliance fosters education, research, and technology transfer in the following areas: (1) production, separation, and purification of radionuclides; (2) development of techniques for radiotracer synthesis and application; (3) radiation protection and safety; (4) waste management and reduction and environmental remediation; and (5) medical imaging.

The College of Engineering is heavily involved in research on waste management, risk assessment, and health physics. Through its Waste management Education and Research Consortium (WERC), the College of Engineering is performing fundamental research in hazardous and radioactive waste, waste management, reduction, and remediation. As an outgrowth of WERC, UNM has established the Center for Radioactive Waste Management (CeRaM). This center is dedicated to the study of radioactive and mixed waste issues—both in the classroom and the research laboratory. The research activities of CeRaM include environmental fate and transport of radionuclides associated with different types of radioactive wastes, environmental restoration and remediation, and health physics and radiation monitoring.

Research Programs of the College of Pharmacy (in collaboration with the College of Engineering and the School of Medicine) include the following: developing new radiopharmaceuticals for clinical use; developing methods for improved targeting of radiopharmaceuticals; investigating factors that affect radiopharmaceutical stability; assessing reliability and enhancing the continued operation of production facilities; exploiting new radioisotopes; optimizing target design; separating radioisotopes; investigating radioisotope imaging/data fusion and image analysis; designing new collimators and detectors for image

analysis; spinning-off new radioisotope technology to industry; and investigating process automation.

7.3.6 Materials Characterization Facilities at UNT

The University of North Texas (approximately ten minutes by car from the proposed site) has existing, excellent faculty and facilities in the physical, life, and computational sciences. UNT's role would be R&D in the basic sciences and engineering technology, including the programs in accelerator technology, accelerator operations, and health physics. Of particular importance in the proposed research program are UNT's strengths in materials characterization, including a wide array of instrumentation capable of analysis at the single atom level. Facilities include standard and high resolution scanning and transmission electron microscopy (to 1.7 Å), scanning tunneling microscopy, electron spectroscopy (ESCA/Auger and X-ray/ion scattering), FTIR, mass spectroscopy, NMR, and X-ray diffractometry.

UNT's Ion Beam Modification and Analysis Laboratory (IBMAL) operates five different accelerators, and is the world's leader in atomic mass spectrometry (AMS) of stable isotopes, having perfected the technology to detect uniquely any element in the periodic table (except indium, which has isobaric interferences) at the sub parts-per-billion level, with the expectation to reach the parts-per-trillion level (one part in 10^{12}) in the near future. This capability will be a tremendous asset to the NBTF program. Currently, the IBMAL group is exploring new techniques to discriminate isobars; i.e., isotopes of different elements with the same atomic mass but different atomic number (different Z). The AMS capability, plus a variety of other accelerator-based analytical capabilities (particle-induced X-ray emission [PIXE], Rutherford backscattering, proton microbeam, nuclear reaction analysis [NRA], etc.) and other state-of-the-art analytical capabilities available in UNT's Center for Materials Characterization, will provide valuable support to the NBTF's research program.

8.0 PROPOSED NBTF EDUCATIONAL AND TRAINING PROGRAMS IN ASSOCIATION WITH KEY AFFILIATES

8.1 Overview

While the research and educational facilities at the NBTF site will be modest, other than the capabilities of a world-class cyclotron, the NBTF and the institutional members of the NBTF Association will mount a vigorous research and training program using the combined expertise and facilities of the Association's consortium, which are considerable in extent. We envision that the Association will ultimately offer a broad educational program, including undergraduate and graduate degree programs, postdoctoral training, continuing education, and performance-based technical training.

We propose a phased-in program of education and training in the disciplines that support nuclear medicine and related industries. An overall plan will be developed that will include the following components:

- Technician-level, performance-based training of industrial workers and support personnel for the radiopharmaceutical and health care industries and institutional settings.
- Baccalaureate-level programs in health physics, waste and environmental management, and in the natural sciences with specializations in areas that support nuclear medicine and related industries.
- Educational programs, typically at the master's level for industry professionals in the areas of radiochemistry, radiopharmaceutical manufacture, health physics, accelerator operations, and research and development. This program will also serve to prepare students for further study at the doctoral level.
- Doctoral and post-doctoral education and training for professionals in industry, academia, and biomedical research and development.
- Combined M.D./Ph.D. education and training for professionals in academic medicine, biomedical research and development, and the health care industry.
- Continuing education for industry and health care professionals in the areas of regulation, technology, industrial and medical practice, and new developments.

8.2 Undergraduate and Graduate Degree Programs

With one exception (Radiochemistry), all degree programs offered through the NBTF Association will be currently authorized and operating programs. Applicable educational programs currently in place at the collaborating institutions include the following disciplines and degrees:

Biochemistry (B.A./B.S., M.S., Ph.D.)
Biomedical Engineering (M.S., Ph.D.)
Biological Sciences (B.A./B.S., M.A./M.S. Ph.D.)
Chemistry (B.A./B.S., M.S., Ph.D.)
Doctor of Medicine (M.D.)
Environmental Science (M.S., Ph.D.)
Hazardous Waste Engineering (M.S.)
Nuclear Engineering (B.S., M.S., Ph.D.)
Nuclear Engineering Technology (B.S., M.S.)
Materials Science (M.S., Ph.D.)
Molecular Biology (M.S., Ph.D.)
Molecular Biophysics (Ph.D.)
Pharmaceutical Sciences (M.S., Ph.D.)
Physics (B.A./B.S., M.A./M.S., Ph.D.)
Radiological Sciences (M.A., Ph.D.)
Radiopharmacy (B.S., Pharm.D., Ph.D.)

A graduate degree program that offers training in Radiochemistry is included under UTSMC's program in Radiological Sciences. In addition, upon approval of the NBTF as proposed in this project definition study, the University of North Texas will seek authorization from the Texas Higher Education Coordinating Board to add a concentration in Radiochemistry under its current authorization to offer the M.S. and Ph.D. in Chemistry. Currently, the UNT Chemistry program is authorized to offer the M.S. and Ph.D. in the traditional subdisciplines of chemistry (analytical, inorganic, organic, and physical chemistry), plus an M.S. in Industrial Chemistry. UNT's M.S. and Ph.D. in Biochemistry are offered through the Department of Biological Sciences.

8.3 Academic Common Market

Currently, fourteen Southern and Southwestern states participate in the Academic Common Market, an interstate agreement for sharing uncommon programs. Residents of these states

who are accepted for admission into selected out-of-state programs may enroll on an in-state tuition basis to programs located outside their home state. Three of the five states participating in this proposal are states that participate in this program, which is managed by the Southern Regional Education Board (SREB).

The mechanism of the Academic Common Market would be used to provide educational opportunities in the above areas through the member institutions of the NBTF Association. In addition, the NBTF Association would approach the SREB and current non-member states to seek a wider compact among participating state academic institutions to make available nationally the unique academic opportunities that the NBTF and the NBTF Association will create. We would also attempt to provide a compact with private academic and medical institutions to provide opportunities for their students.

8.4 Accelerator Technology

We also propose training and educational programs in Accelerator Technology and Accelerator Operations with headquarters in the Ion Beam Modification and Analysis Laboratory (IBMAL) on the nearby UNT campus. Trainees and students would be schooled in the theory, technology, and practical operation of both linear accelerators and cyclotrons. Hands-on experience and thesis/dissertation research would be acquired at both the NBTF and the commercial production linac. On the UNT campus, technical trainees and students would gain experience at IBMAL, which currently operates five different accelerators for research and materials characterization/materials modification in partnership with industrial firms. IBMAL currently is the world's leader in atomic mass spectrometry (AMS) of stable isotopes, having perfected the technology to detect uniquely any element in the periodic table except indium at the sub parts-per-billion level, with the expectation to reach the parts-per-trillion level (one part in 10^{12}) in the near future. UNT's Department of Physics has a 25-year history of excellence in the application of accelerator technology to atomic and nuclear physics and, most recently, in accelerator-based materials characterization. Every two years, UNT hosts the *Conference on the Application of Accelerators in Research and Industry*. It is the premier international conference in the field of low- and medium-energy physics as applied to *both* research and industrial applications.

8.5 Scholarships, Postdoctoral Fellowships, and Exchange Grants

We propose a program of graduate scholarships, postdoctoral fellowships, and grants for faculty and staff exchanges among academic institutions, industry, and the national laboratories. Graduate scholarships and postdoctoral fellowships would be initially funded through the NBTF with DOE funds. However, as the NBTF becomes self-sufficient, the scholarship and fellowship program would be increasingly funded through the revenue from NBTF operations.

We also propose an exchange program among the academic institutions of the NBTF Association and the national laboratories on the model of the program managed by the Oak Ridge Associated Universities (ORAU). However, unlike the ORAU program, the exchange program would work in two directions: university faculty placements at national laboratories *and* national laboratory staff placements at academic institutions of the NBTF Association.

An industry intern program would place appropriately trained masters and doctoral level personnel at industrial sites among participating industrial partners. The benefit for industry would be the opportunity to choose prospective employees from a pool of talented and well trained professionals nurtured through the NBTF's educational programs.

> ***The Scientific Advisory Committee of the Association would annually hold a competition for graduate scholarships, predoctoral internships, postdoctoral fellowships, and grants for faculty/staff exchanges among Association members and the national laboratories. The competition and awards would be managed by the NBTF management entity.***

8.6 Continuing Education

The proposed National Biomedical Tracer Facility (NBTF) and its affiliates in the NBTF Association will form a strong foundation for a program in continuing education, a portion of which will be delivered via distance learning technology. Both UTSMC and UNT and other members of the consortium submitting this proposal currently offer extensive continuing education programs, and each has administrative offices and a variety of facilities to support these efforts, which draw on the expertise of the faculty and other professionals.

The NBTF and the NBTF Association will supply the expertise to staff continuing education events, whereas the continuing education offices at UNT, UTSMC, and other Association members will supply logistical support.

> ***Rather than setting up its own continuing education office, the NBTF will contract with the continuing education offices of UTSMC, UNT, and other Association members to manage conferences, workshops, professional seminars, continuing education courses, and special programs.***

Both the UNT and UTSMC continuing education offices and those of other Association members deal yearly with a large number of such events. They routinely handle scheduling, advertising, mailings, registration, fees, logistics, and all the minutiae of such events, including Continuing Medical Education (CME) credits for medical professionals and Continuing Education Units (CEU) for non-medical professionals.

8.7 Distance Learning Technology in Continuing Education

Continuing education via distance learning technology is expected to play a large role in the NBTF educational program. Both UNT and UTSMC have expertise and facilities for distance learning through interactive video and other technologies. For example, UNT currently offers complete bachelor's and master's programs in Nuclear Engineering Technology at an off-campus site, the Comanche Peak nuclear generating plant of Texas Utilities Electric, approximately 70 miles from the UNT campus.

UNT's Nuclear Engineering Technology program employs a mix of both direct faculty involvement at Comanche Peak and the use of interactive video involving students at both the main campus in Denton and at Comanche Peak and faculty at either site. Thus, faculty members may teach from either site, with mentors and teaching assistants presiding at the other site. This program will expand in the next few years through distance learning technology to a variety of nuclear sites in Texas and across the U.S., both at power generating plants and at other sites that use nuclear technology or process nuclear materials. We envision a similar linkup among the members of the NBTF Association and with other partners, including industrial sites.

> ***We propose to place the NBTF's educational program in the vanguard of the developing electronic "virtual university" that will link and unite educational institutions of the 21st Century.***

Electronic media, fiber optic communication, and satellite communications are revolutionizing our society. These developments will enhance higher education and technical training as well, while inevitably supplanting some traditional forms and methods of information delivery and professional certification. A special effort will be made to link the general academic institutions and medical education centers of the NBTF Association through distance learning technology, so that students at all levels and faculty can access courses and seminars that otherwise would not be available on their local campuses.

> ***The Dean of the University of Missouri's College of Engineering has committed Missouri's leadership in this effort on behalf of the Association.***

Both regular and special courses via distance learning technology will include students and faculty and staff expertise from a variety of academic institutions, national laboratories, and the private sector. For example, the Association might offer an interdisciplinary survey course to give beginning graduate students and industry professionals a comprehensive primer in the field of nuclear medicine in its broadest sense. In this example, individual academic institutions would contribute expertise in health and medical physics (MU), radiopharmacy (OU and UNM), nuclear medicine (UTSMC), accelerator technology (UNT), and reactor technology (MU and UNM). Industrial partners would contribute their practical experience

in the marketplace to such a course through distance learning technology direct from industrial locations.

Finally, the video conferencing capability of the proposed linkages would enable a new level of inter-institutional and interdisciplinary collaboration in research. The technical ability to transmit audio, video, and visual/diagrammatic materials in real time for organized classes can also be used at little extra cost (typically for telephone linkages to support compressed video) in support of research conferences among multiple researchers.

8.8 Performance-Based Technical Training

We propose to work in partnership with the Texas State Technical College System and regional community college systems to establish the feasibility of inaugurating two pilot technical training programs: (1) Accelerator Technician, and (2) Health Physics Technician. Currently, a program in health physics is offered through TSTC, but no program in accelerator operations is currently offered by any U.S. academic institution, to our knowledge. However, we believe that there is a need for such expertise; hence, this proposal for training accelerator operators. These associate degree programs would train technicians primarily for employment in industry. If DOE finds this proposal worthy of pursuing, we will seek partners at the community college level and explore the market for persons trained with the proposed expertise.

9.0 BUSINESS PLAN OVERVIEW

9.1 Introduction

The National Biomedical Tracer Facility (NBTF) and the commercial production facility (AITI) will be the key foundational facilities in the NBTF core facilities. These core facilities, to be located in North Central Texas, will be affiliated with other centers of excellence through an *Association* (the *NBTF Association*), whose membership will include universities, medical centers, national laboratories, and private industry. This business plan is based on the fundamental assumptions listed in the following section.

9.1.1 Basic Elements of the Planned Approach

- The U.S. Department of Energy (DOE), in coordination with the U.S. Office of Management and Budget (MBO) will provide a $25 million interest-free loan to be amortized over 30 years for construction of the NBTF.

- The consortium that prepared this proposal will form an association, to be called the *NBTF Association*, which will help to coordinate the production of critically needed research radioisotopes (and isotope-related research) by the NBTF and other Association facilities to supply the needs of the nuclear medicine research community.

- The North Texas Research Institute (NTRI) will operate the cyclotron for the NBTF and provide the facilities to house the cyclotron, which will have adequate electrical power, water, and sewage services. The existing facilities have a replacement value in excess of $5 million. NTRI will lease beam lines and targets for commercial radioisotope production to AITI and to others on a priority basis that does not impede production of research isotopes.

- AITI will invest over a period of three years up to $15 million to purchase a 70 MeV, 1 mA linac for commercial radioisotope production.

- AITI will lease beam time on the cyclotron from NTRI at a standard commercial rate during linac downtime and maintenance periods. AITI will construct the radioisotope processing facility under a ground lease from UNT and provide processing, marketing and distribution of research radioisotopes to the NBTF through a business contract.

- AITI (and other radiopharmaceutical companies) will provide proprietary research contracts to NTRI.

- AITI will enter into exclusive licensing arrangements with the NBTF for new developments and will pay standard royalties.

Success of the business plans associated with construction and operation of the commercial facility and the NBTF facility depend on a coordinated effort among industry, academia, state, and federal agencies. The proposed DOE $25 million interest-free loan will be used in the construction of the NBTF. A private investment of approximately $28 million from AITI and affiliated industry and investors will be used to construct the commercial facility and purchase the equipment.

9.1.2 Background

The North Texas Research Institute (NTRI), a not-for-profit affiliate of the University of North Texas, in conjunction with AITI (formerly NTR&D), has been involved for several years in a project whose goal is to build and operate a facility much like the NBTF. The previous efforts of NTRI/AITI and the work performed for DOE under a previous contract have led to the conclusions embodied in this business plan.

Our efforts have convinced us that an entity such as the NBTF must address a broad set of issues associated with radioisotope and stable isotope technology. Therefore, we think that it is critical to develop the NBTF in the context of interdependent non-commercial and commercial *core facilities*. Further, the presence of an isotope-using facility among the core facilities, such as the proposed Advanced Medical Imaging Center, will also be of substantial benefit.

The purpose of the core facilities will be to: (1) produce research quantities of radionuclides for the nuclear medicine research community (through the NBTF); (2) produce radionuclides for the radiopharmaceutical industry (through AITI); (3) conduct research into radioisotope production and related technologies (primarily through the NBTF); (4) provide opportunities for education and training in radioisotope production, radiochemistry, radiopharmacy, accelerator operation, and associated disciplines (through the NBTF and members of the NBTF Association); and (5) conduct research into technologies that will benefit from and enhance the market for new radiopharmaceuticals (through the NBTF and the Association).

The North Texas Research Institute, Inc. (NTRI) is a not-for-profit Texas corporation organized in accordance with Section 501(c)(3) of the Internal Revenue Service code. As a separate corporate affiliate of the University of North Texas (UNT), whose sole purpose is to benefit the university, NTRI provides a mechanism through which UNT's outstanding resources may be brought to bear on the regional and national needs in business and industry.

Advanced Isotope Technologies, Inc. (AITI) is the parent company of the originally incorporated NTR&D, a for-profit Texas corporation, chartered in August 1991. AITI's primary purpose is to commercialize technology and intellectual property developed by UNT and other selected institutions. AITI is currently bringing two new technologies to the marketplace. The first is its *Pulsed Sealed Neutron Tube™*, which creates a neutron flux sufficient to convert stable isotopes into isotopically pure radionuclide products in quantity. The second is an *Intense Laser Source* which is expected to advance the art of stable isotope separation.

We propose to manage the NBTF as a division of NTRI. The commercial production facility will be owned and managed by AITI. The two entities will enter into mutually supporting contractual agreements. Future members of the core facilities in North Central Texas will be either not-for-profit or for-profit entities. The previously mentioned Advanced Medical Imaging Center will be managed by the University of Texas Southwestern Medical Center at Dallas (UTSMC) in a not-for-profit context.

The NBTF will provide two basic groups of products and four categories of services.

The groups of products are:

1. Research radionuclides for the nuclear medicine and industrial communities, and

2. Specialized commercial radionuclide products.

The categories of services are:

1. Contract research and development for AITI and other companies,

2. Service irradiations and back-up production for AITI and other companies,

3. Technology transfer of NBTF developed technology, and

4. Education and training.

The availability of research radionuclides and improved radioisotope production technology is critical to the future of nuclear medicine. New imaging techniques, capitalizing on the greatly improved resolution of higher energy gamma photons, hold the promise of revolutionizing the field and providing much more cost-effective diagnostic procedures. The

development of such technologies is very strongly correlated to the ability to use new and specialized radioisotopes. The establishment of the NBTF within the proposed interdependent core facilities creates the critical atmosphere needed for the NBTF to be a truly viable entity.

The main objective of the NBTF and the NBTF Association is to establish the National Biomedical Tracer Facility (NBTF) as a world-class research and development facility with linkages among institutions to advance diagnostic and therapeutic health care through cooperation among universities, nuclear medicine professionals, and the radiopharmaceutical industry.

9.1.2.1 Critical Success Factors

Several factors are critical to the success of the NBTF. The context in which the NBTF is located is crucial to its financial stability. Co-location with a commercial production facility and an advanced imaging facility allows the NBTF to reduce capital and operating expenditures through the availability of shared resources. For example, waste handling and ES&H functions will be operationally shared through business contracts for these services. Also, exchange of specialized personnel support under contract will reduce the labor costs that will be experienced by a stand-alone facility. The commercial production facility will also be a revenue source for the NBTF.

The proximity of good transportation services is also key to the success of the venture. Location near a major hub airport with *easy access to both coasts* from its central national location is very important for the distribution of radioisotopes with various half-lives, some of which may be quite short-lived.

9.1.2.2 Business Environment

Billings by U.S. health care providers for over 11,000,000 nuclear medicine procedures totaled over $8 billion in 1993. Eighty-five percent of these procedures were done in a hospital setting. To generate this activity, the providers purchased approximately $500 million of radiopharmaceuticals, including the cold kits developed by the radiopharmaceutical manufactures to be combined with radioisotopes to create an injected patient dose. Over 75% of this revenue went to the big three radiopharmaceutical companies — Du Pont-Merck, Mallinckrodt, and the Medi+Physics division of Amersham International.

To generate the above revenue, the radiopharmaceutical manufactures make or buy approximately $70 million of bulk radiochemicals for their use in the production of radiopharmaceuticals. Approximately 60% of this bulk radiochemical product's dollar value

is manufactured in the drug companies' own cyclotron facilities, while another 30% is purchased from one supplier, Nordion of Canada. The remaining 10% is acquired from various sources, the chief one being DOE's Isotope Production and Distribution Program (IPDP). The most important single product in the marketplace is the molybdenum-99 generator, whose daughter product, technetium-99m, is used in over 75% of all nuclear medicine procedures. Nordion is the leading producer and marketer of Mo-99.

Nuclear medicine procedures are estimated to be growing at approximately 5% annually; however, cardiovascular studies are growing at 10%, and oncology studies have tripled between 1992 and 1994. Tumor diagnosis and therapy is projected to be the most exciting growth area in the next few years. The advent of high resolution imaging equipment that can use higher energy gamma photons will stimulate the use of a greater range of new radionuclides.

The radionuclide industry, in many ways, is a mature industry, but in other ways, many changes are bringing new challenges to management. Events in recent years have led to concern over the reliability of the supply of even the most widely used radioisotope in nuclear medicine. Commercial production of radionuclides has concentrated on a few products which are highly profitable. These and other factors have combined to put the supply of other radioisotopes, and particularly research radioisotopes, in jeopardy.

Several new technologies are critically dependent on a reliable supply of research isotopes. Changing political and regulatory forces have threatened the research radioisotope supply. DOE has attempted for a number of years to maintain an adequate supply, but the national laboratories have historically had other programmatic priorities which have interrupted isotope production. The growth of the market and the development of new procedures and technologies is intimately tied to the supply of research isotopes.

The principal elements of a regulatory nature which will affect the construction and continued development of the NBTF are state and federal environmental, safety, and health requirements. These will be addressed by both NTRI and AITI simultaneously in a joint effort during the first two years of the project, thus achieving some economy of scale in accomplishing the required ES&H studies, certification, and licensing. Some applications planned for the NBTF will require special permits for the transportation and retention of moderate quantities of radioactive materials. The team assembled by NTRI for this proposal has specific personnel skilled in the transportation, storage, and control of such substances. Hence, the development of procedures necessary to meet state and federal requirements is considered low-risk.

The secondary sources of radioisotopes outside of the NBTF will be the national laboratories and sources outside the United States. Federal policy will strongly impact the interaction between the NBTF and the national laboratories.

It is anticipated that the NBTF and its associated members will be in continued competition for education and research grants. The Association of local and regional universities, medical centers, laboratories, and industries will enhance their competitive position for these grants.

The principal potential *barriers* to achieving the goals of the NBTF are:

1. Timely decisions and funding necessary to maintain program continuity,

2. A coordinated DOE policy toward isotope production with strong support for the NBTF, and

3. Obtaining commitments from key customers to utilize the facilities (once complete) and purchase its products and services at the levels projected in the marketing plan.

9.1.2.3 Risks and Opportunities

The first major strength of the proposal is the presence of a highly qualified team, capable of addressing all aspects of radionuclide and stable isotope production. As summarized in Section 2.1 of the main body of this report, and detailed in Appendices I and II, the team behind this proposal is extremely well qualified and represents an outstanding resource on which to draw.

The second major strength is the context in which we propose to develop the NBTF. Co-locating the NBTF with a commercial production facility is a nessary prerequisite to success. In addition, the proposed imaging research facility will provide a significant advantage to the NBTF that will be both a consumer of the NBTF's products and a partner in research and development. Further, the Dallas-Fort Worth regional location is perfectly positioned for national and North American continental distribution.

The greatest barriers to success of the proposed NBTF are the uncertainty of DOE policy and the international market. By its actions, DOE could choose to support or undermine the NBTF through the national laboratories. This proposal is based on the assumption that DOE supports the mission of the NBTF and the goals contained in the recent Institute of Medicine report, *Isotopes for Medicine and the Life Sciences* (Adelstein and Manning, 1994) and interests expressed by related organizations.

9.1.3 Description of Products and Services

The products and/or services of the proposed NBTF are described in detail in Section 4.0 of this report and further discussed in Sections 7.0 (research) and 8.0 (education).

9.2 Management and Operational Plan

The management and operational plan is discussed in Section 6.0 of this report.

9.3 Financial Plan

The NBTF is expected to operate at a break-even point within four to five years after the installation and commissioning of the cyclotron and associated facilities. The source of funds for NBTF construction are a $25 million government guaranteed interest free loan, and in kind facilities donated by UNT. The sections below describe and analyze the operating revenues and the operating expenses.

9.3.1 NBTF Operating Revenues

The estimated annual revenue by category is shown in Table 9.3-1. These estimates are based on the market size and expected market penetration.

- Income from the sale of research isotopes will grow to be approximately $3.5 million, which is about 40% of the research isotope market, including imaging, therapeutic, industrial, and biomedical/special life sciences radionuclides. The estimate of market penetration is based on a previous market survey commissioned by NTRI, market surveys done in connection with the DOE-funded study of salvaging SSC assets, and a market survey of research isotopes done by NTRI as a part of the NBTF project definition study. The estimate also rests on the assumption that isotope production will decrease at LAMPF. If DOE chooses to limit commercial production of research isotopes at BLIP, the market penetration will be much greater. The market penetration in year one of operation is estimated to be 5%, which will grow to 40% in year five of operation.

Revenue Category	Year 1 Est'd. Rev.	Year 2 Est'd. Rev.	Year 3 Est'd. Rev.	Year 4 Est'd. Rev.	Year 5 Est'd. Rev.	Year 6 Est'd. Rev.	Year 7 Est'd. Rev.
Nuclear Medicine Community							
Imaging Radionuclides	$0	$0	$100,000	$250,000	$650,000	$1,000,000	$1,500,000
Therapy Radionuclides	$0	$0	$48,000	$96,000	$180,000	$360,000	$720,000
Industrial Radionuclides	$0	$0	$225,000	$450,000	$600,000	$750,000	$900,000
Biomedical/Specialty Life Sciences Radi	$0	$0	$50,000	$100,000	$200,000	$300,000	$375,000
Radiopharmaceutical Companies							
R&D Contracts	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Service Irradiations	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Low Demand Comercial Products	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Tech. Transfer and Royalties	$0	$0	$0	$0	$100,000	$175,000	$250,000
Production Rights Advance	$750,000	$750,000					
AITI							
R&D Support	$0	$0	$300,000	$300,000	$300,000	$300,000	$300,000
Backup Production	$0	$0	$278,000	$556,000	$695,000	$834,000	$973,000
Department of Energy							
Education and Training	$0	$0	$250,000	$500,000	$750,000	$900,000	$1,000,000
R&D Grants and Contracts	$500,000	$500,000	$500,000	$750,000	$900,000	$1,100,000	$1,250,000
Other Federal Agencies							
R&D Grants and Contracts	$0	$0	$500,000	$500,000	$500,000	$500,000	$500,000
States of TX,OK,NM							
Support for Education and Training	$0	$0	$150,000	$150,000	$150,000	$150,000	$150,000
Professional Training							
Cont. Educ. & Distance Learning	$0	$0	$25,000	$50,000	$75,000	$100,000	$125,000
Totals	$1,250,000	$1,250,000	$2,726,000	$4,302,000	$6,000,000	$7,669,000	$9,543,000

Table 9.3-1 NBTF Estimated Annual Revenue by Category

- The radiopharmaceutical companies will be a source of R&D contract revenue, service irradiation revenue, revenue from production contracts for specialized products, revenue from technology transfer royalties, and revenue from product rights advances. Discussions with major radiopharmaceutical representatives have resulted in the revenue estimates shown in Table 9.3-1. A variety of outside users and user groups, including but not limited to the radiopharmaceutical companies, will use and support the four beam lines in the amount of $800,000 per year; e.g., for example four major users or user groups at $200,000 per year. (A rate structure will be established that will permit individual researchers and those seeking preliminary data to participate without excessive fees, as appropriate.)

- Commercial radioisotope production as a backup to the linac production facility is estimated to grow to $970,000 annually in year seven, based on projected downtime and maintenance of the linac. AITI will also purchase R&D support from the NBTF. The estimated revenue (by year) is included in Table 9.3-1.

- Continuing support by DOE, NIH, NSF, and other federal agencies for operation is expected to grow to $2,750,000 per year. These funds will be obtained through the standard competitive research grant and contract systems.

- Conversations with state officials indicate that support for education and training is an additional source of revenue as shown in Table 9.3-1. Also shown in the table is a modest amount of revenue from continuing education and distance learning fees.

9.3.2 NBTF Operating Expenses

An NBTF full time equivalent staffing summary is shown in Table 9.3-2. The full time equivalents are separated by labor class and year. The manning summary and the NTRI salary for each labor class are used to calculate the total annual expenses for salaries and wages shown in Table 9.3-3.

NTRI fringe benefits are 23% of the salaries and wages as set by the NTRI standard rates, plus any insurance premium contributions.

The NTRI permanent and expendable equipment are estimated on the bases of the schedule of activities, number of personnel, and past experience.

Labor Class	Yr 1 FTE	Yr 2 FTE	Yr 3 FTE	Yr 4 FTE	Yr 5 FTE	Yr 6 FTE	Yr 7 FTE
Director	1	1	1	1	1	1	1
Research Scientists							
Radiochemist	2	2	2	2	2	2	2
Pharmaceutical Chemist	0	1	1	2	2	2	2
Physicist	1	1	1	2	2	2	2
ES&H Scientist	0.25	0.25	1	1	1	1	1
Research Associates							
Post Doctoral Associates	0	0	2	4	6	8	8
Research Assistants	0	0	1	2	3	4	4
Operations							
Accelerator Operators	0	0.5	1.5	2	2.55	3	3
Health Physics Techs.	0	1	1	1	1	1	1
Process/Chemical Techs.	0	1	2	2	2	2	2
Target Dev.&Prep. Techs.	0	0.5	2	2	2	2	2
QA/QC Staff	0	0.5	1	2	2	2	2
Mechanical Techs.	0	1	1	2	3	3	3
Education & Training Staff	0	0	1	1	1	1	1
Administration	1	1	2	2	2	2	2
Total FTEs	**5.25**	**10.75**	**20.5**	**28**	**32.55**	**36**	**36**

Table 9.3-2 NBTF Labor Full Time Equivalents

Expense Category	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
A. NTRI Salaries and Wages							
Staff Salaries and Wages	$260,000	$527,500	$894,500	$1,269,000	$1,435,750	$1,558,000	$1,558,000
Management Salaries	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000
Technical/Admin. Salaries	$26,000	$26,000	$52,000	$52,000	$52,000	$52,000	$52,000
B. NTRI Fringe Benefits @ 23%	$88,780	$150,305	$240,695	$326,830	$365,183	$393,300	$393,300
C. NTRI Permanent Equipment	$0	$0	$35,000	$20,000	$15,000	$15,000	$15,000
D. NTRI Expendable Equipment	$1,000	$2,000	$3,500	$4,500	$5,000	$5,000	$5,000
E. NTRI Supplies Mat'ls and Serv's							
Equipment Lease	$7,000	$14,000	$5,000	$0	$0	$0	$0
Equipment Maintenance	$0	$0	$50,000	$300,000	$450,000	$450,000	$450,000
Housekeeping	$0	$0	$22,000	$45,000	$46,000	$46,000	$46,000
Utilities	$5,000	$100,000	$200,000	$300,000	$375,000	$450,000	$450,000
Facilities Lease	$6,000	$12,000	$12,000	$0	$0	$0	$0
Office Supplies	$5,000	$5,000	$10,000	$15,000	$20,000	$20,000	$20,000
Professional Symposiums	$1,500	$3,500	$5,500	$6,300	$7,000	$7,000	$7,000
Dues and Subscriptions	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Meetings and Conferences	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Stable Isotopes	$0	$20,000	$100,000	$150,000	$225,000	$300,000	$300,000
F. NTRI Travel							
General Travel	$20,000	$15,000	$10,000	$10,000	$7,000	$7,000	$7,000
G. NTRI Publications	$0	$0	$5,000	$10,000	$10,000	$10,000	$10,000
H. NTRI Reproduction	$2,000	$4,000	$6,000	$8,000	$10,000	$10,000	$10,000
I. NTRI Communication	$6,000	$12,000	$12,000	$8,000	$9,000	$9,000	$9,000
J. NTRI Computer	$1,000	$2,000	$3,400	$4,500	$5,000	$5,000	$5,000
K. NTRI Consultants	$80,000	$125,000	$85,000	$30,000	$20,000	$20,000	$20,000
L. NTRI Subcontracts							
Waste Removal	$0	$0	$5,000	$10,000	$15,000	$15,000	$15,000
Legal Services	$30,000	$20,000	$12,000	$10,000	$10,000	$10,000	$10,000
Liability Insurance	$0	$0	$7,000	$7,000	$7,000	$7,000	$7,000
Licenses	$0	$0	$11,000	$11,000	$11,000	$11,000	$11,000
Marketing & Distribution	$0	$0	$30,000	$80,000	$80,000	$80,000	$80,000
M. NTRI Ind't Costs MTDC def @26%	$144,633	$264,499	$467,895	$697,094	$831,982	$910,078	$910,078
Subtotal Annual Expenses	$785,913	$1,406,804	$2,392,490	$3,483,224	$4,121,915	$4,500,378	$4,500,378
Other Operating Costs							
Amortization	$0	$0	$0	$833,000	$833,000	$833,000	$833,000
Total Annual Costs	$785,913	$1,406,804	$2,392,490	$4,316,224	$4,954,915	$5,333,378	$5,333,378

Table 9.3-3 NBTF Annual Operating Expenses By NTRI Expense Class

The NTRI supplies and materials include equipment lease, equipment maintenance, housekeeping, utilities, facilities lease, office supplies, professional symposia, dues and subscriptions, meetings and conferences, and stable isotopes. The three largest of these subcategories (utilities, stable isotopes and equipment maintenance) are estimated based on the expected products and operating schedules for the proposed equipment.

The NTRI publications, reproduction, communication, and computer expenses are based on long-term experience and the estimated staffing levels.

The NTRI subcontracts include waste removal, legal services, insurance, licenses, and marketing and distribution. The NTRI indirect costs are the standard NTRI off-campus rates. Other operating expenses include amortization of the $25 million, 30-year interest free loan. These Operating Expenses are summarized in Table 9.3-3.

9.3.3 Analysis of Annual Revenues and Expenses

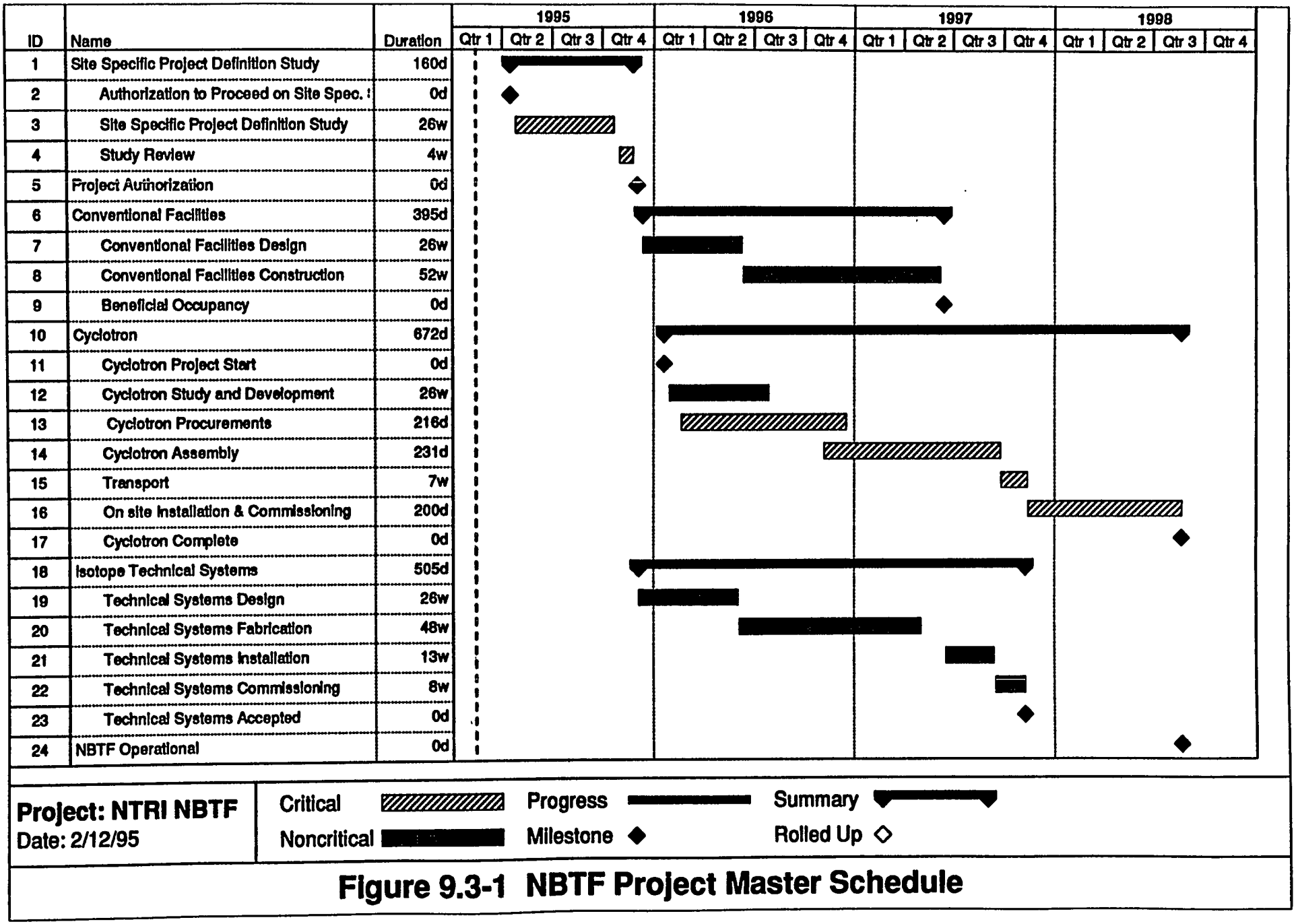
Table 9.3-4 shows an analysis of annual revenues and expenses. The expenses begin in year one, and the isotope revenue does not start until year three when the cyclotron is commissioned. Similarly, the amortization of the 30 year loan does not begin until the fourth year after the NBTF is fully operational. The operating expenses are separated into the standard NTRI expense categories and those that fall outside of the normal NTRI expense categories. No indirect costs are applied to the non-normal categories.

The excess (deficiency) of operating expenses is debited by a depreciation amount of $1.25 million per year. This amount is a straight-line result of depreciating $25 million worth of equipment and facilities over 20 years.

The bottom line excess (deficiency) of revenues over expenses shows a deficit through year five or the third year of cyclotron operation. The deficit averages ~$1 million per year and peaks in year four at approximately ~$1.2 million. Self sufficiency is achieved in year six or the fourth year of cyclotron operation. A project construction master schedule is shown Figure 9.3-1. The cyclotron construction schedule is the critical path for the project. The current cyclotron includes full assembly and testing at the manufacturer's plant before shipping. Substantial time savings may be achieved if the cyclotron is assembled and tested at the North Texas site. A detail of the cyclotron fabrication schedule is also shown in Figure 9.3-2.

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Operating Revenues							
Total Revenues from all Constituencies	$1,250,000	$1,250,000	$2,726,000	$4,302,000	$6,000,000	$7,669,000	$9,543,000
Operating Expenses							
A. Salaries and Wages	$386,000	$653,500	$1,046,500	$1,421,000	$1,587,750	$1,710,000	$1,710,000
B. Fringe Benefits @ 23%	$88,780	$150,305	$240,695	$326,830	$365,183	$393,300	$393,300
C. Permanent Equipment	$0	$0	$35,000	$20,000	$15,000	$15,000	$15,000
D. Expendable Equipment	$1,000	$2,000	$3,500	$4,500	$5,000	$5,000	$5,000
E. Supplies Mat'ls and Serv's	$26,500	$158,500	$412,500	$825,300	$1,133,000	$1,283,000	$1,283,000
F. Travel	$20,000	$15,000	$10,000	$10,000	$7,000	$7,000	$7,000
G. Publications	$0	$0	$5,000	$10,000	$10,000	$10,000	$10,000
H. Reproduction	$2,000	$4,000	$6,000	$8,000	$10,000	$10,000	$10,000
I. Communication	$6,000	$12,000	$12,000	$8,000	$9,000	$9,000	$9,000
J. Computer	$1,000	$2,000	$3,400	$4,500	$5,000	$5,000	$5,000
K. Consultants	$80,000	$125,000	$85,000	$30,000	$20,000	$20,000	$20,000
L. Subcontracts	$30,000	$20,000	$65,000	$118,000	$123,000	$123,000	$123,000
M. Indirect Costs MTDC def @ 26%	$144,633	$264,499	$467,895	$697,094	$831,982	$910,078	$910,078
Total Annual Operating Expenses	$785,913	$1,406,804	$2,392,490	$3,483,224	$4,121,915	$4,500,378	$4,500,378
Excess (Deficiency) of Operating Revenues Over Operating Expenses *Before Other Expenses*	*$464,087*	*($156,804)*	*$333,510*	*$818,776*	*$1,878,085*	*$3,168,622*	*$5,042,622*
Other Expenses							
Amortization	$0	$0	$0	$833,000	$833,000	$833,000	$833,000
Excess (Deficiency) of Operating Revenues over Operating Expenses	$464,087	($156,804)	$333,510	($14,224)	$1,045,085	$2,335,622	$4,209,622
Depreciation			$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000
Excess (Deficiency) of Revenues over Expenses	$464,087	($156,804)	($916,490)	($1,264,224)	($204,915)	$1,085,622	$2,959,622

Table 9.3-4 Analysis of Annual Revenues and Expenses in CY1995 Dollars

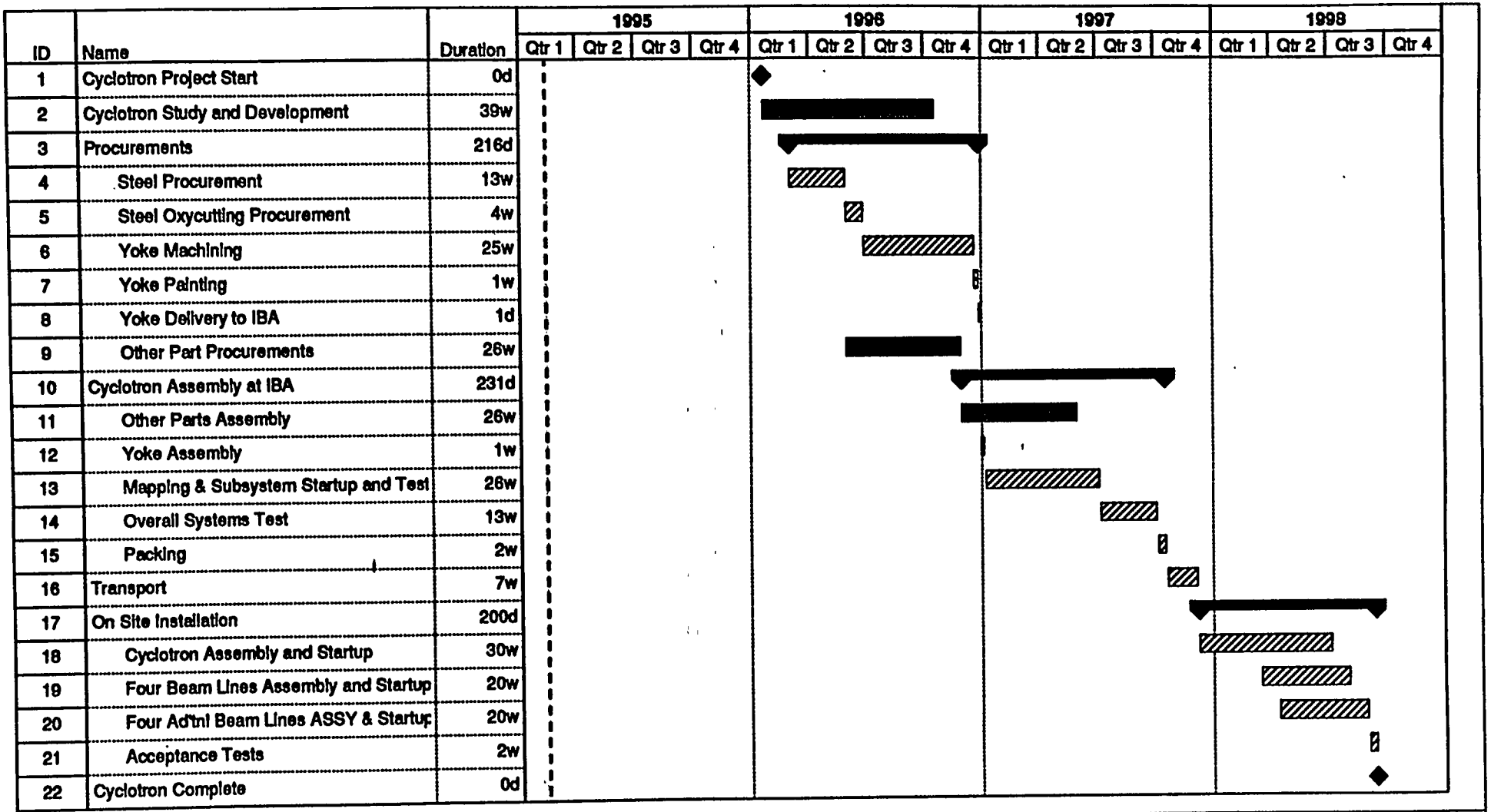


ID	Name	Duration
1	Site Specific Project Definition Study	160d
2	Authorization to Proceed on Site Spec. !	0d
3	Site Specific Project Definition Study	26w
4	Study Review	4w
5	Project Authorization	0d
6	Conventional Facilities	395d
7	Conventional Facilities Design	26w
8	Conventional Facilities Construction	52w
9	Beneficial Occupancy	0d
10	Cyclotron	672d
11	Cyclotron Project Start	0d
12	Cyclotron Study and Development	26w
13	Cyclotron Procurements	216d
14	Cyclotron Assembly	231d
15	Transport	7w
16	On site Installation & Commissioning	200d
17	Cyclotron Complete	0d
18	Isotope Technical Systems	505d
19	Technical Systems Design	26w
20	Technical Systems Fabrication	48w
21	Technical Systems Installation	13w
22	Technical Systems Commissioning	8w
23	Technical Systems Accepted	0d
24	NBTF Operational	0d

Project: NTRI NBTF
Date: 2/12/95

Critical
Noncritical
Progress
Milestone
Summary
Rolled Up

Figure 9.3-1 NBTF Project Master Schedule



ID	Name	Duration
1	Cyclotron Project Start	0d
2	Cyclotron Study and Development	39w
3	Procurements	216d
4	Steel Procurement	13w
5	Steel Oxycutting Procurement	4w
6	Yoke Machining	25w
7	Yoke Painting	1w
8	Yoke Delivery to IBA	1d
9	Other Part Procurements	26w
10	Cyclotron Assembly at IBA	231d
11	Other Parts Assembly	26w
12	Yoke Assembly	1w
13	Mapping & Subsystem Startup and Test	26w
14	Overall Systems Test	13w
15	Packing	2w
16	Transport	7w
17	On Site Installation	200d
18	Cyclotron Assembly and Startup	30w
19	Four Beam Lines Assembly and Startup	20w
20	Four Ad'tnl Beam Lines ASSY & Startup	20w
21	Acceptance Tests	2w
22	Cyclotron Complete	0d

Project: NTRI NBTF
Date: 2/12/95

Critical
Noncritical
Progress
Milestone ◆
Summary
Rolled Up ◇

Figure 9.3-2 NBTF Cyclotron Schedule

9.3.3 Analysis of Cash Flows

Table 9.3-5 shows an analysis of cash flows. The excess (deficiency) of operating revenues over operating expenses is adjusted to determine the total cash provided by (used in) operating activities.

The cash flow from investing and financing activities is summarized and added to that of the operating activities to achieve the net increase (decrease) in cash. The annual net increase (decrease) is then used to determine the beginning and end of period cash balances. Project construction costs, summarized in Table 9.3-6, are accounted for in this category.

In the sixth year, or the fourth year of cyclotron operation, the operating revenues becomes positive as full operational status is approached. At this point, the cash flow begins to accumulate capital for the replacement of equipment, as it reaches the end of its useful life. Thus self-sufficiency, dependent on achieving the estimated market penetration, is achieved in year six or the fourth year of cyclotron operation.

9.3.4 Payback of Government-Guaranteed Loan

Table 9.3-7 shows an analysis of the payback of the $25 million government-guaranteed, interest-free loan and the associated interest cost to the government.

A parallel, but more detailed business plan is contained in Appendix IX.

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Cash Flows from Operating Activities							
Excess (Deficiency) of Operating Revenues over Operating Expenses	$464,087	($156,804)	($916,490)	($1,264,224)	($204,915)	$1,085,622	$2,959,622
Add Adjustments to Reconcile Excess (Deficiency) of Operating Revenues to Net Cash Provided by (Used in) Operating Activities							
Depreciation			$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000
Total Adjustments	$0	$0	$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000
Total Cash Provided by (Used in) Operating Activities	$464,087	($156,804)	$333,510	($14,224)	$1,045,085	$2,335,622	$4,209,622
Cash Flow from Investing Activities							
Construction and Development Costs	($4,000,000)	($8,700,000)	($10,800,000)				
ES&H Expenditures	($800,000)	($800,000)					
Total Cash Provided by (Used in) Investment Activities	($4,800,000)	($9,500,000)	($10,800,000)	$0	$0	$0	$0
Cash Flow from Financing Activities							
DOE Interest Free Loan	$25,000,000						
Total Cash Provided by (Used in) Financing Activities	$25,000,000	$0	$0	$0	$0	$0	$0
Net Increase (Decrease) in Cash	$20,664,087	($9,656,804)	($10,466,490)	($14,224)	$1,045,085	$2,335,622	$4,209,622
Cash, Beginning of Period		$20,664,087	$11,007,283	$540,793	$526,569	$1,571,654	$3,907,276
Cash, End of Period	$20,664,087	$11,007,283	$540,793	$526,569	$1,571,654	$3,907,276	$8,116,898

Table 9.3-5 Analysis of Cash Flows in CY 1995 Dollars

		W.O. Contingency	Contingency Incl.
Project Total		$23,583,000	$24,913,000
Equipment Total		$18,093,000	$18,639,000
Cyclotron	$13,563,000		
Beamlines	$1,800,000		
Target Stations	$300,000		
Target Transfer Systems	$150,000		
Education,Training, &Res. Hot Lab Equipment	$500,000		
*****Processing Equipment Supplied by AITI	$0		
Laboratory Equipment	$575,000		
Laboratory Furniture	$225,000		
General Facility Furnishings	$100,000		
Auditorium Furnishings	$100,000		
Control & Safety Systems	$250,000		
Shop Equipment	$100,000		
Exhaust Systems	$100,000		
Target Station Caves	$200,000		
Chilled Water System	$80,000		
Deionized System	$50,000		
Facilities Total		$3,920,000	$4,704,000
Architect	$180,000		
A-E	$300,000		
Construction Total		$3,440,000	
Below Grade Facilities Total		$480,000	
Accelerator Vault (Modification of Existing Facili	$50,000		
Tunnels	$65,000		
Waste Tank Containment Vault	$50,000		
Above Grade Facilities Total		$2,960,000	
Control Building	$160,000		
Res, Education & Training Building	$2,500,000		
*****Processing Facility supplied by AITI	$0		
Waste Holding & Reduction Facility	$200,000		
Site Preparation	$100,000		
ES&H Total		$1,570,000	$1,570,000
ES&H Systems Total		$570,000	
Storage Tanks	$150,000		
Stack	$100,000		
Stack Monitoring	$80,000		
Water Monitoring	$80,000		
Air Monitoring	$80,000		
Personnel Monitoring	$40,000		
Waste Monitoring	$40,000		
ES&H Compliance Programs		$1,000,000	

Table 9.3-6 NBTF Project Construction Cost Estimate Summary

Year	Amount of loan			Annual NBTF Federal Costs — A —	Amount of loan			Annual NBTF Federal Costs — B —	Difference A - B
	$25,100,000	$25,100,000		$26,355,000	$25,100,000	$25,100,000		$24,489,000	$1,866,000
		Repayment of principal	Principal remaining	▼▼▼ 6%		Repayment of principal	Principal remaining	▼▼▼ 6%	
1	$25,100,000	$0	$25,100,000	$1,506,000	$4,800,000	$0	$4,800,000	$288,000	$1,218,000
2		$0	$25,100,000	$1,506,000	$9,500,000	$0	$14,300,000	$858,000	$648,000
3		$0	$25,100,000	$1,506,000	$10,800,000	$0	$25,100,000	$1,506,000	$0
4		$836,667	$24,263,333	$1,455,800		$836,667	$24,263,333	$1,455,800	$0
5		$836,667	$23,426,667	$1,405,600		$836,667	$23,426,667	$1,405,600	$0
6		$836,667	$22,590,000	$1,355,400		$836,667	$22,590,000	$1,355,400	$0
7		$836,667	$21,753,333	$1,305,200		$836,667	$21,753,333	$1,305,200	$0
8		$836,667	$20,916,667	$1,255,000		$836,667	$20,916,667	$1,255,000	$0
9		$836,667	$20,080,000	$1,204,800		$836,667	$20,080,000	$1,204,800	$0
10		$836,667	$19,243,333	$1,154,600		$836,667	$19,243,333	$1,154,600	$0
11		$836,667	$18,406,667	$1,104,400		$836,667	$18,406,667	$1,104,400	$0
12		$836,667	$17,570,000	$1,054,200		$836,667	$17,570,000	$1,054,200	$0
13		$836,667	$16,733,333	$1,004,000		$836,667	$16,733,333	$1,004,000	$0
14		$836,667	$15,896,667	$953,800		$836,667	$15,896,667	$953,800	$0
15		$836,667	$15,060,000	$903,600		$836,667	$15,060,000	$903,600	$0
16		$836,667	$14,223,333	$853,400		$836,667	$14,223,333	$853,400	$0
17		$836,667	$13,386,667	$803,200		$836,667	$13,386,667	$803,200	$0
18		$836,667	$12,550,000	$753,000		$836,667	$12,550,000	$753,000	$0
19		$836,667	$11,713,333	$702,800		$836,667	$11,713,333	$702,800	$0
20		$836,667	$10,876,667	$652,600		$836,667	$10,876,667	$652,600	$0
21		$836,667	$10,040,000	$602,400		$836,667	$10,040,000	$602,400	$0
22		$836,667	$9,203,333	$552,200		$836,667	$9,203,333	$552,200	$0
23		$836,667	$8,366,667	$502,000		$836,667	$8,366,667	$502,000	$0
24		$836,667	$7,530,000	$451,800		$836,667	$7,530,000	$451,800	$0
25		$836,667	$6,693,333	$401,600		$836,667	$6,693,333	$401,600	$0
26		$836,667	$5,856,667	$351,400		$836,667	$5,856,667	$351,400	$0
27		$836,667	$5,020,000	$301,200		$836,667	$5,020,000	$301,200	$0
28		$836,667	$4,183,333	$251,000		$836,667	$4,183,333	$251,000	$0
29		$836,667	$3,346,667	$200,800		$836,667	$3,346,667	$200,800	$0
30		$836,667	$2,510,000	$150,600		$836,667	$2,510,000	$150,600	$0
31		$836,667	$1,673,333	$100,400		$836,667	$1,673,333	$100,400	$0
32		$836,667	$836,667	$50,200		$836,667	$836,667	$50,200	$0
33		$836,667	($0)	($0)		$836,667	($0)	($0)	$0

10.0 REFERENCES

10.1 General References:

Arthur Andersen & Co. 1993 *U.S. Department of Energy Isotope Production and Distribution Program Management Study*. Washington, DC.

Choppin, G.R. and M.J. Welch (eds.) 1988 *Training Requirements for Chemists in Nuclear Medicine, Nuclear Industry, and Related Areas: Report of a Workshop*. Washington, DC, National Academy Press.

Environmental Protection Agency 1989 *User's Guide for the COMPLY Code*. U.S. Environmental Protection Agency, Office of Radiation and Indoor Air, EPA 520/1-89-003, October 1989

Gardner, P. 1994 Technology at TRIUMF. *Proceedings of EPAC 94, the 4th European Particle Accelerator Conference*, London, June 27-July 1, 1994 (TRI-PP-94-40).

Gibson, D.V. and E.M. Rogers 1994 *R&D Collaboration on Trial. The Microelectronics and Computer Technology Corporation.* Harvard Business School Press, Boston.

Holmes, R.A. 1991 *National Biomedical Tracer Facility Planning and Feasibility Study.* New York, NY, Society of Nuclear Medicine.

Kliewer, K.L. and M.A. Green (eds.) 1992 *Proceedings of the Purdue National Biomedical Tracer Facility Workshop*. Purdue University, West Lafayette, Indiana.

McAfee, J.G. 1989 *Nuclear Medicine. Report for the U.S. Department of Energy Office of Energy Research on the Department's Nuclear Medicine Research Program by the Health and Environmental Research Advisory Committee (HERAC).* Washington, DC, U.S. Department of Energy.

Moody, D.C. and E.J. Peterson (eds.) 1989 *Proceedings of the DOE Workshop on the Role of a High-Current Accelerator in the Future of Nuclear Medicine.* Report LA-11579-C, Los Alamos, NM, Los Alamos National Laboratory.

Oak Ridge Institute of Science and Education 1993 *Status of Graduate Programs in Radiochemistry and Nuclear Chemistry, 1992.* Oak Ridge, TN, Oak Ridge Institute for Science and Education.

University of Missouri Research Reactor Center 1994 *1993 MURR Annual Report.* Columbia, MO, University of Missouri.

U.S. Department of Energy Isotope Production and Distribution Program 1994 *U.S. Department of Energy National Isotope Strategy.* Prepared by the Isotope Production and Distribution Program, August 1994, Publication DOE/NE-0111, Washington, DC 20585.

Verma, V.K. and P. Gardner 1994 Technology Transfer from Accelerator Laboratories (Challenges and Opportunities). *Proceedings of EPAC 94, the 4th European Particle Accelerator Conference*, London, June 27-July 1, 1994 (TRI-PP-94-50).

Yates, S.W. 1993 Future Challenges in Nuclear Science Education. *Journal of Radioanalytical and Nuclear Chemistry* 171: 15-21.

10.2 Targetry References:

"Workshop on Gas Targetry," *Proceedings of the First Workshop on Targetry and Target Chemistry*, Heidelberg, West Germany, October 4-7, 1984 (F. Helus, T.J. Ruth, B.W. Wieland, eds.) Deutsches Krebsforchungszentrum, Institut fur Nuklearmedizin.

"Workshop on Targetry and Target Chemistry," *Proceedings of the 2nd Workshop on Targetry and Target Chemistry*, Heidelberg, West Germany, September 22-25, 1987 (T.J. Ruth, S.A. McQuarrie, and F. Helus, eds.) Deutsches Krebsforchungszentrum, Institut fur Nuklearmedizin.

"Workshop on Targetry and Target Chemistry," *Proceedings of the Third Workshop on Targetry and Target Chemistry*, Vancouver, B.C., June 1989 (T.J. Ruth, ed.) Triumf.

"Targetry '91," *Proceedings of the IVth Workshop on Targetry and Target Chemistry*, Villigen, Switzerland, September 9-12, 1991 (R. Weinreich, T.J. Ruth, and F. Helus, eds.) Paul Scherrer Institut.

APPENDIX I

PRINCIPAL CONTRIBUTORS TO THIS STUDY
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APPENDIX II

INSTITUTIONAL PROFILES AND EXPERTISE
(In Alphabetical Order)

ADVANCED ISOTOPE TECHNOLOGIES, INC. (AITI)

Advanced Isotope Technologies, Inc. (AITI), originally incorporated as the North Texas Research and Development Corporation (NTR&D), is a *for-profit* Texas corporation, incorporated in August, 1991. As the corporation's name implies, its major thrust is commercial development of isotopes for medicine and industry. AITI's primary purpose is to commercialize technology and intellectual property developed by the University of North Texas (UNT), UNT's not-for-profit affiliate, the North Texas Research Institute (NTRI), and other selected corporate, institutional affiliates, and government agencies — including the national laboratories.

Research and Development efforts leading to commercial products is done both through UNT/NTRI faculty, staff, and facilities and by AITI's own staff and facilities. In partnership with UNT and NTRI, AITI acts as an R&D funding source and a holding company and incubator of new companies based on UNT/NTRI developments and those of other universities and technology sources.

AITI's current Board of Directors includes **Dr. George A. Keyworth** (Chair), **Dr. Ira Lon Morgan** (President), **Dr. Edward A. Knapp** (Senior Vice President), and **Mr. Will J. Lepeska** (Vice President for Marketing). In addition, **Mr. Michael G. van Hoye** serves as Chief Operating Officer. Dr. Keyworth, former Science and Technology Advisor to President Ronald Reagan, is currently a Director of the Hewlett-Packard Corporation, for which he also serves in a variety of other roles, and is a member of the Hudson Institute and Trustee of the Santa Fe Institute. Dr. Knapp, former Director of the National Science Foundation and the Universities Research Association, recently moved from the directorship of the Los Alamos Meson Physics Facility (an 800 MeV linear accelerator) to the Presidency of the Santa Fe Institute. Dr. Morgan's 30-year association with the University of Texas at Austin included service as Professor of Physics and Director of the Center for Nuclear Studies. Dr. Morgan is a scientific and technological entrepreneur who has successfully transferred university-originated nuclear technology into the marketplace by founding four successful companies, including Columbia Scientific, Texas Nuclear (later merged with Nuclear Chicago), International Digital Modeling Corporation (industrial tomography), and AITI. Mr. Lepeska is President of Hospital Financial Corporation, an early pioneer in the leasing of nuclear medical equipment to hospitals. Mr. Lepeska was formerly Vice President for Marketing for Nuclear Chicago Corporation and Marketing Manager for G.D. Searle & Co.

AITI will finance, build, and operate the 70 MeV, 1 mA linac and processing facilities proposed for the commercial production facility. **Dr. Edward Knapp**, a

contributor to this study and proposal and AITI Senior Vice President, directed the design, construction, and operation of the accelerator structures of LAMPF and served as its director in 1989-1990. The radioisotope production linac proposed here is based on LAMPF's injector linac.

AITI is currently bringing two new technologies to the marketplace. Its *Pulsed Sealed Neutron Tube*™ uses a dense plasma focus of deuterium or deuterium/tritium to create a neutron flux sufficient to convert stable isotopes to radioisotopes in quantity. This device will permit production of radioisotopes through standard neutron reactions, similar to those performed in a nuclear reactor. The second technology is an *Intense Laser Source*, which couples inexpensive low-power lasers to produce a coherent, high-power beam. This technology may advance the art of isotope separation with the goal of substantially lowering the cost of stable isotopes for which the current suppliers to U.S. companies are foreign.

AMPARO CORPORATION

Amparo Corporation of Santa Fe, New Mexico provides consulting services in physics and computational sciences. The company, which is headed by **Dr. James J. Walker** is staffed largely by recently retired LANL personnel who bring a wealth of experience to bear on technology applications and technical problem-solving. One of the company's strongest areas of expertise is particle accelerator physics and technology and nuclear and atomic sciences. **Drs. Andrew A. Browman, Pierre Grand, Don W. Reid, and Willard L. Talbert, Jr.,** worked with the UNT group earlier on a study to use the Superconducting Super Collider's injector linac as the source of a particle beam for commercial radioisotope production. Dr. Pierre Grand has also participated in the development of this project definition study. In the SSC study, in particular, Amparo personnel contributed often as expert critics of designs and procedures, based on their extensive experience in doing practical physical science. Amparo experts will continue to play the role of institutional devil's advocate, and will also contribute directly to the further development of the plan contained in this study.

Recently, AITI entered into a collaborative agreement with Amparo regarding the development of high current targets for radioisotope production. This R&D effort is based on Amparo's previous work on a high current target to be used in the production of secondary radioactive beams at Oak Ridge National Laboratory. AITI's interest is in a high current, encapsulated, cooled target system for the production of radionuclides in the solid, liquid, or gaseous phases. Such a target system would serve both the production and research capabilities of the proposed accelerator center. Amparo will also participate as a collaborator in the area of other targets, shielding design, instrumentation, and accelerator systems.

BECHTEL RESEARCH AND DEVELOPMENT

Bechtel Research and Development (Bechtel R&D) is a division of the Bechtel Corporation. Bechtel R&D is well qualified to contribute to the scoping of cost estimates, conceptual design, preliminary engineering, final design and costing, construction management, equipment installation, and start-up for the proposed radioisotope production facilities. Bechtel R&D has designed and managed the construction of reactor-based radioisotope facilities, such as the research and commercial isotope facility in Bandung, Indonesia, as well as a similar installation in Thailand. Bechtel R&D is the architect engineer for Los Alamos' proton linear accelerator (linac) program for tritium production, a device that is quite similar to the proton linac proposed for the commercial production facility. Bechtel R&D is also intimately involved in the design, program management and eventual construction of the proton therapy facility for Massachusetts General Hospital in Boston. That facility will employ a cyclotron similar to that proposed for the NBTF, but more energetic (230 MeV), and which requires the same sort of neutron and radiation shielding.

Bechtel R&D's nuclear expertise spans all aspects of nuclear facilities, from handling of water, gaseous, molten salt, and liquid metal coolants, to the design and construction of reprocessing and nuclear test facilities, engineering and design of isotope separation facilities, design and construction of the retention, transportation, and reprocessing facilities for radioactive waste, commercialization of experimental facilities, retrofitting operations that require penetration and resealing of the very thick reinforced concrete nuclear containment shields, generation and management of requirements and specifications, development of safety procedures, commissioning of nuclear facilities, training of operators, clean-up of release accidents, development and deployment of remotely operated equipment for handling radioactive materials, the performance of safety analyses and risk assessments, and assistance in the siting/permitting regulatory process.

Thus, Bechtel R&D brings a wealth of technical capability to the proposed design, engineering, and construction of the NBTF and commercial isotope production facilities. Bechtel would manage the project under contracts with AITI and the NBTF management entity, either the North Texas Research Institute or another not-for-profit entity.

LOS ALAMOS NATIONAL LABORATORY

The Los Alamos National Laboratory (LANL), established during the wartime Manhattan Project in 1942, is one of the premier U.S. centers for nuclear and atomic research. The Los Alamos Meson Physics Facility (LAMPF) has operated a high energy, high current linear accelerator since the early 1970s, including extensive radioisotope production operations, and the commercial production linac proposed here is a lineal descendent of the LAMPF injector. **Dr. Edward Knapp**, a contributor to this study and proposal, directed the design, construction, and operation of the accelerator structures of

LAMPF and served as its director in 1989-1990. We propose collaboration in this project with LAMPF's radioisotope production operation through the U.S. DOE Isotope Production and Distribution Program (IPDP). This collaboration with IPDP would also serve to coordinate the NBTF's production of research isotopes with that of the Brookhaven Linac Isotope Production Facility (BLIP). We also propose collaboration with **Dr. James Stovall** and his staff at LANL's Accelerator Technology Division in optimizing the design of the proposed linac, RF systems, beam transport, and target systems. Currently, AITI is collaborating with LANL through a Cooperative Research and Development Agreement (CRADA) for work on the *Pulsed Sealed Neutron Tube*™, work originally initiated at Los Alamos through a funds-in agreement between LANL and AITI. This project moved from Los Alamos to UNT facilities under contract to AITI in Denton in January 1995. **Dr. Bruce Freeman**, on leave from LANL under the CRADA, is directing the project. The development of a commercial prototype *Pulsed Sealed Neutron Tube*™ has commenced at the Denton site, which is owned by the University of North Texas and leased to AITI.

THE NORTH TEXAS RESEARCH INSTITUTE

The North Texas Research Institute, Inc. (NTRI) is a *not-for-profit* Texas corporation chartered in accordance with Section 501(c)(3) of the Internal Revenue Service code. As a separate corporate affiliate of the University of North Texas (UNT), whose sole purpose is to benefit the university, NTRI provides a mechanism through which UNT'S outstanding academic resources can be brought to bear on Texas' and North America's needs in business and industry. NTRI is UNT's principal means of forming effective R&D partnerships with business and industry.

Through NTRI, UNT researchers work with industry and other R&D organizations, alone or as project team members, under industry policies and on industry timetables. NTRI can also employ scientists directly and establish separate, specialized facilities to enhance UNT resources, as well as participate in cooperative ventures with other private non-profit and government agencies. Like many other university-affiliated research institutes, NTRI solicits federal contracts, including defense-related R&D projects, when appropriate. However, NTRI places its strongest emphasis on research and development partnerships with industry to aid business competitiveness and economic development.

NTRI is governed by a Board of Directors currently chaired by UNT's Chancellor, **Dr. Alfred F. Hurley**. Other members of the Board include UNT's Provost and Vice President for Academic Affairs, **Dr. Blaine A. Brownell**, and citizens from outside the university who bring a variety of talents to the board. These members include **Dr. Kenneth Dickson** (environmental science and technology), **Dr. Albert H. Halff** (engineering), **Mr. J. Jack Hays** (banking and finance), **Mr. C. Dean Davis** (law and state government), **Mr. Roy Appleton** (news media), and **Dr. Norman A. Hackerman** (science). Dr. Hackerman is past president of both Rice University and the University of Texas at Austin, former chair of the National Science Board, and is currently the Chair of the Scientific Advisory Board of

the Welch Foundation. **Dr. Rollie Schafer** currently serves as Executive Director of NTRI. Dr. Schafer is Professor of Neuroscience and also serves as UNT's Associate Vice President for Research and Dean of the Toulouse School of Graduate Studies.

Examples of the institute's areas of research and development activity include large scale studies in environmental toxicology and the fate of agricultural chemicals in the environment, industrial tomography, software development for robotic vision and control, feature recognition, proprietary software, high-speed encrypted communication, and materials characterization focused at the atomic level of materials such as advanced semiconductors structural alloys. The institute's 40-acre Water Research Field Station is currently the second largest facility in the U.S. accredited by EPA for the certification of agricultural chemicals and pesticides.

SANDIA NATIONAL LABORATORIES

Sandia National Laboratories is a Department of Energy multi-program national laboratory employing about 8500 people, including nearly 4000 technical professionals, and having an annual budget of approximately $1.4 billion. Its mission is to provide scientific and engineering solutions to meet national needs in nuclear weapons and related defense systems, energy security, and environmental integrity, and to address emerging national challenges for both government and industry.

Sandia's core competencies are found in its research foundations and integrated capabilities. Its research foundations are: engineered materials and processes, microelectronics and photonics, computational and information sciences, and engineering sciences. Its integrated capabilities are: advanced manufacturing technology, advanced information technology, electronics technology, and pulsed power technology. Sandia's nuclear technology and nuclear facilities are part of the engineering sciences research foundation.

The DOE Isotope Production and Distribution Program (IPDP) selected the Reactor Engineering Technology Center at Sandia National Laboratories for production of radioisotopes for nuclear medicine pending completion of the National Environmental Policy Act (NEPA) process and approval of a detailed resource-loaded schedule. The facilities selected are the Annular Core Research Reactor (ACRR) and the Hot Cell Facility (HCF) at Sandia National Laboratories Technical Area-V, located on DOE land about four miles south of Albuquerque, New Mexico, on Kirtland Air Force Base. The Sandia Pulse Reactor III (SPR III), which is operated in the same technical area, can also be used without modifications to produce research quantities of radioisotopes.

Sandia and the NBTF consortium that produced this proposal have agreed, under a *Memorandum of Understanding*, to cooperate and provide mutual support in research, development, testing, production, and supply of radioactive and stable isotopes and related areas, including detection, imaging, radiopharmaceuticals development, automation of separation and manufacturing processes, information technology, hazards analysis, facility

operations, and environment, safety, and health issues. Under this agreement the parties will provide to each other such quantities of research and other radioisotopes requested by the other party, consistent with the primary missions of the respective organizations.

TECHNOLOGY COMMERCIALIZATION INTERNATIONAL, INC.

Technology Commercialization International, Inc. (TCI) is a for-profit New Mexico corporation incorporated in December, 1993. The corporation is dedicated to *an improved quality of life through technology*. The company's primary business is the commercialization of technology and intellectual property rights developed by its research staff and by its close association with the University of New Mexico faculty, particularly in the Colleges of Pharmacy and Engineering (Nuclear and Chemical Engineering). The company emphasizes the development and marketing of both stable and radioactive isotopes, as well as the concept of centralized radiopharmacies, know-how, training, and implementation.

The corporation's Board of Directors includes H. William Nordyke, M.S., CMC, President and CEO; William M. Hadley, R.Ph., Ph.D., Professor of Pharmacology/Toxicology and Dean, University of New Mexico College of Pharmacy; Arthur H. Guenther, Ph.D., Science/Advisor to the Governor of New Mexico, Member of the Russian Academy of Sciences and former Chief Scientist for the Air Force's Phillips Laboratory; James Thompson, P.E., Ph.D., Professor and Dean, University of Missouri College of Engineering, also elected Honorary Doctor, Institute of Electrophysics, Russia; and William C. Nunnally, Ph.D., Director, Institute of Physical Electronics, University of Texas at Arlington, formerly of Los Alamos National Laboratory.

Through its extensive international contacts, which are reflected by the board membership above, TCI has obtained exclusive marketing and distribution rights for both stable and radioactive isotopes from several Russian institutes. The corporation's proposal to the United States Industry Coalition (USIC) on a *Process for Improved Separation of Mo-99 from Fission Byproducts* has been approved by the USIC and is awaiting final approval from DOE. This proposal, submitted in December, 1994 is a joint project with Sandia National Laboratories and several Russian institutes for the purpose of developing and commercializing an improved process for the generation and separation of Mo-99 and other radioisotopes for medical applications.

TCI intends to provide a backup source of stable and radioactive isotopes for the NBTF program. Using the advanced technology being proposed and developed by the NTRI consortium, the Mo-98 provided by TCI may be valuable for production of Mo-99 for medical applications.

THE UNIVERSITY OF MISSOURI

The University of Missouri at Columbia (MU) maintains the premier university-based nuclear reactor program in the United States. The MU Research Reactor Center (MURR) is a multi-disciplinary center for research and education in the neutron-related sciences and engineering. The facilities are unmatched at any other U.S. university. The central focus of MURR is a 10 MW light water moderated reactor that is the highest power university research reactor in the U.S. The reactor has been in operation for 26 years, and since 1976 has operated more than 150 hours per week, almost 90% of the available time and 95% of the scheduled time. The reactor is a separate, multi-disciplinary research center that is not part of any MU department. It reports to the MU Vice Provost for Research.

MURR has a three-fold mission of promoting basic and applied research in neutron-related science and engineering, education in these fields, and radiation and isotope production services for public and private consumers. Scientific programs at MURR include archaeometry, neutron and gamma-ray scattering, neutron interferometry, neutron activation analysis, human and animal nutrition, epidemiology and immunology, radiation effects, radioisotope studies, health physics, and nuclear engineering.

MURR brings an impressive variety of expertise and facilities to the consortium. Because its irradiation, processing, and research facilities are very different than those of the Sandia reactor facilities, the two reactor facilities each bring complementary capabilities to this proposal. In addition, a strong program in laser optics and physics is available, which includes an ongoing program in laser isotope separation. The university recently received a gift of the patents on the CRISLA laser isotope separation process and approximately $500,000 in CRISLA equipment. This research effort will complement the research on another laser-based isotope separation technology, MLIS, being pursued by AITI and UNT researchers, and the AVLIS process, which has been under development by DOE at its facilities.

The university also brings a strong program in nuclear engineering to the proposed NBTF program. Graduate degree programs leading to the M.S. and Ph.D. are available in nuclear engineering, with concentrations in nuclear power, health physics, and medical physics.

THE UNIVERSITY OF NEW MEXICO

The University of New Mexico's Colleges of Pharmacy and Engineering bring strong programs in radiopharmacy, radiopharmaceutical research, and nuclear engineering to the consortium, augmented by expertise from other academic and research disciplines at UNM and New Mexico's two national laboratories, Los Alamos National Laboratory (LANL) and Sandia National Laboratories (SNL). The College of Pharmacy has one of the oldest and most highly regarded educational programs in nuclear pharmacy and radiopharmaceutical sciences and has been educating professionals in these disciplines since 1972. Pharmacy

facilities include both standard laboratories and a full-function dispensing radiopharmacy. The College of Engineering has some of the best recognized and well-funded programs in waste management, risk assessment, and health physics concentrations in the country. An educational alliance between the two colleges trains students in nuclear pharmacy with specializations in organic and inorganic synthesis, and analytical chemistry and biochemistry with a focus in radiochemical techniques and instrumentation. The College of Engineering established a radiation protection engineering program in 1990 in response to the identified need for trained practitioners. This training program, with concentrations in radiological physics and radiation dosimetry, includes participation by the Medical School, College of Pharmacy, Biology Department, and several engineering disciplines. Students enroll in practica at Kirtland Air Force Base, SNL, and the UNM Hospital, all located in Albuquerque, New Mexico.

UNM has special capabilities are in the following areas: production, separation, and purification of radionuclides for the scientific and nuclear medicine communities, development of techniques for radiotracer synthesis and applications; radiation protection and safety; waste management, reduction, and environmental remediation; and medical imaging. Existing undergraduate and graduate academic programs include programs in radiopharmacy, medicinal chemistry, toxicology, radiological physics and radiation dosimetry, shielding analysis, and radioactive waste management. A cross-disciplinary system of joint faculty appointments has been established to foster multidisciplinary education and research, with a principal educational goal of training highly capable engineers, pharmacists, and scientists and delivering well-informed graduates to U.S. industry. Volunteer faculty from industry and the national laboratories contribute to this mission. UNM is a leader in the Nuclear Medicine Consortium of New Mexico (NMCNM), which is committed to enhance the future of nuclear medicine nationwide.

The Waste management Education and Research Consortium (WERC) is a UNM-led consortium that includes New Mexico State University, New Mexico Tech, Navajo Community College, LANL, and SNL. WERC offers Professional Certificate programs in conjunction with B.A., B.S., M.S., and Ph.D. degrees in biology, chemistry, geology, pharmacy, public administration, law, and engineering. As an outgrowth of WERC, UNM has established a Center for Radioactive waste Management (CeRaM). This center studies radioactive and mixed waste issues, including research on the environmental fate and transport of radionuclides associated with different types of radioactive wastes, environmental restoration and remediation, and health physics and radiation monitoring.

Most recently, the Colleges of Engineering and Pharmacy have established a technology commercialization venture to provide technology transfer to the commercial market. The venture is also designed to return a significant portion of its profit to UNM in support of education and research in nuclear medicine.

THE UNIVERSITY OF NORTH TEXAS

The University of North Texas (UNT), one of Texas' *Big Five* universities, is the largest and most comprehensive university in the North Texas region, with ten schools and colleges and approximately 50 doctoral programs, 100 master's programs, and 150 undergraduate concentrations. The enrollment of approximately 26,000 includes students from throughout the United States and the World. The Robert B. Toulouse School of Graduate Studies enrolls about 6,800 graduate students, placing it among the top three graduate schools in size among universities in Texas and neighboring states. The programs in science and technology are an area of strength, which is complemented by strong programs in arts and letters, business administration, the community service professions and psychology, education, visual arts, and nationally-acclaimed programs in music and information science.

Bachelor's through doctoral programs are available in all of the physical, life, and computational sciences. Of particular relevance to this proposal is UNT's Department of Physics, which has a 25-year history of excellence in the application of accelerator technology to atomic and nuclear physics and, most recently, to accelerator-based materials characterization. Every two years, UNT hosts the *Conference on the Application of Accelerators in Research and Industry*. It is the premier international conference in the field of accelerators applied to *both* research and industrial applications. For example, in the most recent 13th Conference (November 1994), entire sessions were devoted to atomic and nuclear physics, isotope production for medical applications, biological and medical applications of AMS, targetry, accelerator-based neutron for boron neutron capture therapy, radiation processing, materials analysis, accelerator technology, radiation safety, and other areas.

UNT's Ion Beam Modification and Analysis Laboratory (IBMAL) operates five different accelerators, and is the world's leader in atomic mass spectrometry (AMS) of stable isotopes, having perfected the technology to detect uniquely any element in the periodic table (except indium because of isobaric interferences) at the sub parts-per-billion level, with the expectation to reach the parts-per-trillion level (one part in 10^{12}) in the near future. This capability will be a tremendous asset to the NBTF program. Currently, the IBMAL group is exploring new techniques to discriminate isobars; i.e., isotopes of different elements with the same atomic mass but different atomic number (different Z). The AMS capability, plus a variety of other accelerator-based analytical capabilities (particle-induced X-ray emission [PIXE], Rutherford backscattering, proton microbeam, nuclear reaction analysis [NRA], etc.) and other state-of-the-art analytical capabilities available in UNT's Center for Materials Characterization, will provide valuable support to the NBTF's research and quality control/quality management program.

The programs in Environmental Science (M.S., Ph.D.), Materials Science (M.S., Ph.D.), Nuclear Engineering Technology (B.S., M.S.), and Physics (B.A./B.S., M.A./M.S., Ph.D.) provide a strong base for educational programs in health physics and waste management, and can provide a unique source of strength to research in these areas to complement the effort in Radiological Sciences based at the University of Texas

Southwestern Medical Center at Dallas (UTSMC) and the educational programs at Missouri, New Mexico, and Oklahoma. UNT offers degrees in Nuclear Engineering Technology in partnership with and at a nuclear utility company. The Department of Chemistry's principal strength is in the area of organometallic chemistry, with ten faculty who work in this area in the Center for Organometallic Research and Education (CORE). This will provide a strong foundation for NBTF research that requires organic synthesis and labelling. UNT will also provide expertise in Radiochemistry through the graduate program in Chemistry.

THE UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER COLLEGE OF PHARMACY

The University of Oklahoma (OU) was founded in 1890 by an act of the first legislature of the Territory of Oklahoma. Presently, the main campus, located in Norman, Oklahoma, and the Health Sciences Center, with campuses in Oklahoma City and Tulsa, offer more than 150 baccalaureate, 100 master's and 90 doctoral degrees through 16 colleges. Research and other sponsored projects on these campuses is expected to exceed $100 million in fiscal year 1995. The Health Sciences Center campus in Oklahoma City contains two major programs of importance to the National Biomedical Tracer Facility: Nuclear Pharmacy and Nuclear Medicine Technology.

Nuclear pharmacy is located within the OU College of Pharmacy, which offers M.S. and Ph.D. degrees in Pharmaceutical Sciences. Nuclear Pharmacy is one of five specialty areas in this college, whose programs combine formal course work with research experience to prepare graduates for careers in education, research, or specialized practice. The college is housed in a modern, 75,000 square-foot building which contains well-equipped research laboratories and specialized support facilities. Faculty in the OU nuclear pharmacy area have varied backgrounds and interests, but all focus primarily in three major areas: radiopharmaceutical chemistry, clinical nuclear pharmacy, and nuclear pharmacy management. Currently, the College of Pharmacy operates a full-function nuclear pharmacy, which serves a dozen hospitals in the Oklahoma City area. The primary individuals who will work with NTRI on NBTF are **Dr. O. Ray Kling**, Vice Provost for Academic Affairs and Dean of the Graduate College, **Dr. Stanley L. Mills**, Associate Professor of Nuclear Pharmacy, and **Dr. Garo P. Basmadjian**, Professor of Nuclear Pharmacy.

The OU College of Pharmacy offers both master's and doctoral degree programs in nuclear pharmacy. Appendix VIII contains a description of the graduate nuclear pharmacy program at OU. Emphases include radiopharmaceutical chemistry, clinical nuclear pharmacy, and nuclear pharmacy management. Currently, the focus of radiopharmacy research at OU is the development of new radiopharmaceutical agents labeled with Tc-99m and I-123 for use as diagnostic agents for imaging the heart and brain, and the development of radiolabeled monoclonal antibodies for diagnosis and therapy.

In addition to nuclear pharmacy capabilities, OU also offers a program in nuclear medicine technology, which is taught within the College of Medicine. Nuclear medicine

technology addresses *in-vivo* and *in-vitro* techniques of utilizing radiopharmacy. *In-vivo* training relates to functional imaging, combined with anatomical imaging. *In-vitro* nuclear medicine deals with the laboratory analysis of blood or body fluids that have been "tagged" with a radiopharmaceutical agent for analysis and evaluation outside the body. These radioimmunoassay laboratory techniques determine the level of various drugs, hormones, and other organic materials in body fluids. Nuclear medicine technology is one of four radiologic technology areas in the OU Department of Radiologic Technology of the College of Allied Health. The other three are radiography, radiation therapy technology, and sonography.

THE UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER AT DALLAS

The University of Texas Southwestern Medical Center at Dallas (UTSMC) now ranks among the top academic medical centers in the nation. The center includes three degree-granting institutions: Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences, and Southwestern Allied Health Sciences School. The three institutions currently train more than 2,800 medical, graduate, and allied health students, residents, and postdoctoral fellows each year. The Medical Scientist Training Program integrates medical research and training at the graduate level leading to both the M.D. and Ph.D. degrees. Faculty members and residents provide care for approximately 63,000 hospitalized patients and over one million outpatients each year.

UT Southwestern celebrated 50 years of service in 1993. Its major growth has occurred in the last 20 years as a result of a philosophy of developing targeted research efforts based on identifying, recruiting, and supporting the best available investigators in carefully selected fields of medical importance. By building a core of world-class basic science experts in the fields common to all state-of-the-art biomedical research — immunology and monoclonal antibodies, molecular biology and genetics, cellular biology and metabolism — Southwestern has become a world leader in building interdisciplinary teams of scientists and physicians in areas such as arthritis research, cholesterol abnormalities and heart research, diabetes research, endocrine research, neuroscience, and nuclear medicine.

In the past 15 years, this strategy has led to four faculty members winning Nobel Prizes (three of whom were entirely home-grown); nine faculty members elected to the National Academy of Sciences and three to the Royal Society; and an eight-fold increase in competitively-awarded external research grants, which now total more than $115 million annually (the most rapid rate of increase of any major medical school). On 30 acres donated by the John D. and Catherine T. MacArthur Foundation, the first of six new research towers nears completion on the new North Campus. Over the next 20 years, these new facilities will double Southwestern's capacity. The Rogers Magnetic Resonance Imaging Center, occupied in early 1990, was the first structure on the North Campus and houses clinical and research facilities for Radiology.

Affiliated with Southwestern are other major medical facilities: the Zale Lipshy University Hospital, a teaching and referral hospital; Parkland Hospital, the Dallas County Hospital and the major teaching unit of the medical school; Saint Paul Medical Center; and Baylor University Medical Center. The contiguous facilities of both Parkland and Saint Paul have extensive medical imaging centers.

Individual research facilities important to this proposal include the Nuclear Medicine Center, which conducts research on the circulation of the brain and the heart in health and disease using experimental imaging methods. The director of the Center is Frederick J. Bonte, M.D., Professor of Radiology and holder of the Cain Distinguished Chair in Diagnostic Imaging — and a major contributor to this study and proposal. The Animal Resources Center (ARC), a state-of-the-art facility for the production, procurement, conditioning, maintenance, and health status of experimental animals, also provides extensive experimental surgery facilities to support animal research.

APPENDIX III

AITI Commercial Isotope Production
(For Reviewers Use Only)

I. THE COMPANY

Advanced Isotope Technologies, Inc., (AITI - the "Company") is an advanced technology company organized primarily for the exploitation of emerging technologies used in the manufacturing and marketing of products and services for the radiopharmaceutical, industrial and research markets.

The Company supplies products and services for the vertically integrated market chain that starts with chemical elements (isotopes). The isotopes are activated by energetic particles (protons or neutrons) into radioisotopes which are then chemically processed into radiochemicals for use by pharmaceutical companies to prepare radiopharmaceuticals. The radiopharmaceuticals are used by the medical doctors in diagnostic and therapeutic procedures which, in some cases, generates a low-level waste. The low level waste is then transmuted by the Company, through a proprietary process, to ZERO WASTE. The underlined terms indicate specific areas addressed by the Company in its business.

The Company's operations are conducted through its operating divisions ISORAD, ISOSEP, ISOGEN, and ISOTRANS. The Company is engaged in the manufacturing, marketing, development and commercialization of innovative products and related research activities. The Company's radiochemical processing capabilities produces radiochemicals from the neutron or proton produced radioisotopes. The radiochemicals that are produced are for medical diagnosis and therapy as well as process control and process monitoring in industry. An Intense Neutron Source manufactured by the Company will be used in radioisotope production and the Company plans to purchase or lease, and place into operation, a 70 MeV Proton Linear Accelerator (Linac) for the production of radioisotopes. A Laser Isotope Separator is being manufactured and will be employed for the separation and production of extremely pure stable isotopes necessary in the production of radioisotopes. The Company's primary services include radioisotope transmutation for waste management and trace analysis in geophysics and material sciences. The Company plans to offer complete waste management of radioactive products from the medical industry and provide transmutation of waste to stable products. The Company's research efforts will primarily focus on research and development of technologies, devices and facilities that will more efficiently produce radioisotopes that are incorporated into radiopharmaceuticals for medical diagnostics and therapeutics in the nuclear medicine market as well as isotopes used in industrial applications.

Manufacturing and production procedures are used to obtain high efficiency and maximum productivity of standard and new products using the Company's advanced proprietary technology. Research will be conducted on the production of radioisotopes generated by the interaction of energetic protons and neutrons with highly enriched stable isotopes. The state of

the art products manufactured and marketed may ultimately be used to supply various radiotherapy modalities for the treatment of cancer.

The Company intends to produce standard radioisotopes currently approved by the FDA for use in medicine and conduct research and product development on new radioisotopes which are used in medical diagnostics and therapeutics for brain, heart, lung, kidney, bone and other organs. The Company's products will have the potential to contribute to the development of agents which have diagnostic and therapeutic potential for treating various medical disorders including cancer. The Company also plans to produce radioisotopes used in industry and will conduct product development on new isotopes to be used in process monitoring and process control.

II. MARKETING

The marketing of AITI's proprietary products and services from each division will be coordinated through a corporate marketing organization composed of AITI's Vice President of Marketing and the marketing managers of ISORAD, ISOGEN, ISOSEP and ISOTRANS. The marketing managers will be responsible for establishing direct sales, OEM distribution through established manufacturers or representatives.

A. RADIOISOTOPES/RADIOCHEMICALS

Initially, most of the radioisotopes produced by the ISORAD and ISOGEN divisions will be marketed as radiochemicals through the ISORAD marketing channels to commercial radiopharmaceutical companies. There is also the potential for distribution through the existing isotope distribution network of the U.S. Department of Energy. In parallel, AITI will develop a marketing plan and distribution system to supply isotopes to medical research institutes and to private firms. The major radiopharmaceutical manufacturers have expressed great interest in purchasing isotopes directly. Based on extrapolation from existing market surveys for the period of 1989-1993, and proprietary information provided by the principal radiopharmaceutical companies regarding their projected need for radioisotopes and radiochemicals used in diagnostic imaging and therapy, AITI predicts a market niche of up to $30 million per year by 1999. Specific radioisotopes which this facility intends to produce through its proprietary processes will be unique and AITI will be the only independent commercial producer in the U.S.

The radioisotopes used in the nuclear medicine market for diagnostic imaging and therapy are defined in the following section which describes the general use of radioisotopes in medicine and the current size of the commercial market. In particular, discussions are given of specific radioisotopes which are of major importance in the current market. It is anticipated that the emerging market of radiation therapy being developed through use of radioisotope tagged monoclonal antibodies will substantially expand the demand for radioisotopes during the next five years. The following extensive discussion presents an estimate of the present and future demand for specific radioisotopes currently in use in nuclear medicine.

B. NUCLEAR IMAGING ISOTOPES

- **^{201}Tl (Thallium-201)** is one of the primary accelerator produced isotopes for nuclear medical imaging and represents 35% of the dollar value of the current medical radioisotope imaging market. The domestic supply of Tl-201 is predominantly supplied by the pharmaceutical companies through in-house production using cyclotrons. Approximately 2.4 million medical imaging procedures were performed for diagnosis of thyroid disease, brain tumor location, cardiac imaging, myocardial profusion and stress analysis. The Company's 70 MeV Proton Linear Accelerator will produce this product through the (p,3n) and (p,5n) reactions in stable isotopes of thallium at a much higher efficiency and lower cost than is currently available in the U.S.

- **^{111}In (Indium-111)** an accelerator produced radioisotope represents approximately 2% of the dollar value in medical diagnostic imaging. This isotope is extensively used for imaging of cerebrospinal fluid, hematologic, musculoskeletal infections, AIDS diagnosis, liver and kidney function transplant evaluation, peripheral vascular and bone marrow. A large number of indium-111 tagged monoclonal antibodies have been developed for prostate, ovarian, colorectal, breast and other melanomas and are being evaluated for clinical utility.

- **^{67}Ga (Gallium-67)** an accelerator produced radioisotope represents approximately 10% of the dollar value in medical diagnostic imaging. This isotope tagged to a citrate is extensively used for imaging to determine transplant evaluations, head and neck tumors, genitourinary and GI tract tumors, melanoma, hepatomas, lung carcinoma, neoplasia, musculoskeletal infections and pulmonary infections. The Company plans to produce this product using the Proton Linear Accelerator to irradiate Zn-68 to produce Ga-67 at a high efficiency.

- **^{82}Sr/^{82}Rb (Strontium-82/Rubidium-82)** generators are used to produce ^{82}Rb for heart imaging, with a U.S. demand currently at approximately 1 Ci per month. FDA approval of a new drug application (NDA) for the clinical use of the ^{82}Sr/^{82}Rb generator for PET scan heart imaging was approved in late 1989, and all recent industry forecasts predict a dramatic increase in its use based upon possible availability.

- **^{123}I (Iodine-123)** is currently in high demand as a SPECT scan brain imaging agent, which is used -- for example -- in assessing the extent of damage after a stroke, and represents 4% of the current market. Iodine's chemical properties also make it ideal as a radiotracer for a variety of brain imaging agents and for use in the new generation of diagnostic and therapeutic agents based on the emerging monoclonal antibody technology. However, U.S. companies make only a limited amount of ^{123}I using their existing low energy cyclotrons, and most ^{123}I comes from outside the U.S. Because of the supply situation and the resulting high cost, ^{123}I imaging utilization has been retarded in the U.S. However, economically viable production of ^{123}I is possible using an existing accelerator-based method starting with 100% enriched ^{124}Xe. A much more economical production

method should be possible using a less costly starting material (^{127}I subjected to the (p,5n) reaction). A strong advantage of the Company's high-current 70 MeV Proton Linear Accelerator will be the ability to simultaneously produce several different radioisotopes for the radiopharmaceutical market while still providing ample beam time for the development of new production methods, such as creating ^{123}I from ^{127}I.

- **^{68}Ge (Germanium-68)** is used in PET scanning for image correction during imaging of the radiopharmaceutical. As the number of PET centers grows, the demand will steadily increase.

- **^{127}Xe (Xenon-127)** was used in lung imaging until the national laboratories became unable to sustain continuous production of the isotope, when the physics accelerators at Brookhaven and Los Alamos ceased year-round operation due to budget constraints. However, the reintroduction of ^{127}Xe into the market place would be welcomed by the many nuclear medicine physicians who consider ^{127}Xe superior to the radioisotope that replaced it, ^{133}Xe.

- **^{57}Co (Cobalt-57)** is used extensively in nuclear medicine as an energy source for calibrating imaging instruments. An authoritative recent report lists the demand for ^{57}Co at more than 8 Ci per year.

- **^{99m}Tc (Technetium-99m)** is the primary radioisotope for nuclear medical imaging and represents approximately 70% of the current medical radioisotope procedures but only 36% of the market dollar value. There is no domestic source of ^{99m}Tc, and all U.S. radiopharmaceutical manufacturers and radiopharmacies must rely on a foreign source. This radioisotope is currently produced from reactor fission products and is chemically separated through a so-called radioisotope generator from the parent radioactive element ^{99}Mo. ^{99m}Tc can be produced directly by the Company's 70 MeV Proton Linear Accelerator through the (p,2n) reaction on ^{100}Mo, at a rate of 2,000 Ci (Curies) of ^{99m}Tc in a 24 hour period. The estimated current market price of this radioisotope is approximately $140-150 per Ci. This process would provide a local and regional supply of a high purity product free of other isotopes (carrier free).

- **^{99}Mo (Molybdenum-99)** is the precursor radioisotope for the production of ^{99m}Tc through the use of $^{99}Mo/^{99m}Tc$ radioisotope generators located in clinical sites or radiopharmacies which distribute ^{99m}Tc to clinical sites. The primary method of production is by means of thermal and fast neutrons using the ISOGEN I. The availability of the high purity, separated stable isotope ^{100}Mo permits the use of the (n,2n) reaction to produce hundreds of Curies of this radioisotope within a period of one week. The market price of this radioisotope is also approximately $140-150 per Ci. Various nuclear reactions, at proton energies within the range of the AITI 70 MeV Proton Linear Accelerator, can be used to produce this radioisotope. The Company's calculations of production costs indicate that 70 MeV Proton Linear Accelerator production of ^{99}Mo is economically viable for routine isotope production however the ISOGEN I is more efficient.

C. NUCLEAR THERAPY ISOTOPES

Radioisotopes produced through neutron reactions using the Company's ISOGEN I system will be processed by ISORAD to supply the radiation oncology market with radiochemicals which are normally made from radioisotopes in nuclear reactors and are procured from sources outside the United States. These products are highly enriched in the specific isotope and are generally tagged to specific drugs, peptides or monoclonal antibodies in order to provide detailed radiation therapy to a specific organ or site. The market demand for therapeutic drugs used in radiation therapy is equivalent to the market for imaging radioisotopes and is estimated to be approximately $60 million annually. Radioisotopes specifically used for radiation therapy are as follows:

- **^{32}P (Phosphorous-32)** a neutron produced radioisotope using the ISOGEN I system will be produced 1000 times more efficiently and with a specific activity 100 times greater than currently available from nuclear reactors. The primary use of this radioisotope is in the treatment and pain abatement of bone cancer. Proprietary market data indicates that over 200,000 procedures were utilized which require $20 million of the P-32 radioisotopes. The Company's proprietary processes will efficiently produce this product through the fast neutron irradiation of S-32.

- **^{131}I (Iodine-131)** a neutron produced radioisotope using the ISOGEN I system through the neutron interaction with Xenon-131. The primary use of the radioisotope is in the treatment of thyroid diseases and in particular graves disease similar to that experienced by former President Bush and his wife.

- **^{186}Re (Rhenium-186)** a neutron produced radioisotope using the ISOGEN I system and produced at very high specific activity through the (n,2n) reaction. The primary use of this radioisotope is in the labeling of monoclonal antibodies for the treatment of lung cancer. The demand for an effective radiation therapy in the treatment of lung cancer is paramount, due to the pollution in the environment, and extensive clinical testing is in process. The fast neutron production of this isotope will be a unique facility within the United States.

- **^{67}Cu (Copper-67)** is currently marketed in moderate amounts for research purposes, for example bone imaging, but its ready availability from a domestic U.S. source would rapidly increase its use in clinical medicine in other organs, according to a recent authoritative report. Its decay produces both beta particles for treating cancerous cells and gamma rays for imaging, making it an ideal radioisotope for simultaneous cancer therapy and imaging using monoclonal antibody technology.

- **^{103}Pd (Palladium-103)** is an accelerator produced radioisotope and will be manufactured by ISORAD however the ISOGEN I system can efficiently produce this isotope through the (n,2n) reaction in Pd-104. This product is currently used clinically for the treatment of prostate cancer and is estimated to have an annual market of approximately $2 million.

- ^{111}Ag (Silver-111) is a neutron produced radioisotope of high specific activity which is primarily used in the treatment of lymphnode diseases and cancers.

- ^{198}Au (Gold-198) is a neutron produced radioisotope of high specific activity primarily used in the treatment of prostate cancer.

D. INDUSTRIAL RADIOISOTOPES

Industrial radioisotopes are widely used in radiation processing, non-destructive evaluation (NDE) radiography and gamma gauging, tracer diagnostics, wear diagnostics and diffusion analysis in the semiconductor industry. Industrial isotopes are also used in x-ray fluorescent analyzers and MÖSSBAUR analyzers.

- ^{60}Co (Cobalt-60) this neutron produced radioisotope emits high energy gamma rays and has a half-life of 5.3 years. Its primary commercial use is in providing megarad irradiation sources for the processing and sterilization of food and other products. It is extensively used in gamma ray radiography for castings and heavy industrial machinery.

- ^{137}Cs (Cesium-137) this neutron or fission produced radioisotope emits a monoenergetic gamma ray and has a half-life of 30 years. Its primary commercial use is in providing dimensional gauging in process control, fluid flow density measurements, liquid level measurements and mass flow measurements. This isotope is extensively used in the petrochemical industry for oil well logging to provide porosity measurements of geological strata.

- ^{192}Ir (Iridium-192) this neutron or proton produced radioisotope emits multiple gamma rays in the region of 300 keV and possess a 72 day half-life. The principle use is in gamma ray radiography for oil field pipe lines and high pressure steam pipes in electric power plants. Its primary advantage is in the high specific activity (800 Ci/gm) which provides small sources for high resolution radiography.

- ^{109}Cd (Cadmium-109) this neutron or proton produced radioisotope emits low energy protons in the regions of 22 keV and 100 keV for use in x-ray fluorescent diagnostics of the elemental concentration in materials. It is extensively used throughout the steel, aluminum and metals industry for quality control and analysis.

- ^{57}Co (Cobalt-57) this radioisotope can be produced by either neutrons or protons and has a half-life of 271 days. It emits several intense gamma rays in the region less than 140 keV. The 14.4 keV gamma ray is used in the MÖSSBAUR analyses to resonantly excite Fe-57. In addition, Co-57 is used as a calibration source.

- ^{22}Na (Sodium-22) can be produced by either neutrons or protons and has a half-life of 2.6 years. It decays by positron emission and thus is a good source of 511 keV annihilation radiation. It is principally used for fluid flow studies in a variety of process streams. It is easily dispersed in liquids, thus it is used for assessment of oil reservoirs and aquifers.

E. MARKET ESTIMATES

The present worldwide market for medical radioisotopes use in imaging and therapy provided in bulk, semi-processed, form is approximately $200 million, based on wholesale pricing. Fifty percent (50%) of the total dollar market value is produced by reactors, the remaining fifty percent (50%) by accelerators. The U.S. market is approximately fifty percent (50%) of the world market, or $100 million. Approximately fifty percent (50%) of that total is for medical imaging and research and fifty percent (50%) is for therapeutic radiation treatment of diseases and cancer. The U.S. market for the radioisotope molybdenum-99 (^{99}Mo) is approximately $20 million, which is one half the estimated world market of $40 million. The U.S. market requires 2,500 curies of ^{99}Mo, each week, at a current market price of $140 to $150 per curie.

The production of radioisotopes for industrial usage in process control, process monitoring and tracer diagnostics is approximately $20 million world wide. The predominant isotope in this industrial market is Co-60 used for radiography and radiation processing and is also used in radiation cancer therapy.

The predominant isotopes Mo-99 and Co-60 are produced in nuclear fission reactors and must be obtained from foreign sources. The ISOGEN I and ISOGEN II systems will produce these products and provide nuclear medicine and industry with a stable supply.

Independent calculations, by a major pharmaceutical company, has substantiated the AITI calculations that the potential radioisotope productivity of this facility will be approximately $700,000 per week or $30 million annually. The potential income from individual isotopes is shown in Table II-1. The relative short half-life of the radioisotopes produced requires prompt distribution from a major international airport. The facility, located near DFW Airport, will be able to distribute radioisotopes to the major pharmaceutical companies within an eight hour time frame. The estimated production of various isotopes are shown in Tables II-2 and II-3.

Table II-1
Potential Individual Isotope Income
[1999]

Isotope	Half Life	Production Energy (MeV)	Potential Production/Yr ($millions)	15% Market Penetration ($millions)
Mo-99	65.9h	70	29.0	4.35
Tc-99m	6.0h	70	45.0	6.75
Ga-67	78.3h	70	13.0	1.95
In-111	67.0h	70	25.0	3.75
Pd-101	8.5h	20	24.0	3.60
I-123	13.2h	70	30.0	4.50
I-131	8.0d	70	3.0	0.45
Tl-201	73.0h	30	26.0	4.35

Table II-2
Radioisotope Production Facility Products.

Product	Target	Enriched	BeamLine	Estimated Beam Current	Estimated Yield/Hr
In-111	Cd-112	Y	30 MeV	200 μA	800 mCi
Ga-67	Zn-68	Y	30 MeV	150 μA	500 mCi
I-123	Xe-124	Y	30 MeV	75 μA	400 mCi
Pd-103	Rh-103	N	30 MeV	500 μA	125 mCi
Co-57	Ni-58	Y	30 MeV	500 μA	15 mCi
Xe-127	I-127	N	30 MeV		
Tl-201	Tl-203	Y	30 MeV	150 μA	300 mCi
Ge-68	Ga-69	N	50 MeV	100 μA	6 mCi
Cu-67	Zn-70	Y	50 MeV	150 μA	
Tc-99m	Mo-100	Y	70 MeV	200 μA	
W-178	Ta-181	N	70 MeV	500 μA	
Sr-82	Rb-85	Y	70 MeV	100 μA	25 mCi

research expertise is in the field of biophysics and neuroscience, and he contributes expertise in biomedical science to AITI, having taught at two medical schools and four universities during his career.

The technical staff is composed of Mr. Wayne B. Cloud and Dr. William J. Courtney. Mr. Cloud, a professional mechanical engineer, has extensive experience in large project scheduling, management, and facilities planning, design and construction. He is a registered Professional Engineer in Texas and Oklahoma. Mr. Cloud holds a MSME degree from Rice University and retired from Mobil Research and Development Corporation in 1992. He was employed 27 years with Mobil.

Dr. Courtney, a physicist, joined the company as a Research Scientist upon leaving IBM. At IBM he provided technical marketing support to high technology organizations including the Superconducting Super Collider Laboratory and Electronic Data Systems. Dr. Courtney's research expertise is in the field of nuclear physics and in the application of physics techniques to environmental science research. Prior to IBM, his research career was in both academic and industrial organizations.

AITI consultants include Dr. Norman Hackerman, Mr. Joe Beaver, Dr. Wyatt W. Givens, Dr. Floyd D. McDaniel, and Dr. Homer Hupf.

Dr. Norman Hackerman, a chemist, is President Emeritus and Distinguished Professor Emeritus of Chemistry of Rice University. He is also a former president of the University of Texas at Austin where he served on the chemistry faculty for 25 years. Dr. Hackerman is currently the Chair of the Scientific Advisory Board of the Welch Foundation. When he served as a faculty member of the University of Texas at Austin he was involved in the founding of Tracor Corporation with colleagues and students.

Mr. Joe Beaver, a radiochemist, recently retired from the Oak Ridge National Laboratory where he was in charge of radioisotope production and distribution. In his career he developed the Mt. Siani Medical Institute cyclotron radioisotope facility and Mallincroft's radioisotope and radiopharmaceutical facilities. Mr. Beaver has agreed to join the company in the position of Manager of Radioisotope Production and Distribution.

Dr. Wyatt W. Givens, a physicist, having served in the employ of Mobil Research and Development Corporation for 31 years, recently retired and joined AITI. He attained the highest technical level of Scientist within Mobil while his inventions resulted in 48 issued U.S. patents, numerous internal publications and 21 publications in scientific journals. He received numerous professional society awards and honors. His technical expertise is nuclear well logging using neutron generators, nuclear magnetic resonance, and electrical properties of geologic materials.

Dr. Floyd D. McDaniel, a physicist, is Professor of Physics in the Department of Physics and Center for Material Characterization at the University of North Texas, Denton, Texas.

He is also Director of the Ion Beam Modification and Analysis Laboratory as well as Director of the Industry University Cooperative Research Center at the University. He provides experimental expertise in nuclear physics, neutron physics and linear accelerators. He has over 115 publications in technical journals.

Dr. Homer Hupf, a radiochemistry, has 30 years experience in research and development and commercial production of radiochemicals, radiopharmaceuticals and related products. He was formerly associated with Oak Ridge National Laboratory, Mount Sinia Hospital and Hybertech. Dr. Hupf has agreed to join the company in the position of Manger of Radiochemical Production and Radiopharmaceutical Development.

B. ORGANIZATION

The organizational chart is shown below in Table III-1 and represents the organization and lines of authority. The Chief Operating Officer is responsible for all of the general operations and performance of the divisions. The Senior Vice President for Research and Development is responsible for all the planning for research leading to products and services. The Vice President of Marketing is responsible for the marketing and distribution of all products and assists the Chief Financial Officer in finance relating to production, market research and analysis relating to acquisitions and technology transfer. The Chief Financial Officer is responsible for financial planning, cost control, internal audit and financial reporting as well as the analysis of acquisitions. The President is responsible for the overall operation of the company, execution of business plans, goals and objectives and long range planning. The President recommends to the Chairman and CEO for presentation to the Directors, the strategic plans as developed by the senior officers.

Table II-3
Diagnostic Products For Medical Imaging (Positron Emission Tomography) 30-Mev Targets Stations.

Product	Target	Enriched	Beam Line	Estimated Beam Current
F-18	O-18	Y	30 MeV	25 μA
O-15	O-16	N	30 MeV	25 μA
N-13	O-16	N	30 MeV	25 μA
C-11	N-14	N	30 MeV	25 μA

III. Organization

A. Management and Key Personnel

Name	Position
George A. Keyworth, Ph.D.	Founder, Chairman of the Board & CEO, Director
Ira Lon Morgan, Ph.D.	Founder, President, Treasurer, Director
Michael van Hoye	Chief Operating Officer
Edward A. Knapp, Ph.D.	Founder, Sr. V.P. Research, Director
Will J. Lepeska, M.A.	Founder, Vice President Marketing, Director
Bruce L. Freeman, Ph.D.	Vice President ISOGEN Division

The five current officers, consultants and science advisor noted below, provide a variety of expertise, including business management (Keyworth, Morgan, van Hoye) physical science and technology (all), technology-based business start-ups (Hackerman, Lepeska, and Morgan), marketing (Lepeska and Morgan), research, development and technology (Knapp) and biomedical science.

Dr. Keyworth, a physicist and former science advisor to President Reagan, is currently associated with the Hudson Institute and the Santa Fe Institute, both private research

institutes that promote advancement of science and technology for the benefit of humankind. He is an affiliate of the Los Alamos National Laboratory and is a director of the Hewlett-Packard Corporation and other corporations for which he also serves in a variety of roles.

Dr. Morgan, is the Founder of International Digital Modeling Corporation of Austin, Texas, a company that applies nuclear and computational technology to tomographic imaging in industrial settings. During his 30-year association with the University of Texas at Austin, Dr. Morgan served as Professor of Physics and directed the Center for Nuclear Studies. In this period he transferred technology to four different companies which he founded. For 20 years he has served as co-chair of the Conference on the Application of Accelerators in Research and Industry. This biennial conference is the premier international meeting on accelerators and their industrial applications.

Mr. Michael van Hoye, is the former Founder and President of Identics a major manufacturer of process monitoring and analytical analysis instrumentation for the aerospace industry. He is also President of Triton Limited an engineering firm which has performed major systems engineering and operations in the U.S., Great Britian, France and Spain in the transportation and manufacturing industries.

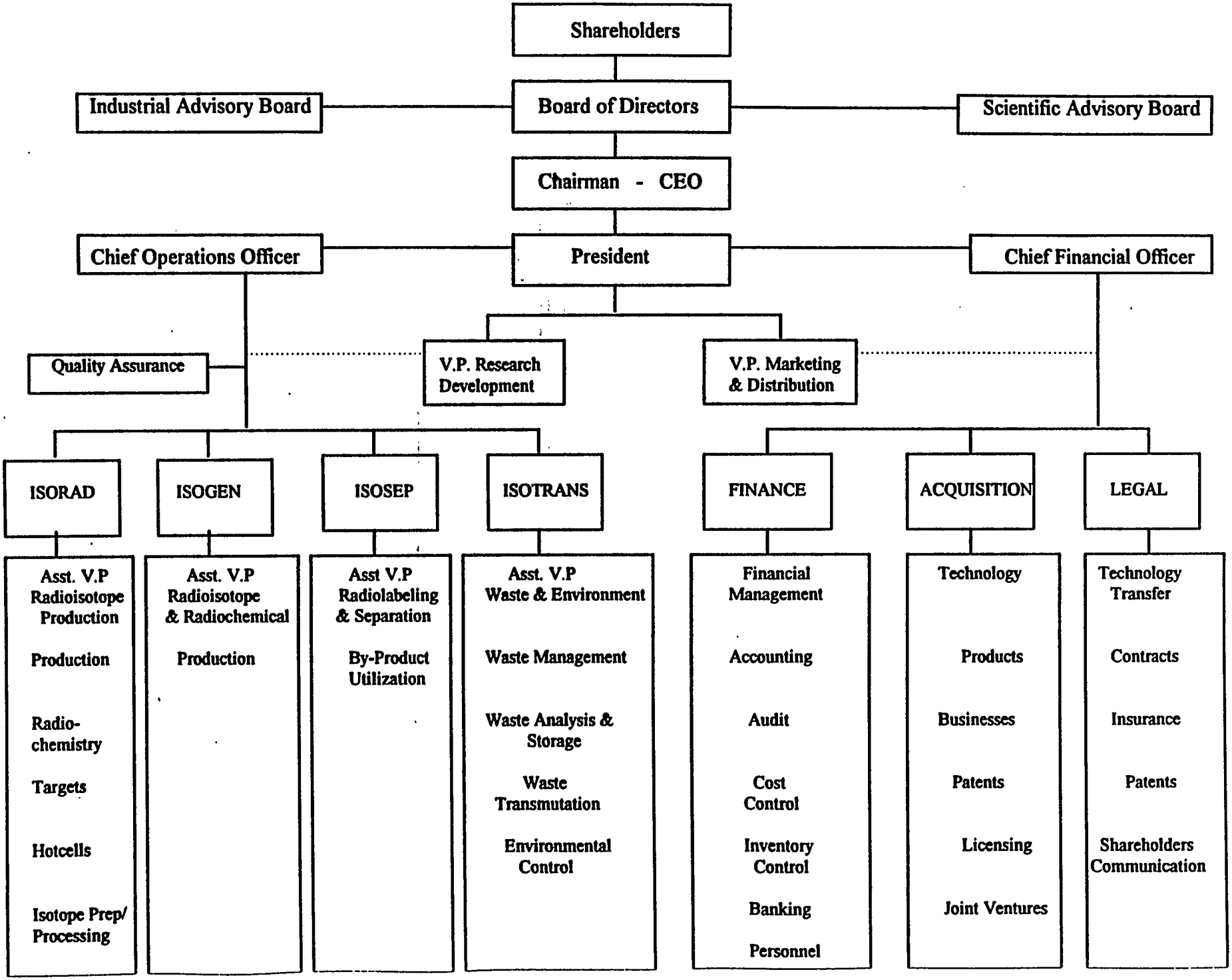
Dr. Knapp, a physicist, is a former director of the National Science Foundation and the Universities Research Association, the management consortium of Fermilab and the Superconducting Super Collider Laboratory. He recently moved from a directorship of the Los Alamos Meson Physics Facility (an 800 MeV proton linear accelerator) to the presidency of the Santa Fe Institute. Dr. Knapp is the inventor of the drift tube linac technology that will be applied in the radioisotope production facility.

Mr. Lepeska is currently President of Hospital Financial Corporation, an early pioneer in the leasing of nuclear medical equipment to hospitals. Mr. Lepeska was formerly Vice President of Marketing for Nuclear Chicago Corporation, a major producer of radioisotope imaging equipment and subsequently marketing manager for G.D. Searle. Now he serves on the Board of Directors of several medical instrumentation, electronics and marketing corporations.

Dr. Bruce Freeman, a physicist, has 20 years experience in experimental physics ranging from underground nuclear testing, to high-explosive testing, to extensive work with plasma focus devices at the Los Alamos National Laboratory as a Technical Staff Member. In 1991 he received a LANL Distinguished Performance Award in Pulsed Power Research. Dr. Freeman has recently joined the Company as a Vice President in charge of the ISOGEN division.

To provide expertise in the biomedical sciences, AITI has been assisted on a pro bona basis by Dr. Rollie Schafer, science advisor. Dr. Schafer is the chief research officer of the University of North Texas where he has served the past five years as Associate Vice President for Research and Dean of the Toulouse School of Graduate Studies. Dr. Schafer's

AITI ORGANIZATIONAL CHART



IV. MANUFACTURING AND PRODUCTION

A. Intense Neutron Source Devices

AITI has entered into an agreement with a major pharmaceutical company to demonstrate Proof of Principle for the development and construction of a prototype Intense Neutron Source. AITI has entered into a Funds-In agreement with the U.S. Department of Energy and Los Alamos National Laboratory to develop a prototype device. This completed prototype is the basis of ISOGEN I and was transferred to AITI's facilities in Denton, Texas in January of 1995. AITI retains proprietary rights and patent rights to the developments funded under this agreement. AITI has filed patent disclosures on the independent proprietary technology developed regarding methods of radioisotope production. The primary objective of the ISOGEN I is the more cost effective localized production of radioisotopes, for nuclear medicine, which have previously been produced by research reactors at a few locations.

The Intense Neutron Source, ISOGEN I, previously described provides the primary AITI production facility for ^{99}Mo, ^{32}P, ^{131}I and other neutron produced radioisotopes. ISOGEN I will also be built for lease and operation to the radiopharmaceutical companies. The regionally located ISOGEN I can provide the industry and their medical customers with localized production of short-lived radiopharmaceuticals throughout the world.

The first commercial Intense Neutron Source will be constructed starting in mid 1996 for $1.4 million under an internal manufacturing program in coordination with a CRADA with Los Alamos. Subsequent units will be manufactured at a turn key manufacturing cost of $2 million starting in 1997. A total of seven Intense Neutron Sources are shown in the Proforma projections in Table VI-3 in Section VI, Operations and Finacial Plans.

B. Intense Neutron Source Produced Radioisotopes

The ISOGEN I system will be used as a primary production facility for a variety of radionuclides. The initial production for this device is being directed at the efficient production of ^{99}Mo, the most successful medical radioisotope, with a worldwide market approaching $40 million based on wholesale prices. The Proforma projections for Intense Neutron Source Produced Radioisotopes reflect production from this unit starting in 1997. The secondary isotopes produced by this system are outlined in the marketing section. The ISOGEN I system is a product which produces intense beams of deuterons with energies up to 10 MeV. These intense beams are very efficient in the production of positron emitting isotopes which are used in the functional diagnostics of the heart and brain. Recent FDA regulations indicate that radioisotope positron emitters should be produced at the hospital or diagnostic center due to the short half-life and the required medical procedures. AITI has entered into a Small Business Initiative with Sandia National Laboratory to study the use of the Fast Burst Reactor as a source of fast neutrons for radioisotope production.

C. Royalty on Intense Neutron Source Production

The seven ISOGEN I systems reflected in the Proforma will be operated by various radiopharmaceutical companies throughout the world. Because of the proprietary technology involved, AITI will require a five percent (5%) royalty payments on all production from these devices. The royalty flow is projected for late 1996 when the first commercial Intense Neutron Source is projected to go on-line.

D. 70 MeV Proton Linear Accelerator Produced Radioisotopes

AITI will purchase a 70 MeV Proton Linear Accelerator which will be used by the ISORAD division, with production power equivalent to 100 kW, to economically produce radioisotopes for commercial sale to radiopharmaceutical companies. The 70 MeV Proton Linear Accelerator selected is modelled after a similar linear accelerator being operated as a research machine at Los Alamos National Laboratory. The AITI facility will have four times the production capability of current commercial cyclotron systems.

The 70 MeV Proton Linear Accelerator will be able to produce the standard isotopes such as ^{99}Mo, ^{201}Tl, ^{111}In, ^{67}Ga and ^{123}I at multi-Curies per week. Radioisotope production from this 70 MeV Proton Linear Accelerator is projected for late 1996, after a eighteen-month construction period. The annual production is anticipated to increase to $15 million and proprietary technology can double the production if market conditions demand.

E. Monoclonal Antibodies/Therapeutics

Market research studies have indicated that radiation therapy for the treatment of cancer and other diseases will become very effective through the tagging of radioisotopes to monoclonal antibodies and peptides. Market research indicates the market should grow to approximately $1 billion. The achievement of these therapeutic procedures would require a three fold increase in the demand for radioisotopes. Various projections have been made indicating that the most useful radioisotopes of the future will involve monoclonal antibodies for the selective aiming of radioactive labelled proteins to destroy cancerous cells. Examples include:

- The Coulter Corporation radioimmunotherapy (using radioiodine) for blood lymphoma in work done at the University of Michigan Medical Center, as reported in the August 13, 1993 New England Journal of Medicine. This is the early stages of development of this technique.

- Metastron, a treatment for cancer pain, utilizing Strontium-89, is manufactured by Amersham and marketed by them to nuclear medicine, radiopharmacy and radiation oncology departments, which is also marketed by Zeneca. A single injection of Metastron provides significant pain relief, lasting three months or more, with fewer side effects than previous treatment methods.

- The Proforma projects the beginning of commercial production of radioisotopes to be tagged to these materials in 1998.

F. Laser Isotope Separator / Stable Isotopes

AITI has received a Phase I SBIR (Small Business Innovation Research) contract from the U.S. Navy for development of an intense laser source which may advance the art of isotope separation technology. This development of a Laser Isotope Separator could substantially improve the economics of radioisotope production by providing lower cost stable isotopes. Foreign sources are currently the major suppliers of stable isotopes, due to the closing of the Oak Ridge electromagnet separation facilities (Calutrons).

An internal manufacturing budget estimated at $500,000 is projected in the Proforma, Table VI-3 in section VI Operations and Financial Plans, for starting in early 1995. Thereafter, the projections reflect the successful application of this new technology to the commercial production of stable isotopes by ISOSEP for use by ISORAD and ISOGEN in the production of products for the radiopharmaceutical industry. Direct sales of stable isotopes to the pharmaceutical industry by ISOSEP will provide a domestic supply. AITI through a CRADA with the University of California Los Alamos National Laboratory is in the process of obtaining technology and patent rights to use certain laser isotope separation processes.

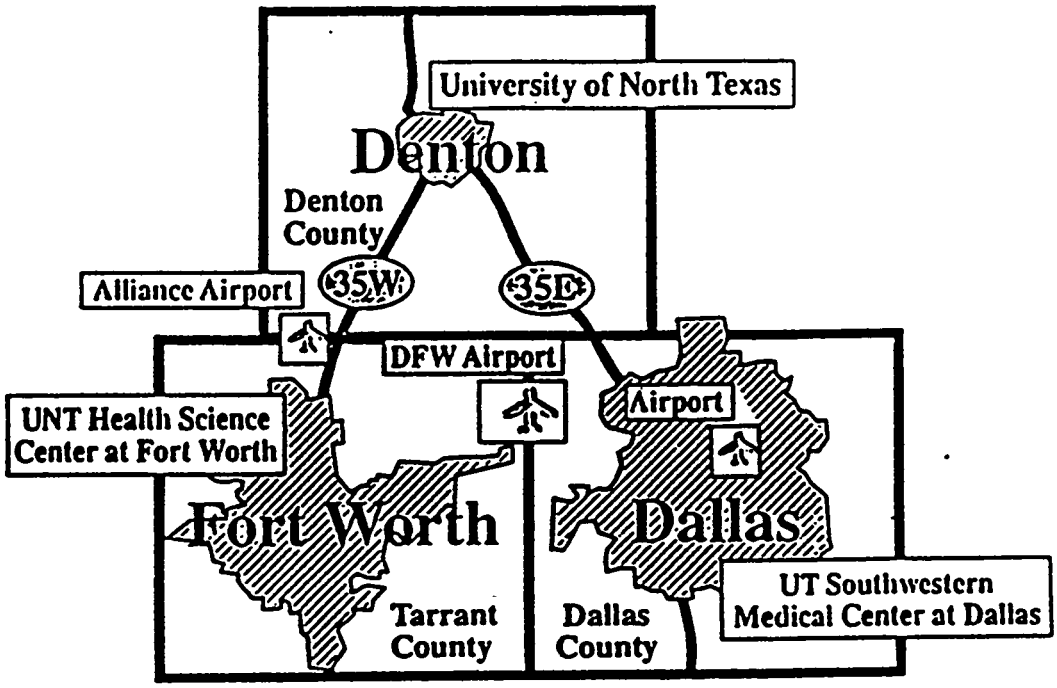
G. AITI Production Facility

1. Facilities

a. Site Plan

The AITI commercial isotope production facility is located at 9103 North Locust Street, Denton, Texas in the near proximity (5 miles) of the University of North Texas. In Figure IV-1 locations are shown for the UTSWMC in Dallas, The UNTHSC in Ft. Worth, UNT, NTRI and AITI in Denton along with DFW international and Alliance commercial airports. The facility has complete security in that it maintains the structure of a former Hercules NIKE Site. AITI leases approximately nine acres of the NIKE site which contains three large underground concrete structures. The underground concrete rooms are ideal for housing the intense neutron source, linac and radioisotope target area. The site plan is shown in Figure IV-2. Access to the area is gained off of North Locust Street (Highway FM 2164) along Able Street through the guard gate and within the double security fence area. A second guard gate and restricted access to the radiation processing facility is maintained prior to entering the vault area.

The Phase I site plan of the National Biomedical Tracer Facility, AITI's commercial production facility as shown in Figure IV-3. The primary commercial radioisotope production and irradiation is housed in the two west vaults labeled 5 and 6. The intense neutron source control room and linac control room are located above ground adjacent to



Dallas-Fort Worth-Denton Metroplex

Figure IV-1

1 NIKE MISSILE SILO
2 SILO DOORS
3 BERM
4 GENERATOR BUILDING
5 WARHEAD BUILDING
6 STORAGE SHED
7 UNT ENVIRONMENTAL RESEARCH
8 UNT ASTRONOMY FACILITIES
9 UNT ASTRONOMY CLASSROOMS
10 PUMP HOUSE

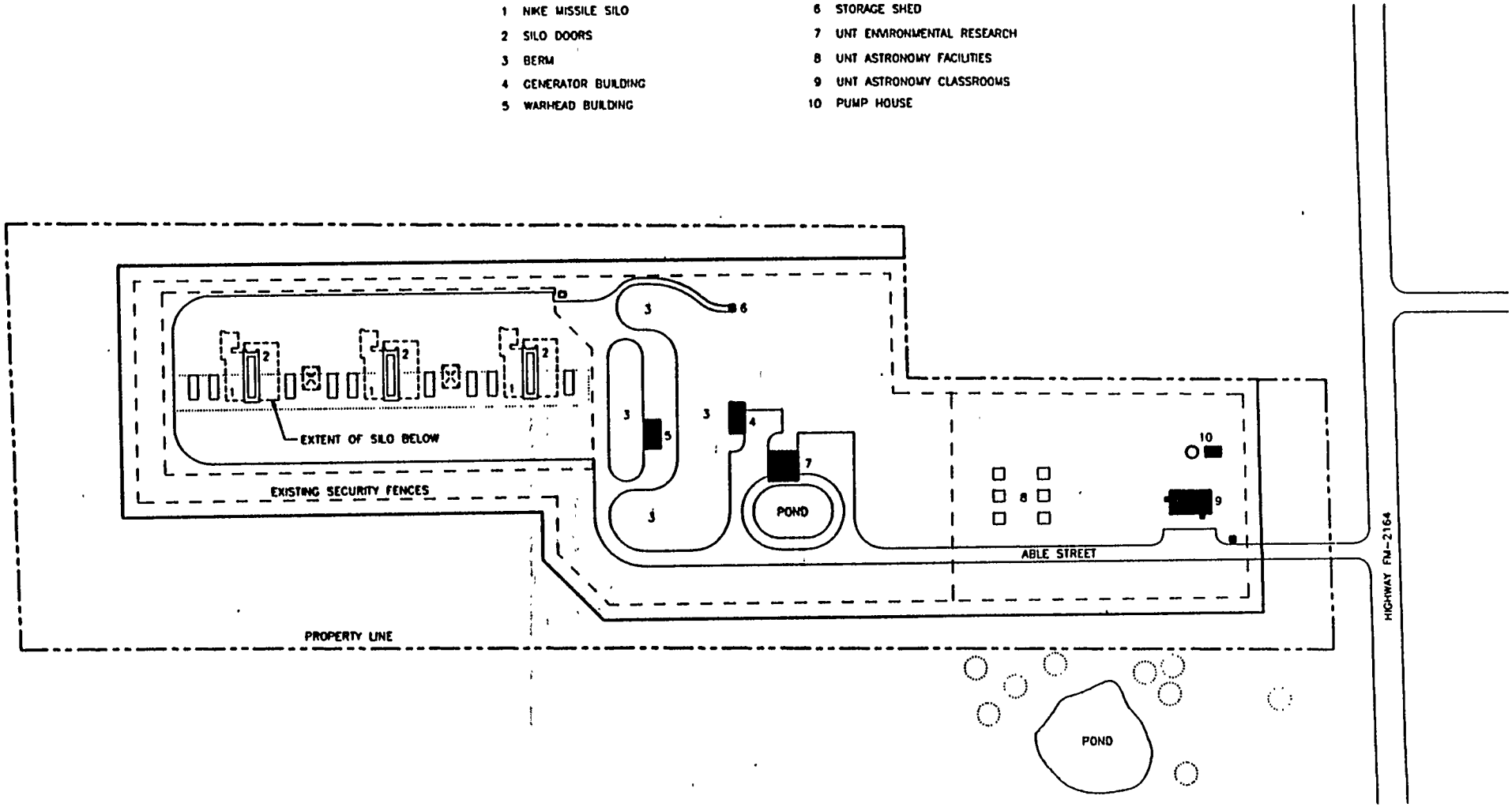


Figure IV-2 Existing Site Plan

NATIONAL BIOMEDICAL TRACER FACILITY

James E. Langford, Architect

1 ADVANCED ISOTOPE TECHNOLOGIES, INC.
2 NATIONAL BIOMEDICAL TRACER FACILITY
3 SERVICE COURT (RESTRICTED ACCESS)
4 PARKING
5 NEUTRON SOURCE IN SILO
6 TARGET STATIONS IN SILO
7 CYCLOTRON IN SILO
8 LINAC VAULT BELOW
9 CONTROL ROOM
10 KLYSTRON GALLERY
11 WASTE HANDLING & RETENTION FACILITY
12 ACCESS TO LINAC TUBES
13 EXISTING BERM EXPANDED (15' HIGH)
14 ENTRY GATE WITH GUARD
15 GENERATOR BUILDING
16 UNT ENVIRONMENTAL RESEARCH
17 EXISTING POND ENHANCED
18 UNT ASTRONOMY FACILITIES
19 PUMP HOUSE
20 UNT ASTRONOMY CLASSROOMS

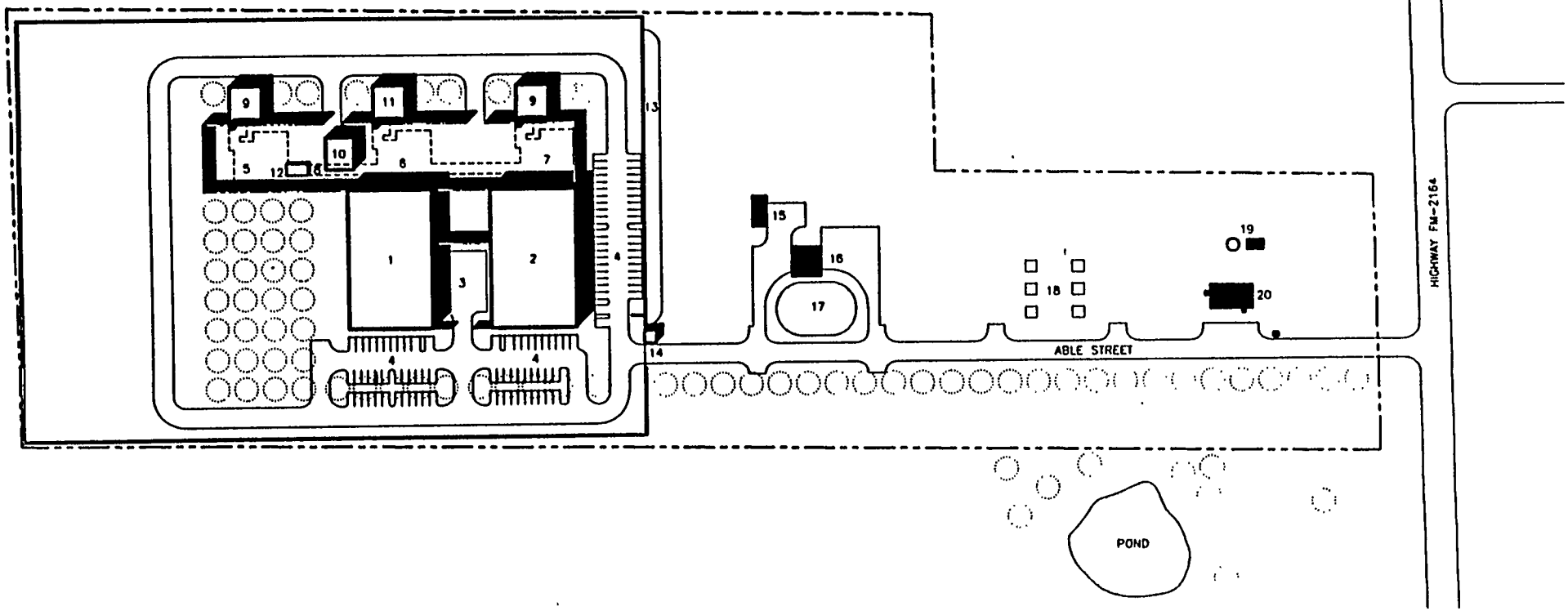


Figure IV-3 Phase One Site Plan

NATIONAL BIOMEDICAL TRACER FACILITY

James E. Langford, Architect

vault labled 5 in Figure IV-3. The vaults are underground structures 70' X 70' located 18' below grade and are constructed of 1' thick reinforced concrete with a reinforced concrete roof and 3' of earthen overburden. The intense neutron source is located in the western side of vault labeled 5 with the associated electronics for operation as well as the electronics for operation of the linac. A 10' X 10' tunnel 80' long connects vault labeled 5 with vault labeled 6 and houses the 70 MeV linac. The klystron gallery is located above ground and adjacent to the linac with RF waveguide feedthroughs to the DTL tanks. In vault labeled 6 is located the target area for radioisotope production. Waste handling and retention is located above ground and located near the radioisotope processing facility. The radioisotope processing facility is a 20,000 square foot building located above ground and south of the target vault and labelled 1 in Figure IV-3.

b. Linac Target Area

The target area located in the middle vault is shown in Figure IV-4. High level studies have also indicated the preferred approach, to provide beam to the radioisotope production facility (RPF), is to extract all beam energies at the end of the 70 MeV DTL section of the Linac. The beam line is also centered 4 ft 2 inches above the floor-slab and is 78 inches south of the inside north wall of the tunnel. Current beam extraction design has the 70, 50 and 30 MeV beam lines moving out from the beam centerline location at angles of 35, 42.16 and 55 degrees, respectively.

c. Intense Neutron Source DPF Layout

The intense neutron source for radioisotope production located in the western portion of the vault is shown in Figure IV-5. The dense plasma focus (DPF) fusion source is well shielded within a cylindrical borated polyethylene shell. Adjacent to the DPF are three capacitor banks providing 750 KJ of energy and a 120 Kv DC power supply. The system is again shielded with 2' of high-density concrete walls. Radioisotopes produced in this system are transported to the radioisotope processing facility and are processed in coordination with the radioisotope production from the linac.

d. RPF Surface Processing Building

The third area of conventional construction is the Surface Processing Building containing Radiochemistry Processing, Target Preparation, Laboratory space and Office Area. The conceptual adjacency requirements are indicated in Figure IV-6. This is an approximately 20,000 sq ft facility. Specific room sizes and spaces are identified in Table IV-1 Surface Processing Facility Square Footage. Assumed construction is tilt wall external walls, concrete masonry walls for lab areas, bar joist roof beams spanning approximately 30 ft each with suspended fiberglass mat type false ceilings, ducting and piping run through the bar joist with access panels for servicing. HVAC systems within a portion of the lab will be once through air. Other lab areas may use auxiliary (outside) make-up air for portions (70%) of their fume hood air. Exhaust of all rooms and fume hoods will be combined into a single facility exhaust stack that will also accommodate the Target Area exhaust.

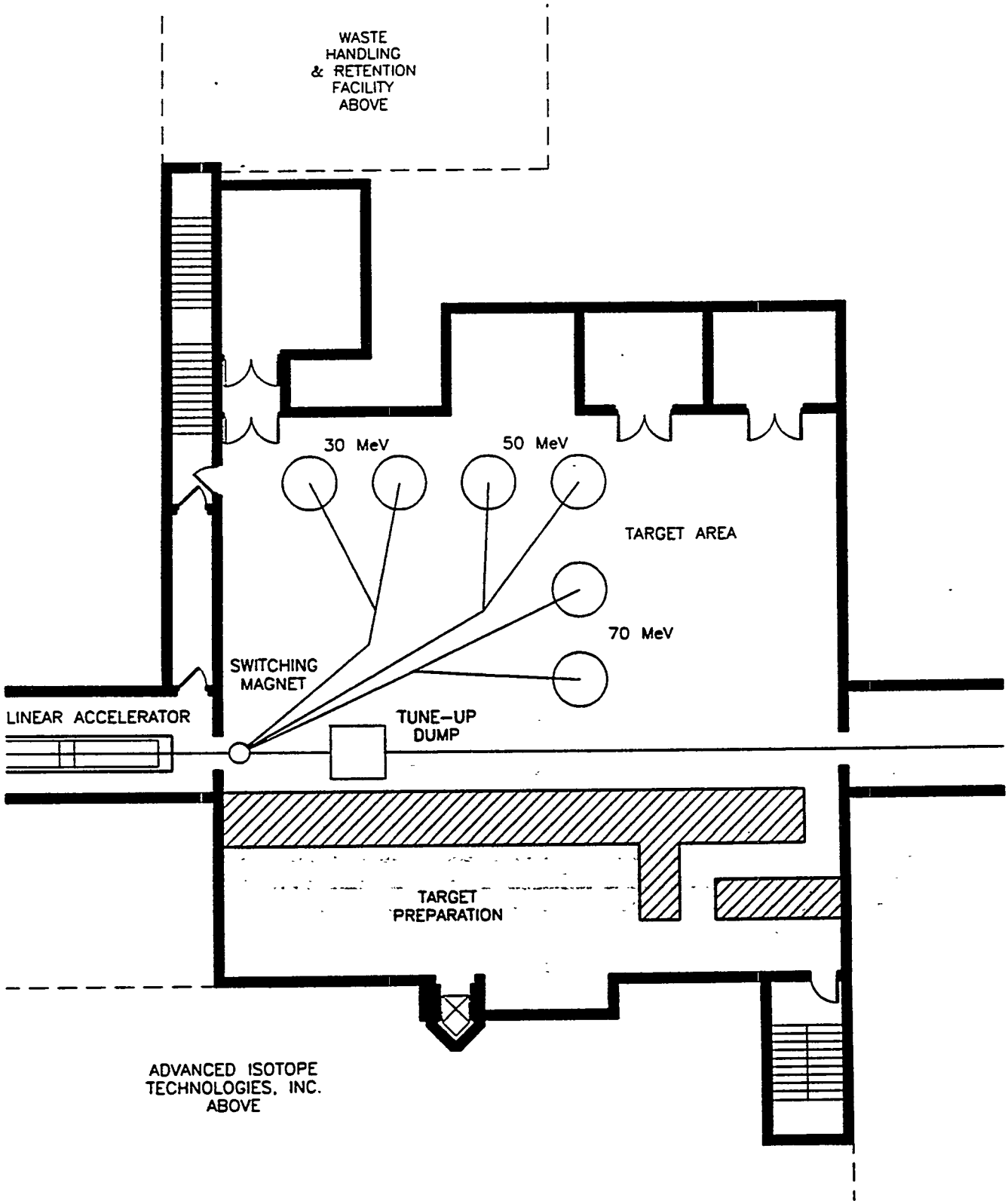


Figure IV–4 Modified Missle Silo #2

N A T I O N A L B I O M E D I C A L T R A C E R F A C I L I T Y

0 4 8 12 16

James E. Langford, Architect

North

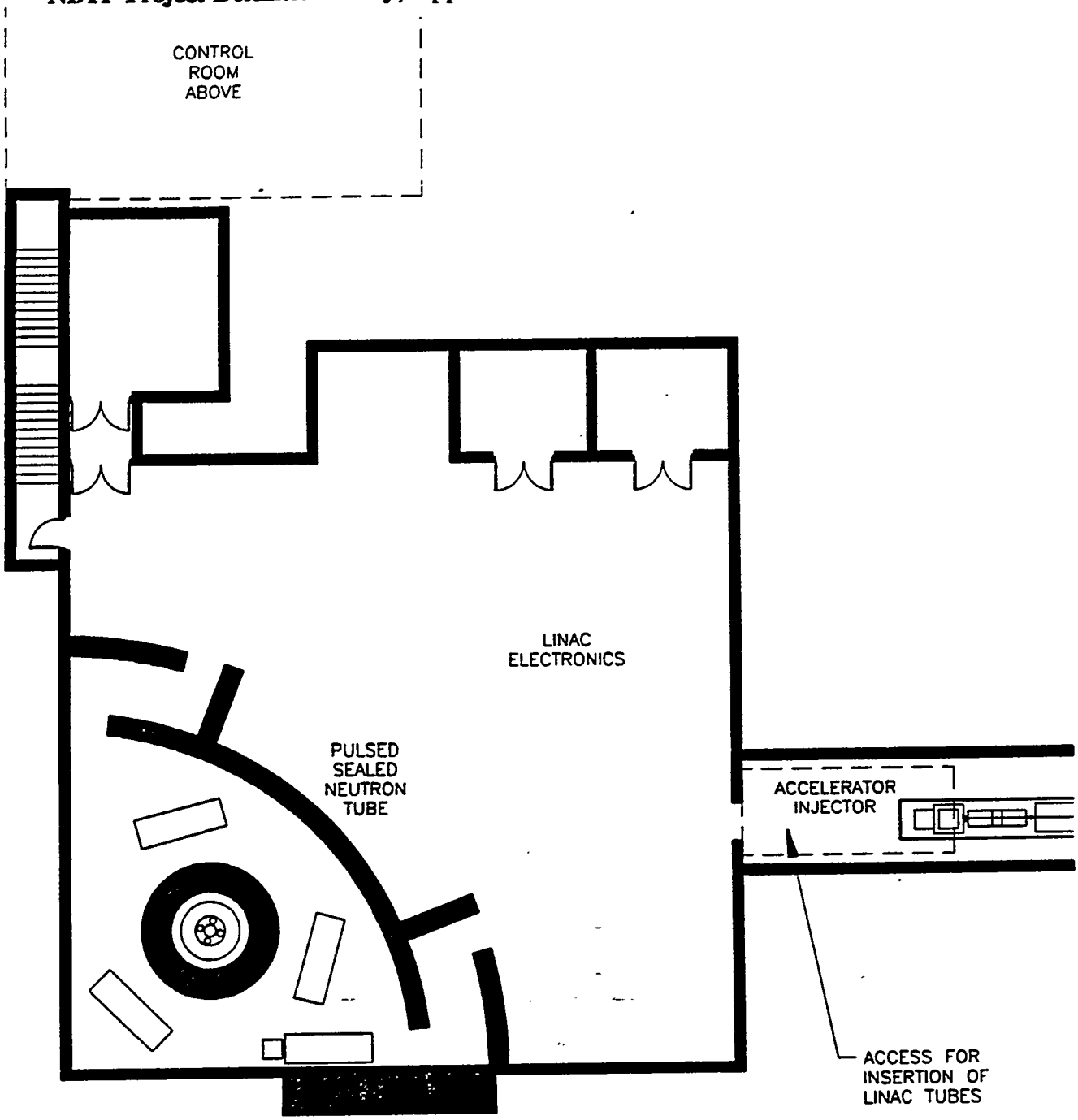


Figure IV-5 Modified Missle Silo #1

NATIONAL BIOMEDICAL TRACER FACILITY

0 4 8 12 16

James E. Langford, Architect

North

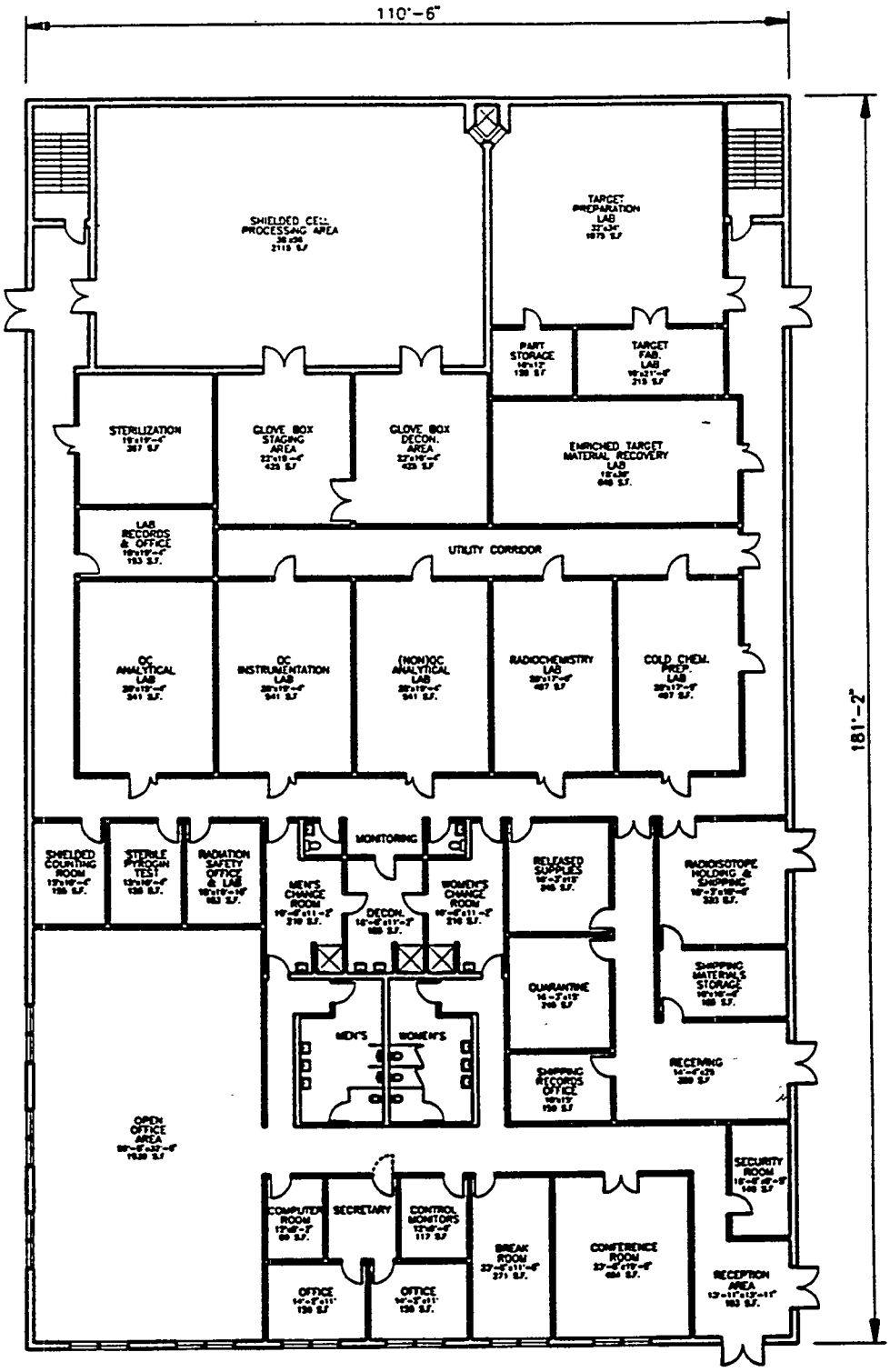


Figure IV-6 Commercial Radioisotope Processing Facility

ADVANCED ISOTOPE TECHNOLOGIES, INC.

For the National Biomedical Tracer Facility Center

James E. Langford, Architect

0 5 10 20

North

Table IV-1

SURFACE PROCESSING FACILITY SQUARE FOOTAGE	
1. Cold Chem Prep Lab	497
2. Receiving	360
3. Quarantine	244
4. QC Analytical Lab	540
5. QC Instrumentation Lab	540
6. Sterile Pyrogen Test	155
7. Enriched Target Material Recovery (8 hoods)	648
8. Target Prep Lab	1075
9. Target Fab Shop	215
10. Target Part Storage	120
11. Shielded Cell Processing Area (8 processing hot cells, 1 TRF cell)	2115
12. Glove Box Staging	425
13. Glove Box Decontam *Connects to Three 5000 gal Exterior Tanks for Rad Waste Retention	425
14. Sterilization	280
15. Radioisotope Holding & Shipping	338
16. Shipping Office Records	150
17. Personnel Decontam/Shower	185
18. Womens Change Room/Shower	215
19. Mens Change Room/Shower	215
20. Shielded Counting Room	155
21. (NON) QC Analytical Lab	540
22. Radiochemistry Lab	497
23. Radiation Safety Office/Lab	162
24. Released Supplies	235
25. Interconnecting Hall Controlled area (6ft wide for fork pallet lift access)	1860
26. Utility Corridor - Lab	530
27. Ship Materials Storage	185
28. Lab Records & Office	280
29. Office Area	
a. Conference Room	518
b. Break/Lunch Room	236
c. Offices Area, Halls, Reception Area	3255
d. Rest Rooms - Men & Women & Hallways	742
e. Computer Room	100
f. Security Monitor Room	121
30. Monitors & Restrooms	150
31. Walls/Stairways and Other Spaces	1710
TOTAL IDENTIFIED AREA FOR SURFACE FACILITY - SQUARE FT	20,018.00

Shielded Cell Processing Area Equipment

The surface processing facility contains a shielded cell (hot cell) processing area for the hot targets. This equipment is not part of the building but is discussed to illustrate the special requirements for the building. This area will consist of two banks of hot cells. The two banks of four processing hot cells will be installed on the legs of a horseshoe configuration with backs (containing access doors into the cell) facing each other, and the windows facing out so that when a hot cell door is open the radiation shines to the rear of the opposite bank. The closed end of the horseshoe has a long transfer hot cell across the end interconnecting each bank of hot cells. The transfer cell contains manipulators on each side with the pneumatic target transfer tubes from the Target Area entering in the middle portion of the cell. Each bank will have one waste disposal cell at the end of the bank of processing cells. In addition, one of the banks of hot cells will have an additional storage/dispensing cell. The dispensing hot cell will be equipped with manipulators. One of the processing cells will be equipped with through-the-wall manipulators. The waste handling cells will have a single over-the-wall manipulator. All other processing hot cells will be equipped with manipulator plugs, so manipulators can be added as necessary in the future.

Each cell in the bank will be connected with a conveyor belt system. This conveyor belt system is capable of moving in either direction, and the system will have a clear opening of 8" wide and 10" high. This allows material to be transported along the various cells in the bank.

The rear of each of the processing cells will have a door capable of accessing the entire interior of the cell. Each of the processing cells will have a removable enclosure that acts as a separate liner. The waste disposal cell will be equipped with a shielded interlock to allow waste containers to be removed from the cell without exposing personnel. The back of the transfer cell will have a door opening into the horseshoe area.

Ventilation for the processing cells will be connected through the removable inner liners. The transfer, processing, waste, and storage/dispensing hot cell will have a 12" x 12" x 6" shielded HEPA filter on the roof. The transfer cell and processing cells will be equipped with quick connects for air, water, vacuum, gas, and one extra. All cells will be equipped with a low profile fluorescent light and accessory plugs on the roof for control cables and access lines.

Each hot cell will be equipped with a appropriate size lead glass window to allow viewing of the inside of the cell.

Additional Details of Construction for the Surface Processing Building:

The clear ceiling height in Laboratories is 12 ft. The foundation is reinforced-concrete drilled piers bearing in the limestone substrata. The ground floor slab is a reinforced-concrete slab on select fill. The slab is thickened at the shielded cell processing area to accept heavier hot

cell loading.

The roof structure is light steel framing on steel columns with steel roof decking and built-up roofing. Exterior walls are tilt-up river rock wall panels bearing on drilled pier foundation. Exterior walls are furred with concrete masonry units with epoxy paint. Aluminum windows are used in office area. Interior partitions in the laboratory area are concrete masonry units to roof structure with epoxy paint. The office partitions are standard drywall painted and the interior of exterior walls are furred with drywall and painted. The interior doors are painted wood doors in hollow metal frames.

Ceilings in the Surface Processing Building include:

Laboratory area - Suspended fiberglass mat with vinyl cladding
Office area - Exposed grid acoustical
Ceiling height - Office 10 Ft., Lab areas 12 Ft.

Toilet Rooms have ceramic tile floor and wet wall. Other walls are vinyl wall covering. Typical toilet fixtures and accessories are used.

Mechanical

Air conditioning is based on "once through air" for the Shielded Cell Processing Area and Sterilization Room and on ASHRAE standards for the remainder. Particulate filtering of 300,000 parts per million is required for the Shielded Cell Processing Area and Sterilization Room. The effluent from all labs will be ducted to the centrally located exhaust stack . The exhaust stack will discharge at an elevation* of no less than 2.5 times the RPF building height relative to ground level, and will include filtering/monitoring for radioactive content.

The seven (7) laboratories include twenty six (26) exhaust hoods and three sinks supplied with hot and cold water. The hoods are rated at 750 cfm each. Their nominal operating flow rate is 500 cfm. Approximately eighteen (18) of the hoods will use 70% auxiliary (outside) air and only 30% of the air conditioned room air. Each lab will also be supplied with distilled water taps. Office air will be supplied by a conventional variable volume air control system.

Laboratory and decontamination room plumbing is connected to three (3) 5,000 gallon retention tanks located adjacent to the RPF building. Toilet rooms are connected to a septic system also located adjacent to the RPF building. Laboratory equipment interconnects and fire protection/sprinkler systems have been included in the cost appraisal.

Electrical

Lighting level -	Lab area	80 Fc Pendant mounted high efficiency fixtures
	Office area	One parabolic fluorescent fixture per 80 SF max.

Service -	Lab area	Allow 5 watts per SF for equipment and outlets
		Include 1-120 V duplex outlet per 100 SF
		Separate electrical panel in each lab
		Provide 1 phone outlet per 200 SF
		Seal all floor, wall, and ceiling penetrations
	Office area	Allow 5 watts per SF total
		Include 1-120 V duplex outlet per 100 SF
		Provide 1 phone outlet per 200 SF
	General	Include service for exhaust and AC equipment
		Lighting protection system included

The adjacency requirements in the processing area are extensive and drive the floor plan configuration. A combination of operational/radiation safety and Good Manufacturing Practices requirements also drive many building considerations. A substantial number of these considerations are delineated in the RPF Radiation Safety Manual located elsewhere in this report. It covers in detail controlled areas, regulated zones, radiation areas, supervisory/instrumentation/interlock safety systems, door monitoring and alarms, air handling and filtering systems, and liquid waste storage. The sections on air handling and waste retention are repeated here in slightly revised form for information.

Air handling system and filters

The various exhaust systems involving the target station area and the hot cells in adjoining laboratories are designed in such a manner as to provide a fixed pattern of air flow in the direction of the target station area, under normal or abnormal conditions. All rooms in the radioisotope production facility are evaluated with respect to their relative contamination potentialities in decreasing order of severity. These rooms comprise the RPF so designated because of their locations with respect to the Target Station Area. All air exhausted to the atmosphere from these room is passed through two absolute filters into a manifold to a single exhaust stack. It is possible to preassign and maintain different negative pressure values in each room so that the nearer the room is located to the target station area the greater is the negative pressure assigned and maintained in that particular room.

All rooms supplied with conditioned air are provided with dampers capable of adjustment, as well as being capable of automatic shut-off. Similar dampers are located in the exhaust ducts. If the air supply to any of the occupancies service is shut-off because of an emergency condition caused by some accident, the quantity of air ordinarily delivered to the room is automatically recirculated through the bypass section of the air handling unit, allowing the unit's blower to continue normal operation. This feature is also provided in the exhaust unit associated with the system. This method allows constant operation of all systems, both supply and exhaust, irrespective of disruption of source to one or more rooms connected to the system, as well as providing a dilution factor for any radioactive gas escaping the occupance into the exhaust duct.

Separate absolute filters are installed on the air exhaust ducts from the following areas:

Target Area

Target station assembly area
Irradiation room isotope production station
Transfer line to radiochemistry area

Surface Facility

Target transfer cell and processing cells
Laboratory areas

All of these separate air exhaust ducts feed into a single exhaust stack which is vented to the atmosphere at the top of the RPF building.

Separate radiation sensors are situated down stream of each absolute filter for the purpose of monitoring activity levels in the exhaust air from the different locations listed and also the total activity level in the air vented to the atmosphere. All of the remote readouts are displayed on a single control console in the Health Physics office. It is possible to preset any particular reading on a monitoring instrument as an "alarm level" so that if the activity level exceeds this level visible and audible warning will be given at the Health Physics Control Console. In addition, air flow rates and operating conditions of the exhaust fans can be monitored from this console. Schedule for the replacement of filters will be under the control of the Health Physicist, who will first check any activity levels, for the protection of maintenance personnel, and who will keep records of changes and of activities detected. Calibration and maintenance of the radiation sensors in the exhaust system shall be the responsibility of the Health Physicist.

Liquid Waste Storage

Liquid radioactive waste, - resulting from the processing of accelerator products or from the washing down of hot cells or other decontamination procedures, - will be contained in liquid retention tanks outside the RPF building. Three glass-lined storage tanks, with a combined capacity of 15,000 gallons, are located here for this purpose. It is possible to route the liquid waste to any one of the three tanks and also to pump from one tank to another. The outlet from the tanks feeds into the septic tank system via a lockable valve. The key to this valve will be held by the Safety and Security Department of the facility. Before the key can be released, a written request must be submitted containing the signature of the Radiation Safety Officer. Before this request is made, samples from each tank will be assayed by the Health Physicist to ensure activity levels do not exceed allowable limits. Results of all assays will be kept on file. It is anticipated that the capacity of the storage tanks will be

sufficient to permit the holding of radioactive wastes until decay to negligible levels has taken place and that it will not be necessary to discharge the tanks more than once very three or four months. Trade-offs must be evaluated for placement of this tankage above or below ground level.

V. AITI Commercial Production Equipment

A. Linear Accelerator for Commercial Radioisotope Production

1. Overview

The baseline requirements for the radioisotope production accelerator are 70 MeV at 1 mA average beam current, with the potential for upgrading to 2 or 3 mA. Beams of 30, 50 and 70 MeV must be provided for commercial production. Economic viability of the radioisotope production enterprise requires 24 hour a day operation, seven days a week with 200 μA-hrs of beam for each of four radioisotopes every week to insure a steady supply of basic radioisotopes. To keep the power delivered to a target at a reasonable level, based on current target technology and the available beam power, the beam must be split among at least four targets on a time scale that is short compared to thermal time constants. Two accelerator technologies have been considered, linear accelerator (linac) and cyclotron.

Radioisotope production on a commercial scale suggest that a linac is preferred over a cyclotron. The linac is easily capable of delivering 1 mA beams, and there are straight forward upgrade paths to much higher currents. However, no manufacturer is willing to guarantee more than 1 mA extracted beam from a standard cyclotron. The linac proton beam is inherently completely extracted for simple transport to external targets, and the pulsed H^+ beam is readily distributed to multiple targets on a pulse-by-pulse basis.

The linac consists of cascaded accelerator tanks with energies of 30, 50 and 70 MeV. The multiple energy requirement is met by turning on rf power only to the tanks required to reach the desired energy for a particular pulse. The beam focusing is designed so that the 30 and 50 MeV beams can be drifted through the unexcited tanks to the end of the linac. The beams are simply split into separate beam lines for each energy by an bending magnet at the end of the linac.

AITI intends to purchase (or lease) a 70 MeV - 1.0 mA linac with guaranteed specification, performance and delivery from a bonded commercial vendor. In our studies, at least three linac technologies would be evaluated. Our approach is the traditional, proven commercial linac (AccSys, J.P. Accelerator Works) which consists of an RFQ accelerator from an injection energy of 30-50 keV to 2-3 MeV followed by a traditional post-stabilized drift tube linac (DTL) with permanent magnet quadrupole (PMQ) focusing. An alternate technology,

proposed by Los Alamos National Laboratory (LANL), is to use a long coupled section RFQ (Young 1994) from the injection energy to the 10-13 MeV level, followed by a coupled cavity DTL (CCDTL) (Stovall 1994). The principle advantage of this technology is that the PMQs are placed between cavities and not in the drift tubes, simplifying construction. A third alternative, proposed by Linac Systems (Swenson 1994) is the electric focused DTL. This requires a short RFQ to an energy of 1 MeV or so followed by a DTL that has electric quadrupole rf focusing elements inside the drift tubes. These elements are excited by the normal drift tube currents. The advantage of this technique is the elimination of PMQs entirely. At this time, either of the latter two approaches would require an accelerator development program to construct the system and prove the technology.

The ion source, RFQ and DTL tank can be obtained from commercial sources, with performance guaranteed by the manufacturer. The same commercial vendors are capable of performing the modifications to increase the average beam current capability of the remaining components.

The DTL will be operated in a pulsed mode with a peak beam current of 50 mA, requiring a duty factor of 2% for 1 mA average current. The choice of pulse width and repetition rate to obtain 2% duty factor is a compromise between conflicting requirements. Efficiency favors long beam pulses because of the power lost during the cavity fill time when no beam is accelerated. Thermal cycling between beam pulses favors a high repetition rate to minimize problems due to thermal transients. The repetition rate on each target ideally should be at least 60 pps. Also, it is good to have the beam repetition rate set at a multiple of the power line frequency. For a beam split between four targets this suggests a 240 Hz repetition rate and a beam pulse length of 83 msec. Since this length is short, considering a DTL fill time of about 15 msec and the requirements for upgrading the current, the baseline design is for a 110 msec beam pulse at 180 Hz, with a 125 msec rf pulse.

The average beam current can be upgraded by increasing the peak beam current, increasing the duty factor, simultaneously accelerating H^+ and H^- beams, or a combination of these factors. Increasing the beam current by increasing the duty factor can be accomplished by increasing the pulse width, the repetition rate or both. Either choice requires that the rf system supply not only the additional beam power, but also additional cavity power. Increasing the repetition rate alone is attractive because the energy storage requirement remains the same and only additional dc power need be supplied. Increasing the peak beam current requires additional rf power equal to the added beam power, but is limited by the initial design current limit of 50 mA. This limitation can be overcome by simultaneous acceleration of H^+ and H^- which increases the peak beam current without increasing the beam space charge forces that limit the peak current, because the two beams are separated longitudinally. This approach also requires that the rf power system supply only the additional beam power. While this technique increases the complexity of the low energy beam transport, before and after the RFQ, adding to the initial construction cost, it is cost effective to make minimal provision for this capability to decrease the down time required for future upgrading of the beam current.

To determine the incremental cost for a current upgrade, a comparison has been made between two approaches to doubling the average current. This comparison does not include the effect on the initial capital cost of including the required peak and average power capability in the accelerator structures and rf power systems. An estimate of the operating ac power costs and relevant capital equipment costs is presented in Table V-1. Mode I is the baseline operation with 50 mA peak current at 2% duty factor. Mode II is a 2X current upgrade by doubling the repetition rate. The results for doubling the pulse length (not tabulated) are similar. A slight increase in efficiency is obtained because the fill time is a smaller fraction of the rf pulse length. The capital cost of the upgrade is slightly higher because of the increased energy storage requirements, but the difference is not significant for this estimate. Mode III assumes that the average current is doubled by simultaneous acceleration of H^+ and H^-. Such an upgrade is assumed to add \$200k to the ion source/low energy beam transport (LEBT) cost. The power handling capacity of the accelerator structure and klystron rf power sources is assumed to be built into the initial construction, with a negligible effect on the original construction costs. The capital equipment costs are assumed to be paid for at 10% interest over a 25 year period and depreciated to zero over a 25 year life time. An operating year is assumed to be 6000 hours. Differences in ion source operating costs have been ignored. Other assumptions are made about klystron efficiency, power supply efficiency, cooling tower cost, power supply cost and ac power cost.

The analysis shows that ac power cost dominates the cost of doubling the current. There is a net reduction of beam cost of about \$0.02 per mA-hr obtained in mode III. An increase of \$1,000,000 in the upgrade cost only affects the beam cost by \$0.01 per mA-hr. If the beam can be produced at \$0.30 per mA-hr, the savings may be worthwhile, provided that there is no other significant increase in operating costs due to the complexity of accelerating two beams simultaneously.

Table V-1
Estimate of Differential Costs for 2X Current Upgrade

Mode	I	II	III
Peak beam current (mA)	50	50	100
Beam duty factor	0.02	0.04	0.02
Avg. beam current (mA)	1	2	2
Peak beam power (kW)	3500	3500	7000
Avg. beam power (kW)	70	140	140
Peak cavity power (kW)	7000	7000	7000
RF duty factor	0.0225	0.045	0.0225
Avg. cavity power (kW)	157.5	315	157.5
Klystron efficiency	0.5	0.5	0.5
HVPS efficiency	0.9	0.9	0.9
AC power (kW)	506	1011	661
Cost of power ($/kWh)	0.1	0.1	0.1
Cost of power (k$/7200 h)	364	728	476
Cooling tower (k$)	101	202	132
Power supply (k$)	329	657	430
Ion source & LEBT (k$)	100	100	300
Total capital costs (k$)	530	959	862
25 year payout (k$/y)	58	106	95
Interest (k$/y)	37	67	60
Total (k$/y)	- 422	834	571
Milliampere hours/year	7200	14400	14400
Incremental cost ($/$\mu$A-h)	0.059	0.058	0.04

The initial cost for ensuring 2 mA capability by doubling the duty factor is negligible and it will be less than $100,000. The klystrons will handle 4 MW at the 4.5% rf duty factor required for 2 mA operation at 4% beam duty factor.

The cost differential for manufacturing the linac for easy upgrading by adding an H^- beam will exceed the costs for the increased duty factor technique. It is desirable to minimize the down time required to add an H^- beam, the approach would have to be built into the RFQ-DTL transition region from the beginning, which would increase hardware costs. The benefit of increasing the beam current from 1 mA to 2-3 mA is significant due to the increased productivity and production of radioisotopes. The above incremental costs indicates the production would increase by 100% for a 20% initial manufacturing cost.

2. Linac Components

a. Ion Source and Injection

The primary ion source will be a 60 mA H^+ duoplasmatron that is available commercially from several sources. One such source is AEA Technology of Culham, England. (Their budgetary quote for an ion source without power supplies was less than $100,000 (Proudfoot 1995).) If a H^- ion source is purchased it would be one of the SSCL H^- ion sources if available, it may be possible to consider dual beam operation soon after startup. There are some beam dynamics issues that must be considered up front if dual beam operation is to be implemented without a major interruption to radioisotope production. A choice must be made between combining the two beams ahead of the RFQ or after the RFQ. The latter choice requires two RFQs. Combining RFQ beams at the 2.5 MeV level may simplify the low energy beam transport from the ion source to the RFQ, but is complicated by the probable need for buncher cavities in each leg to preserve the beam emittance. Combining the beams at the ion source extraction energy requires attention to the effects of space charge on transverse emittance. However, this possibility should be considered because the high beam current already rules out short, electrostatically focused beam lines between the ion source and the RFQ. Also, because a new RFQ will be built, there is some flexibility in selecting the RFQ injection energy.

With the electric quadrupole focusing of the RFQ, the difference in charge sign between the two beams affects the beam shape. Whether there is one RFQ or two, the beam transport between the RFQ and DTL must be carefully designed in order to match both beams into the DTL. Furthermore, the charge sign difference affects the direction the beams are steered by misalignment of the DTL quadrupoles. Error tolerance studies need to be performed to determine the required quadrupole alignment accuracy. If dual beam operation is envisioned, the technical and economic impact of these features must be addressed. It will not be feasible to shut down a production linac for the time required to realign the drift tubes.

b. RFQ

AITI will select a commercial vendor such that it is more cost effective to go with a commercially produced RFQ, using the manufacturer's design. The LANL RFQ mechanical design can be produced by LANL or through technology transfer manufactured by a commercial vendor. The physics design affects only the details of the RFQ vane tip shapes and the structure length and is basically independent of the other mechanical and electrical design features of the RFQ structure.

A major simplification of the rf power system is possible if the RFQ power is obtained from the first DTL klystron. This has already been done at one major RFQ installation (BNL) and should be feasible for the radioisotope production facility. Using two RFQs for dual beam operation requires separate RFQ power systems, both to provide the necessary rf power and to permit phase control for combining the beams. This will be an additional capital cost for upgrading to 2X beam current. The RFQ power will be extracted from the DTL by an added power coupling loop, similar to the RFQ drive loop. A mechanical or ferrite-tunable phase shifter in the transmission line between the DTL and the RFQ will permit setting the RFQ phase relative to the DTL. The rf feedline will not be evacuated to avoid multifactoring problems. A vacuum window in the power coupling loop and in the RFQ drive loop will isolate the transmission line from the RFQ and DTL vacuum. The RFQ amplitude will be adjusted by rotating the power coupling loop in the DTL. This technique has better performance and is simpler than an adjustable power splitter in the rf feedline.

c. DTL System

Based on the experience at LANL and other laboratories and in the opinion of commercial vendors, a linac can be manufactured for operation at 3.5% duty factor. If 4.5% duty factor is feasible, it will be possible to double the beam current by doubling the duty factor. The proposed modifications to the tank wall cooling, adding extra cooling channels between the existing channels, should support 4.5% duty factor if the coolant flow is increased. Analysis of the drift tube cooling suggests that some drift tubes do not have to be modified for 3.5% duty factor. However, improved drift tube body cooling is a necessity for 4.5% duty factor. The impact of improving the drift tube body cooling is not as great as it might seem, since the stem cooling changes require rebuilding the drift tube bodies in any case. Thus, it is feasible to manufacture or use existing components without compromising the possibility of upgrading to 2 mA beam current.

The required work (as quoted by commercial vendors) to utilize the SSCL components and manufacture a linac to guaranteed specifications are as follows: Finish machine work is required on the penetrations of the top beam for mounting the drift tubes on some tank sections. All the tank sections must be modified by adding penetrations for the tuning bar cooling tubes. All sections of these tanks must be copper plated.

For high duty factor operation, the end walls must be modified to improve cooling to both

the drift tube and the wall between the nose and the flange. The existing tank frames and alignment struts can be used without modification.

The drift tube stems must be modified to have re-entrant cooling channels to improve the heat removal from the stems. In the present scheme the cooling tubes are too small for adequate coolant flow to the drift tubes and make only haphazard contact to the stem. This modification requires replacing the drift tube body. The current drift tubes have a body on the order of 1" long which is the only cooled portion of the drift tube. The remaining drift tube length is in the noses, which are cooled by conduction to the body through the electron-beam welds. By lengthening the drift tube bodies, more cooling can be provided to the drift tube and the conduction cooled noses can be much shorter, reducing the heat flow across the weld joint. Shortening the noses also allows reworking the weld joint for better heat flow. Because of the increased coolant flow requirement, the drift tube water manifolds must be replaced or modified to permit parallel feed of coolant to all drift tubes.

The post stabilizers are designed for conduction cooling and must be modified for active cooling. The post stabilizers will have an axial hole bored nearly the full length of the stabilizer. The coolant will be supplied through a concentric tube, with the return flow between the supply tube and the stabilizer wall. Adding post stabilizer cooling requires additional water manifolds for the water supply and return.

The tuning bars must be modified to have a cooling channel. A cooling tube will be brazed to the underside of the tuning bar. The water supply and return are provided by passing the ends of the cooling tube through the tank wall. A vacuum seal will be made between the tank wall and the outside of the cooling tube. This technique avoids water to vacuum joints. The cooling tubes complicate the installation of the tuning bars. However, the tuning bar size will be determined by using uncooled tuning bars when the tanks are cold tuned. The permanent tuning bars will then be machined to the required finished size. Any discrepancies in frequency due to the uncertainty in this process will be accommodated by the slug tuners.

Because of the thermal gradients introduced by the high duty factor operation, it is not feasible to control the tank frequencies by varying the tank or drift tube coolant temperature. Some form of active tuning is required. This can be in the form of motorized slug tuners. The slug tuners must also be cooled because of the high duty factor operation. An alternative to motorized slug tuners is coupled ferrite tuners. Such tuners would be loop coupled to the cavity fields, using the slug tuner wall penetrations for access to the cavity field. A reactive current flowing in the tuners would be varied by varying the bias field on the ferrites in the tuner, changing the tank resonant frequency. While such tuners are expected to cost more than motorized slug tuners, they are attractive because there are no moving parts. The improved reliability in a production environment may offset the higher initial cost.

Commercial quotations from vendors (exclusive of the beam transport systems) indicates the purchase or manufacturing price of the 70 MeV 1.0 mA linac is approximately $10.8 million. The utilization of existing SSCL components indicates the manufacturing price to be $9.95 million.

The Linac system required for reliable radioisotope production to supply the needs of the radiopharmaceutical industry and other commercial purposes has been well established. In general, the system must supply proton beams of 30, 50 and 70 MeV at beam currents of up to 1.0 mA. The system must be capable of delivering these beams to at least four targets and possess the capability of expanding to eight targets in the future. Reliability is a critical factor in that the system must operate 24 hours per day, 6 days per week on an annual basis in order to be commercially viable. The radioisotope production facility must be commercially operated and supply radioisotopes using GMP, guaranteed delivery and comply with all FDA and industrial customer requirements. General Requirements for the RPF Linac are shown in Table V-2.

Table V-2

Linac Requirements For Radioisotope Production.

Ion Type	H^-
Output Energies (Kinetic)	30, 50, 70 MeV (nominal)
Peak Output Current (up to 70 MeV)	≥ 30 to 50 mA
Average Output Current (up to 70 MeV)	1 mA (nominal)
Beam Pulse Length (up to 70 MeV)	80 μs
Repetition Rate (up to 70 MeV)	330 Hz
Dispersion, nominal h,h' (E = all)	0,0
Output Beam Energy Spread	± 250 keV
Transverse Jitter	TBD
Energy Jitter	TBD
Synchronous Phase (Time) Jitter	TBD

d. Beam Extraction System

The beams will all be extracted from the high energy end of the 70 MeV DTL tank. Vendors indicate that 30 and 50 MeV beams can be transported to the end of the linac with little or no loss. A simple magnet would split the beams by providing an energy dependent deflection.

e. Diagnostics

The linac would be provided with simple beam current and beam spill monitors for safe operation. Elaborate scanners and beam position monitors will not be necessary, except for initial tuning of the machine. One set of portable beam diagnostic instrumentation will be adequate for the linac.

f. Controls

The accelerator control system is essential to safe operation of the linac. For commercial operation it is imperative to avoid the creation of a control system "empire." This means that commercial hardware and software should be used to the greatest extent possible. The issues to be addressed are facility and personnel safety, response time for readback of controlled parameter changes on critical adjustments, automatic operation, data logging, and remote monitoring and troubleshooting.

While the control system does not need to be as complex as the system planned for the SSCL linac, much of the control system hardware can be used for the radioisotope production linac. Requirements include multiprocessor, network, fiberoptic data links, commercial hardware, commercial software.

g. Klystrons and Gallery

The RF power system may consist of upgrade klystrons (from the SSCL) or due to the power requirements for dual beams and higher efficiency it may prove economical, both because of the initial cost and the long term operating cost, to use new, high efficiency klystrons designed specifically for the application.

To minimize construction and equipment costs, as shown in Figure V-1, the klystrons will be operated using a single, large power supply and energy storage system, with separate modulators for each klystron. The power supply, energy storage, high voltage crowbar, klystrons and modulators will be located together in a single room, along with a spare klystron and modulator. The capacitors and crowbars will be housed in an interior, metal-walled room with interlocked doors that prevent access unless there is no high voltage present and the capacitors are discharged. A single overhead crane is available for moving the modulators and klystron oil tanks and for removing klystrons from their sockets for servicing. The klystrons will be arranged so that a spare can quickly replace a unit requiring

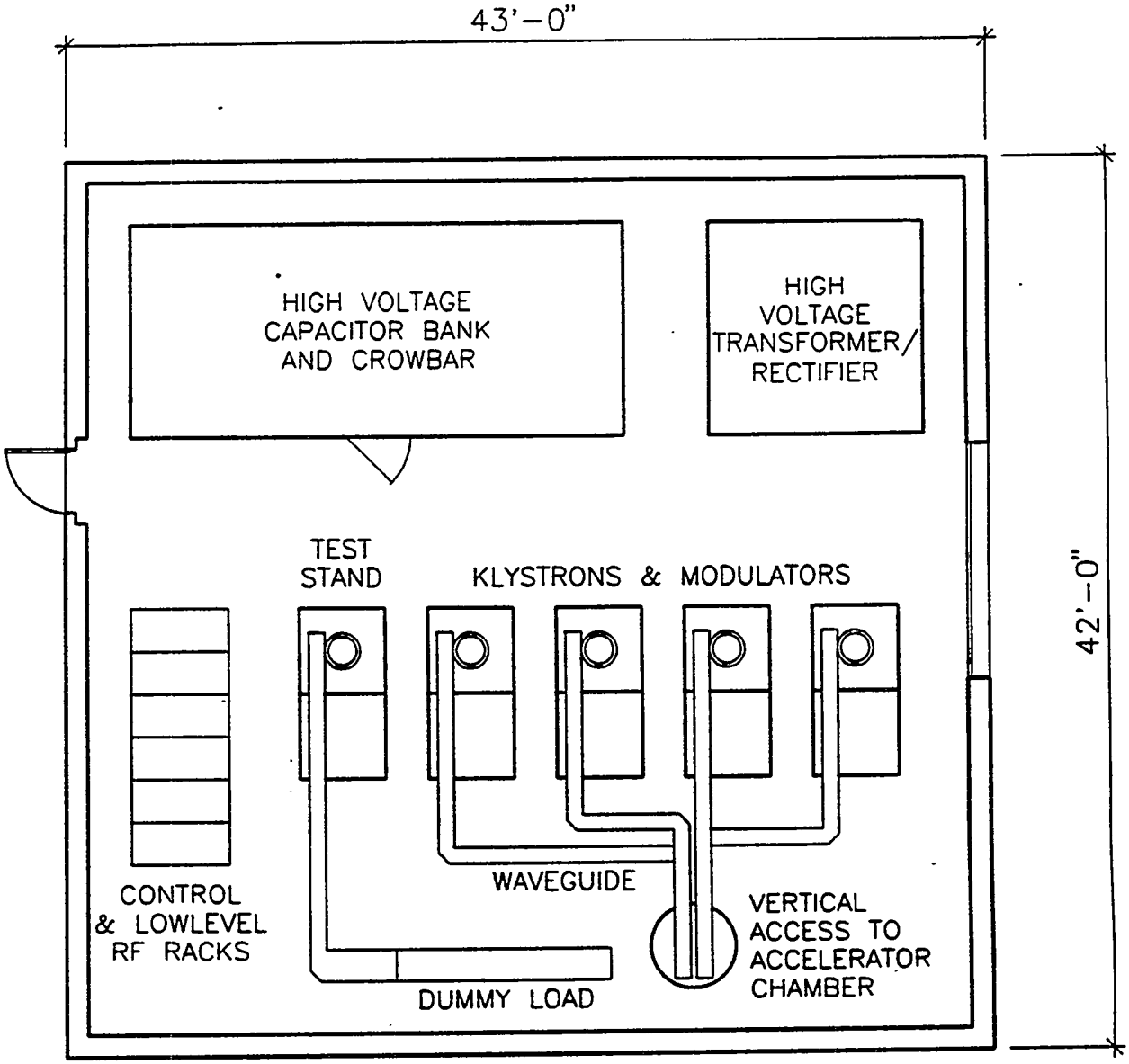


Figure V-1 Klystron Gallery Plan

NATIONAL BIOMEDICAL TRACER FACILITY

0 2 4 6 8

James E. Langford, Architect

service. The spare will sit in a test stand so that it can be kept conditioned, permitting a rapid return to full operation when it is placed into service.

The rf power from the klystrons will be distributed through WR-1800 waveguides along the linac tunnel wall. At 428 MHz the waveguide loss is negligible for the length of waveguide required. The waveguides will use a single passage from the klystron building to the linac tunnel. This arrangement reduces construction costs, simplifies the control system and is more convenient for maintenance than spacing the klystrons along the linac.

h. Ancillary Systems

The cooling system for each accelerator tank, both RFQ and DTL, will consist of a closed loop recirculating system with built in heaters for quick turn on. A water-to-water heat exchanger will transfer the heat to the house water system. The house water system will also directly cool the klystron anodes, which are operated at ground potential. The accelerator water system will be used to maintain the RFQ and DTL temperature constant. Slug tuners, or, equivalently, ferrite reactive tuners, will be used to maintain the resonant frequency of the linac.

3. Linac Beam Lines and Beam Transport

The linac parameters required to produce beams of the required energies, (nominally 30, 50 and 70 MeV) and average current (approximately continuously adjustable for each energy) is described above. The pulsed nature of the linac is ideally suited for the production of different discrete energies and currents. The pulsed nature further allows beams of the same energy to be delivered to different targets through the use of fast kicker magnets.

All beam energies are delivered to the end of the linac where the different beam energies are deflected by a DC bending magnet into three different beam lines for transport to the individual target stations. This magnet may be turned off so the beam can be delivered to a separate line for tune up and commissioning of the linac. The diagnostic devices can be removed from the beam allowing transport to a neutron multiplier target as shown in the facility overview, Figure IV-4. The beam will never operate out of a vacuum environment.

The layout of the linac beam lines and target area, Shown in Figure IV-4, is predicated by the need to achieve adequate separation between the individual target stations. The three nominal beam energies of 30, 50 and 70 MeV are deflected into different beam lines by the bending magnet. Additional bending magnets are needed to achieve adequate separation between these beam lines so that the overall size of the target area can be contained within the available site dimensions. The layout shown is very preliminary and much refinement and optimization is required. For example, the choice between a larger kicker magnet or a small kicker and DC septum magnet needs to be examined.

Each beam line will include a number of quadrupole and steering magnets to focus and align the beam. Diagnostics will consist of toroid current monitor, beam profile and position monitors as well as assorted loss monitors to detect any unexpected beam losses. The beam size on target will be adjusted with the final pair of quadrupoles and the area will be nominally 3-5 cm^2. A set of wobbler magnets will be just downstream of these quadrupoles so that the power per unit area on target can be maintained at the desired level which will be different for different targets.

The number of target stations indicated in Figure IV-4 is predicated by economic considerations and the different radioisotopes that will be produced. Each beam line will be

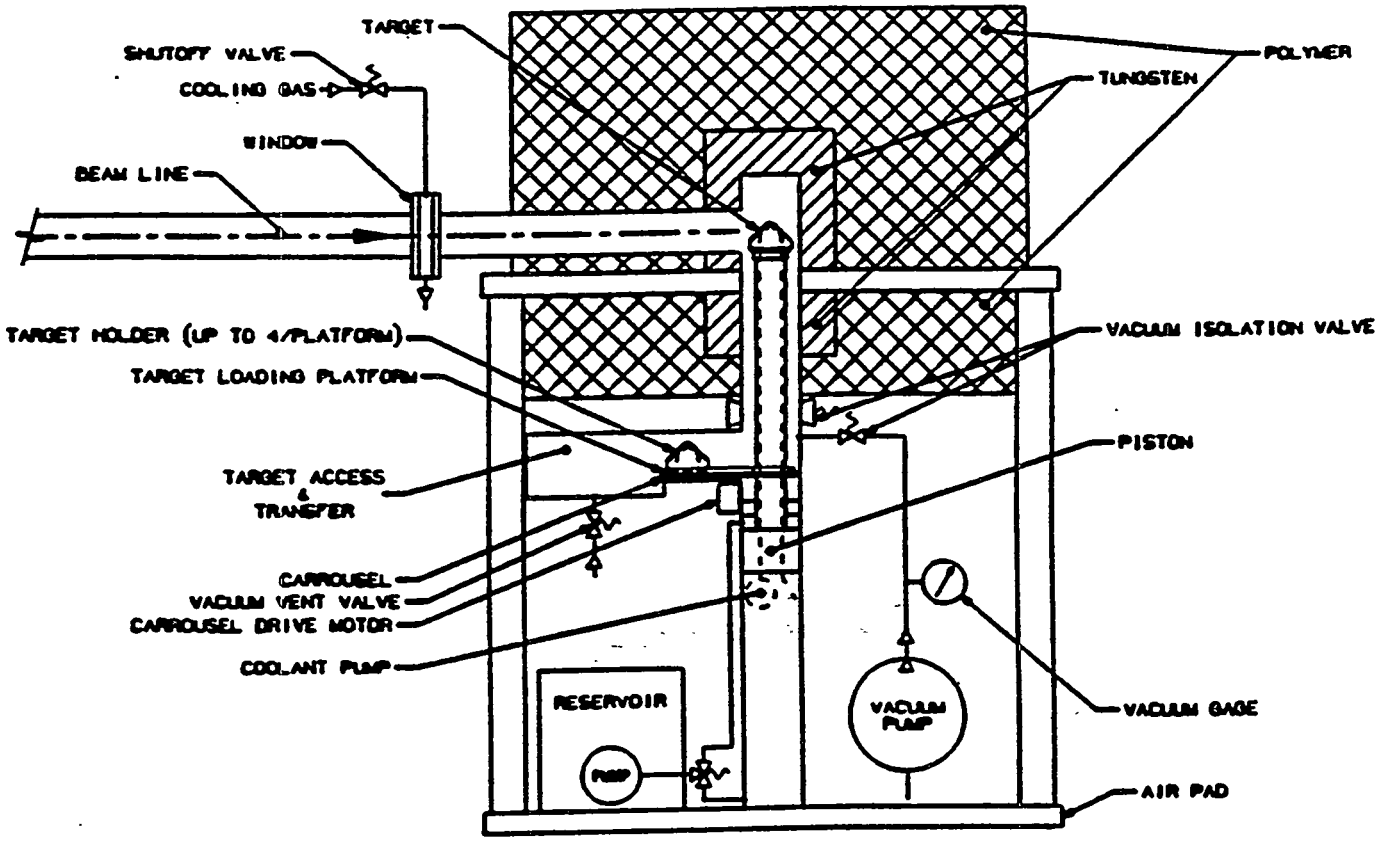
designed to accommodate at least two target end stations. One of these target end stations can be dedicated to a specific isotope; the other will contain a carousel capable of holding up to four targets, as shown in Figure V-2 only one of which will be activated while the others are waiting on the carousel. The beam transport line will include sufficient diagnostics to monitor the beam current, the beam centroid position, and the beam profile. Each target station will have a dedicated beam current toroid. Additional external diagnostics, such as radiation monitors, will detect excessive beam losses. These monitors will be used to activate interlock systems and help ensure safe operation.

Radioisotope target irradiation occurs only over an energy range that is defined by the physics of the nuclear reaction and the need to avoid impurities and contaminants caused by competing nuclear reactions. As a result, the incident beam energy from the linac will often have to be reduced or degraded. The double-foil window at the entrance to the target chamber will define the highest available beam energy for a given target station. There will be reactions, however, for which the emergent beam energy is too high, and further energy reduction is required. This energy reduction will be accomplished by one of the two techniques described below.

- Clad the target material with a thin foil.

- Install a ladder assembly just upstream of the target chamber with helium-cooled, double-foil windows so that the total thickness of this assembly and the target isolation windows reduces the beam energy to the desired value.

Technique 1 offers some potential advantages in the amount of stable isotope required and elimination of sputtering. Technique 2 is more straightforward. It is likely that some target stations will be dedicated to a specific radioisotope, and no further energy reduction will be required other than that designed into the isolation window.



Target Chamber

Figure V-2

4. Target Systems

Typical target systems and the production targets will, in general have similar characteristics. A concept for a target station carousel has been developed, as indicated in Figure V-2. This arrangement will reduce the external shielding and building requirements and will aid the manufacturing and production cycle. The design will be developed in detail and complete costs will be developed. The use of heavy local shielding surrounding the target station for radioisotope production targets has been studied in detail by Steyn et al. (1992) for a beam energy of 72 MeV. A complete design description of this type of target station is presented by Mills et al (1991). This radioisotope production target station described by Mills does not include the additional features of an air pad for installation or a carousel assembly as described below.

The use of the carousels will, in principle, allow unattended change-out of the individual targets. Replacement of carousels is, however, considered in the proposal as a manual operation. From the personnel safety standpoint as well as the operational standpoint, the potential of designing systems that incorporate the possibility of unattended carousel change-out will be investigated. In fact, the question of necessity for carousels themselves can be argued if target change-out can be accomplished in an unattended manner.

When a target is changed out, the newly-inserted target may require different beam characteristics, such as beam shape or macropulse sequence. It is necessary, therefore, to have a remotely-activated "tune-up target" as an integral part of the beam transport and diagnostic system preceding the production target in order to validate the desired beam characteristics before irradiation of the new target commences. Specific attributes of these target stations include:

- Self-Contained Target Stations
- Self-Shielded
- Quick Disconnect and Movable
- Six Target Stations - two for each beam line, four targets in each target station carousel, and two target stations for preparation
- Remote Target Positioning (water-cooled)
- Remote Target Replacement and Transfer to Hot Cell
- Weight approximately 5000 lb
- Neutron Dose at Surface of about 75.0 r/h (@300 mA)

- Gamma Transmission of 3×10^{-15}

The target area layout in, **Figure** IV-4 shows a staging area for installing and maintaining the target stations. This area is connected to the above ground processing area through a dumb-waiter.

A separate Low Conductivity Water (LCW) system shall be used for the target cooling. This system will include holding tank provisions to accommodate decay of activated ingredients in the water, such as leeched activated copper and tritium. The detail designs will address the levels of activation anticipated and the size of the holding tanks. This system will be located within the area containing the targets and beam lines and will be completely separate from the linac LCW system.

5. Target Handling and Transport to Hot Cell

The target mounted in the carousel is attached to a rotary remote-target positioning rod and is automatically positioned in-line with the proton beam for irradiation. The rotation of the target is variable between 1 and 3 revolutions/sec. At the end of bombardment (EOB), the target is retracted back to the carousel and removed from the positioning rod, and a new target is rotated into position. The irradiated target is then deposited in the transfer mechanism for transport to the hot target processing cell. The transfer mechanism is projected to be a link belt mechanism with irradiated target-holding chambers. Targets intended for bombardment will be assembled in the radioisotope processing area and transported to the target station by a pneumatic or mechanical automated system. Irradiated targets will be similarly transported by an automated system to the transfer cell located in the high-level radiochemistry processing area. From this station, each irradiated target will be routed remotely by a mechanical system to the appropriate shielded enclosure or glove box for chemical processing.

6. Target Processing

Chemical separation and purification of the irradiated targets will be performed in specially designed moveable glove boxes contained within fixed shielding cells. Procedures for the chemical processing of commercial radioisotopes have, for the most part, been developed and reported in the literature. Some development will be necessary to facilitate robotics processing procedures. Processing of each product will be conducted according to an approved batch record documentation, including in-process and final product sampling for analytical analysis.

7. Target Recovery

Chemical recovery and external reuse of isotopically enriched target material will be performed in a separate laboratory, following appropriate holding for decay. Recovered target material used to make new targets will be tested for identity and purity by activation

analysis.

8. Target Plating

A laboratory for target assembly and preparation will include the necessary equipment for plating specific targets with the enriched isotope.

9. Target Preparation, Isotope Costs, and Analysis

A Drug Master File (DMF) will be filed with the Food and Drug Administration (FDA) for each commercial human-use product supplied to radiopharmaceutical companies. The DMF is a compilation of information about the proposed product requested by the FDA to determine the identity, purity, strength, and manufacturing documentation used for the product. It also requires analytical methods documentation and compliance with established specifications. The DMF does not contain any clinical information that must be supplied by the distributor of human-use final product. In some cases, it may be necessary for the customer to generate clinical data using product prepared from the starting radioisotope.

10. Robotics

Robotics systems will be used wherever possible when handling highly radioactive material. These systems will be installed in the hot cells and in other areas in the high-level radiation area of the RPF.

11. Construction

The anticipated time line for construction and commissioning of the linac is shown in Table V-3 Model PI-70 production schedule. (AccSys)

Schedule 1. Model PL-70 production schedule.

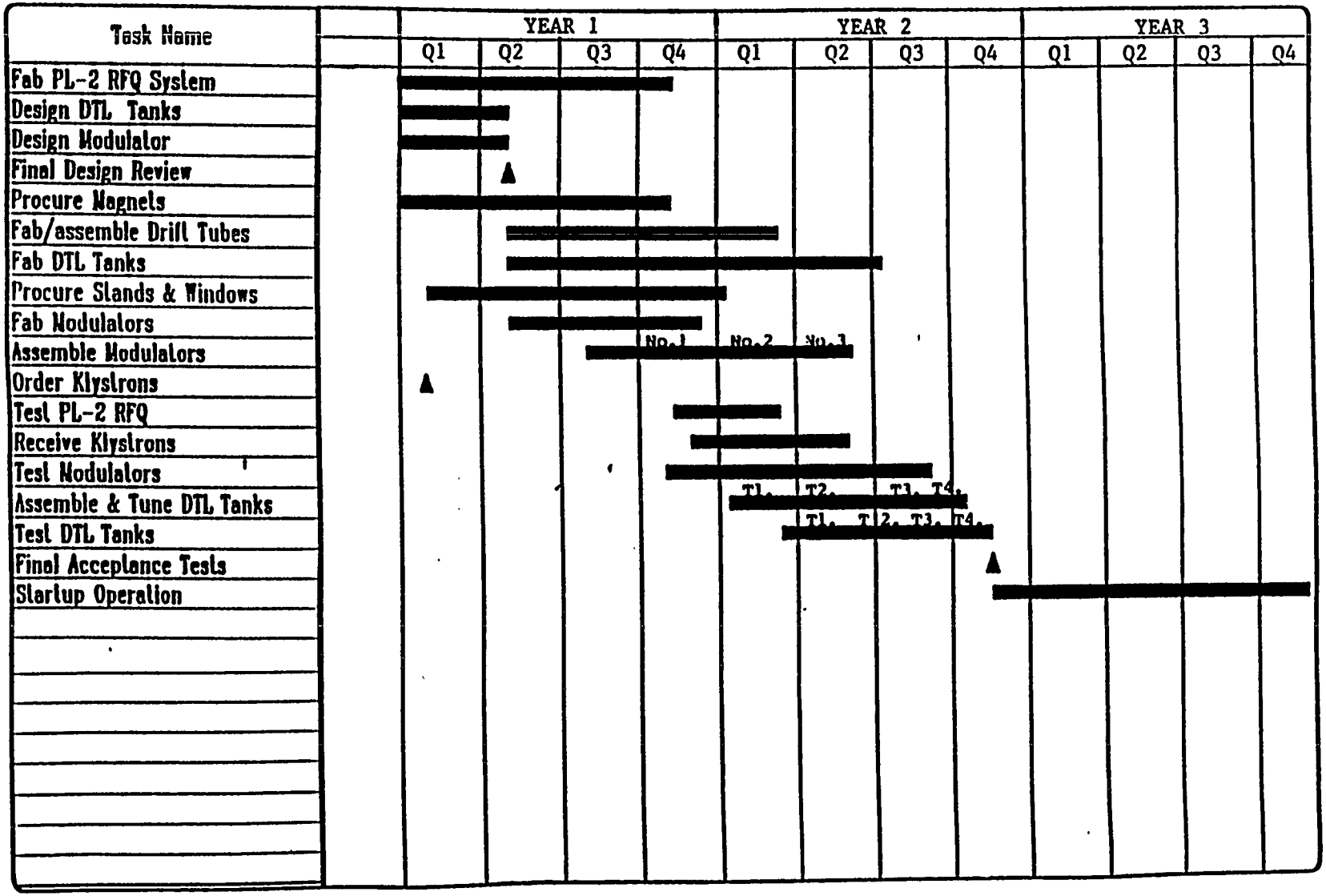


Table V-3

B. Dense Plasma Focus Neutron Source for Commercial Isotope Production

1. Overview

A dense plasma focus (DPF) is a magnetically driven, magnetized-fuel fusion device. The AITI DPF is a Mather-type system that can be fired repetitively to produce a large yield of neutrons for many applications. Ware et al (1973) has produced 2 x 10^{12} D-D neutrons per pulse. A 50% deuterium-50% tritium mixture should increase the neutron yield by a factor of 80-100 (Mathur et al (1970).

A 1.0 MJ ultraclean DPF device is being developed by AITI to produce 3 x 10^{15} D-T neutrons per pulse for radioisotope production. At a repetition rate of 0.33 Hz, the average neutron yield will be $\sim 10^{15}$ neutrons per second. The 0.33 Hz repetition rate will allow 25,920 shots per day or approximately 100,000 shots in a four day activation period. The total D-T neutron yield for the four day activation would be $\sim 3.4 \times 10^{19}$ neutrons.

The AITI Dense Plasma Focus (DPF) operating at 0.75 MJ has the capability of producing a fast neutron yield of 10^{15}n/shot. The neutron output increases as a function of pinch current ($\approx I^5$) and total system energy. AITI is in the process of research and development activities to manufacture DPF systems with high currents, repetition rates and system energies which will be capable of producing commercial quantities of radionuclides. In Table V-4 is listed the fast neutron reactions (n,2n), (n,p) and (n,α) which produce radionuclides of interest to the medical research community. Investigations by Freeman et at, (1993), Mather (1971), Gullickson and Sahlin (1975), Brzosko, et al (1992), Jäger and Herold (987), Filippov (1980), and others have studied the yield and energy distribution of energetic ions. The D(d,n)^{3}He and D(t,n)^{4}He reactions produce intense bursts of 2.45 and 14.1 Mev neutrons. The D, ^{4}He and ^{3}He ions are accelerated to energies of several MeV. Various investigators have observed ions up to and greater than 10 MeV. Intense electromagnetic fields generate large electrostatic fields and relativistic electrons and general collective ion acceleration. In Figure V-4 is shown a calculated deuteron ion distribution.

Freeman et al (1993) have observed the energetic production of deuterons in a 125kJ DPF discharge. Measurements were made by observing the positron annihilation (0.511 MeV gamma) from the decay of ^{13}N. The ^{12}C(d,n)^{13}N reaction (Q = -0.283 MeV) was created by few MeV deuterons produced by the very steep electrical gradients within the core of the pinch. Instabilities in the plasma filaments as well as the large electron current (2 MA) also provides collective ion acceleration of deuterons to MeV energies.

Deuterons (^{2}H$^+$) and helium ions ^{3}He^{++}, ^{3}He^{++} accelerated to several MeV may produce positron emitters required by nuclear medicine. Table V-5 list the possible reactions which can be produced in the DPF for producing radioisotopes for PET studies.

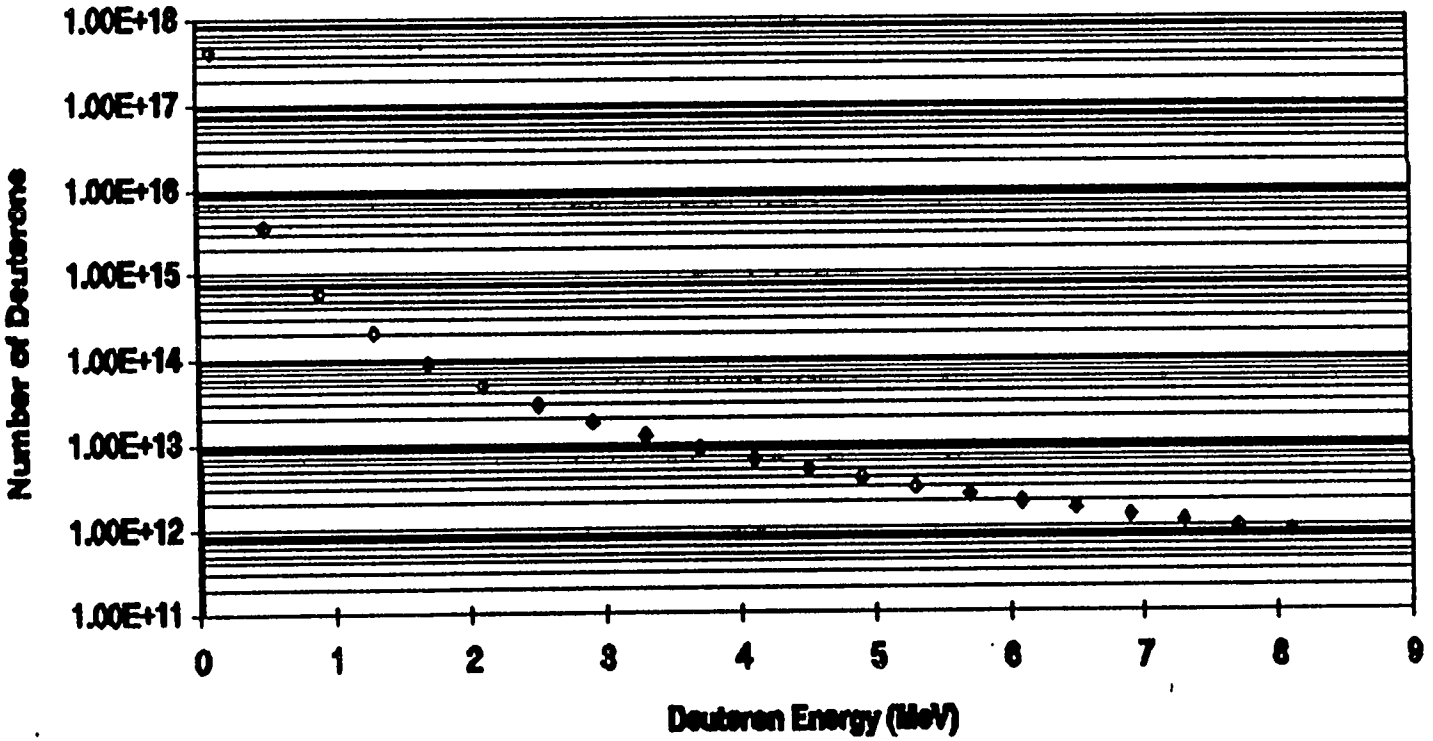
Table V-4.
Radioisotope yields produced with fast neutrons.

Radioisotope	Half-life	Target Element	Isotopic Abundance (%)	Nuclear Reaction	σ (mb)	Yield* (Ci)
^{3}H	12.33 y	^{3}He	0.000137	(n,p)	140	0.69
^{3}H	12.33 y	^{6}Li	7.5	(n,α)	28	0.08
^{7}Be	53.29 d	^{9}Be	100	(n,3n)	54	10.8
^{14}C	5730 y	^{14}N	99.6	(n,p)	43	.00014
^{13}N	9.97 m	^{14}N	99.6	(n,2n)	6.9	13
^{18}F	109.77 m	^{19}F	100	(n,2n)	43	61
^{22}Na	2.602 y	^{23}Na	100	(n,2n)	18	0.081
^{24}Na	15.02 h	^{24}Mg	79	(n,p)	197	195
^{24}Na	15.02 h	^{27}Al	100	(n,α)	122	121
^{28}Al	2.24 m	^{28}Si	92.2	(n,p)	252	221
^{28}Al	2.24 m	^{31}P	100	(n,α)	121	104
^{31}Si	2.62 h	^{31}P	100	(n,p)	142	122
^{32}P	14.26 d	^{32}S	95	(n,p)	254	47
^{32}P	14.26 d	^{35}Cl	75.8	(n,α)	137	22
^{33}P	25.34 d	^{33}S	0.75	(n,p)	214	22
^{35}S	87.51 d	^{35}Cl	75.8	(n,p)	137	3.9
^{44m}Sc	58.6 h	^{45}Sc	100	(n,2n)	120	58
^{44}Sc	3.927 h	^{45}Sc	100	(n,2n)	240	143
^{42}K	12.36 h	^{45}Sc	100	(n,α)	54	32
^{48}Sc	43.7 h	^{48}Ti	73.8	(n,p)	58	29
^{45}Ti	3.08 h	^{46}Ti	8	(n,2n)	9.6	4.8

Radioisotope	Half-life	Target Element	Isotopic Abundance (%)	Nuclear Reaction	σ (mb)	Yield* (Ci)
^{54}Mn	312.5 d	^{55}Mn	100	(n,2n)	719	4.1
^{55}Fe	2.68 y	^{56}Fe	91.7	(n,2n)	439	0.7
^{61}Cu	3.408 h	^{64}Zn	48.6	(n,α)	18	6.6
^{64}Cu	12.701 h	^{64}Zn	48.6	(n,p)	182	67
^{67}Cu	61.92 h	^{67}Zn	4.1	(n,p)	90	29
^{72}Zn	46.5 h	^{75}As	100	(n,α)	10.1	3.6
^{69}Ge	39.05 h	^{70}Ge	21.2	(n,2n)	407	135
^{74}As	17.78 d	^{75}As	100	(n,2n)	950	65
^{88}Y	106.64 d	^{89}Y	100	(n,2n)	848	8.7
^{89}Zr	78.43 h	^{90}Zr	51.5	(n,2n)	611	123
^{95m}Tc	61 d	^{96}Ru	5.5	(n,np)	180	2.5
^{97}Ru	2.9 d	^{98}Ru	1.9	(n,2n)	1027	200
^{127}Xe	36.4 d	^{128}Xe	1.9	(n,2n)	1376	25
^{139}Ce	137.66 d	^{140}Ce	88.4	(n,2n)	1833	8.4
^{153}Gd	241.6 d	^{154}Gd	2.2	(n,2n)	1980	4.6
^{199}Au	3.139 d	^{199}Hg	16.9	(n,p)	4.6	0.4

*Yield is calculated for 2.2×10^{15} n/cm^2/sec @ 14 MeV.
The sample size is 100 g.
Isotopic abundances < 90% are assumed to be 90%.
Irradiation times are the smaller of 96 hours and $2*t_{1/2}$.

Figure V-4



Calculated deuteron energy distribution produced by a Dense Plasma Focus.

Table V-5
RADIOISOTOPES FOR PET USING DPF

RADIOISOTOPE	DIRECT REACTION	Q VALUE (MeV)
^{11}C	^{10}B (d,n)	+6.465
^{11}C	$^{9}Be(^{3}He,n)$	+7.557
^{13}N	$^{14}N(n,2n)$	-10.553
^{13}N	$^{12}C(d,n)$	-0.280
^{13}N	$^{10}B(^{3}He,\gamma)$	+21.636
^{13}N	$^{11}B(^{3}He,n)$	+10.183
^{15}O	$^{14}N(d,n)$	+5.073
^{15}O	$^{16}O(^{3}He,\alpha)$	+4.915
^{18}F	$^{19}F(n,2n)$	-10.431
^{18}F	$^{17}O(d,n)$	+3.383
^{18}F	$^{16}O(^{3}He,p)$	+2.032
^{18}F	$^{20}Ne(d,\alpha)$	+2.792
^{18}F	$^{19}F(^{3}He,\alpha)$	+10.147
^{22}Na	$^{23}Na(n,2n)$	-12.418
^{22}Na	$^{21}Ne(d,n)$	+4.513
PARENT-DAUGHTER		
^{68}Ge	^{66}Zn (^{3}He,n)	4.940
^{82}Sr	^{80}Kr (^{3}He,n)	4.964
^{62}Zn	^{60}Ni (^{3}He,n)	3.560
^{52}Fe	^{50}Cr (^{3}He,n)	4.934
^{44}Ti	^{42}Ca (^{3}He,n)	5.861
^{72}Se	^{70}Ge (^{3}He,n)	4.196
^{118}Te	^{116}Sn (^{3}He,n)	2.987
^{122}Xe	^{120}Te (^{3}He,n)	2.524

Research and development will be done by AITI to determine scaling of neutron yield with DPF current. For this high power DPF, the neutron yield is expected to increase with the fourth or fifth power of the current as shown in Figure-V-5 for various DPF devices (Zucker, et al. 1975). In parallel with the research and development to verify scaling of DPF neutron yield with DPF current, a small, compact Pulsed Sealed Neutron Tube™ (PSNT) for radioisotope production is being developed. In many cases, the fast neutrons cross sections for production of selected radioisotopes is quite favorable and competes well with reactor-based fission production of radioisotopes. In addition, radioactive wastes associated with reactor-based fission production are considerably greater than with fast neutrons from a DPF device.

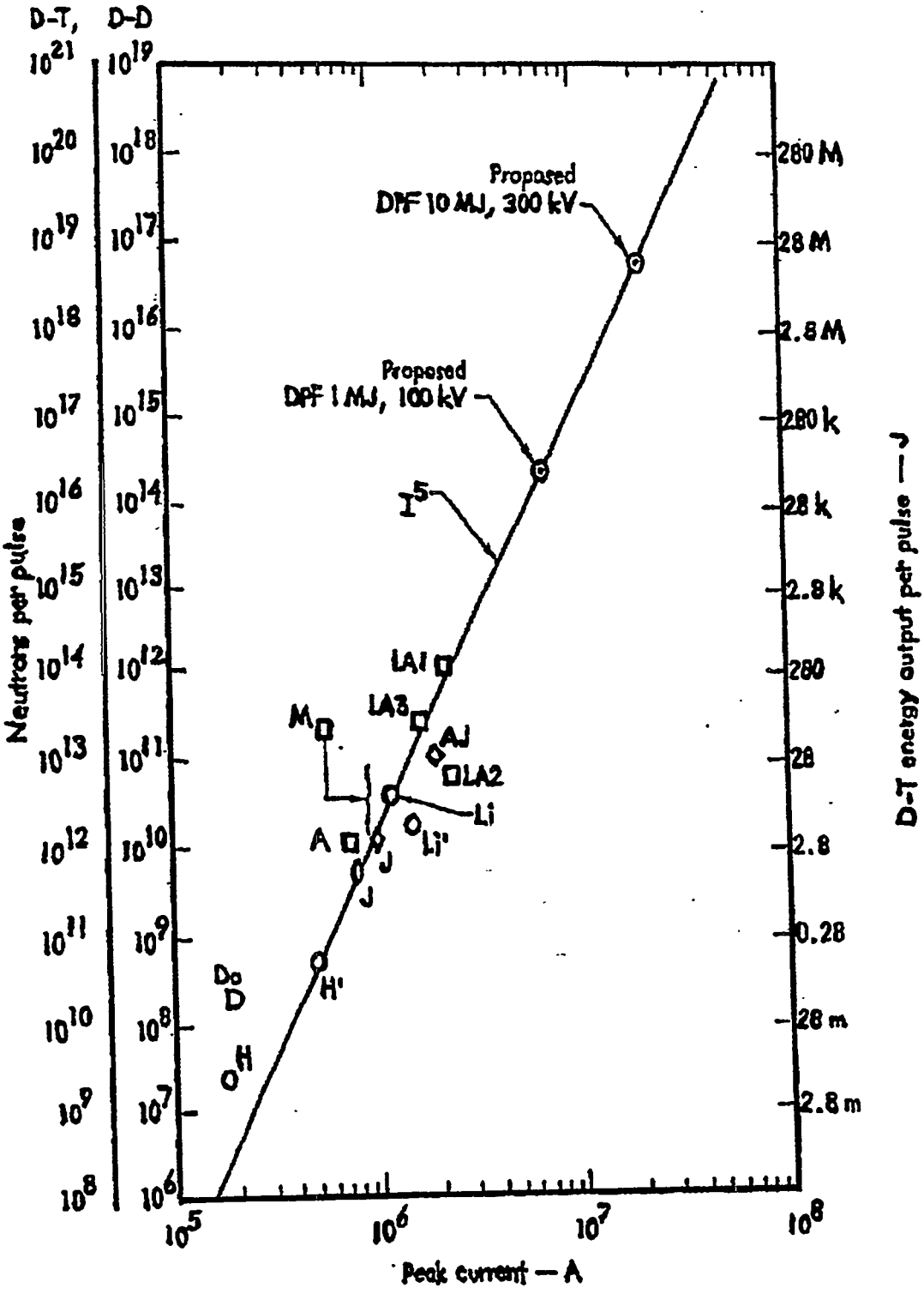


Figure V-5. Neutron yield vs peak current per pulse and corresponding energy output.

2. Requirements

The characteristics of the PSNT required for radioisotope production to supply the needs of the radiopharmaceutical industry and other commercial purposes have been established. In general, the PSNT must be capable of producing 3 x 10^{15} neutrons/pulse at a repetition rate of 0.33 Hz for an average neutron yield of $\sim 10^{15}$ neutrons/s for thousands of shots. The PSNT must be small and compact in order to locate materials to be activated near the pinch of the DPF. Reliability of the PSNT is a key component as it must be able to produce and deliver high fluxes of neutrons 24 hours a day, four to five days a week, fifty-two weeks a year to be commercially viable. The PSNT radioisotope production facility must be commercially operated and supply radioisotopes using Good Manufacturing Practice (GMP), guarantee delivery and comply with all Federal Drug Administration (FDA) and industrial customer requirements. The processing of radioisotopes from the PSNT DPF facility will be accomplished using the commercial isotope processing facilities as outlined in Section IV.G.1.d.

a. Space Requirements

The space requirements for the research and development and commercial operation are $\sim$10m x 22m. In addition, a 4m x 5m electromagnetic and radiation shielded control room is adjacent to the research and commercial area. The space to be used for the DPF facility is an existing Nike missile site five miles North of the University of North Texas (UNT) campus. The Nike site is owned by UNT and leased to AITI. The site contains three highly shielded concrete bunkers $\sim$20m x 22m located 6m below grade separated by $\sim$37m from each other. The research and commercial area will include space initially for research and development using the existing Los Alamos National Laboratory (LANL) DPF system including 750 kW, 120 kV power supply, three 250 kJ capacitor banks, 120 kV trigger, DPF chamber, D_2 gas feed system, control system, and diagnostic detectors and electronics. Prototype PSNT systems will be developed in the same space. After development and testing of the commercial PSNT system with a D-T gas mixture, the space will be used for commercial production of radioisotopes. Shielded space will be provided for maintenance and repair of equipment.

b. Power Requirements

Initially, the 120 kV system from LANL will be employed for research and development. A new and innovative high voltage power supply will be developed by AITI that will be capable of charging a 1 MJ capacitor bank in one second using the principle of "bucket charging" which results in a simpler, more reliable system. The power requirement for this power supply will be 1 MW while it is energized. During development of the commercial PSNT, the current will be increased to $\sim$4 MA. If neutron yield scaling is confirmed to increase with I^5, then the neutron yield should correspond to $\sim$2-4 x 10^{15} neutron per pulse. If the neutron yield per shot does not increase as expected, the repetition rate will be increased to possibly one shot every second. The increased repetition rate will require active

cooling of components. If a 1 Hz repetition rate is not attainable because of heat dissipation or power supply limitations, another alternative to be considered would be to construct ten DPF systems each with their own capacitor banks charged by the original 1 MW power supply in a round robin mode.

c. Shielding

Shielding for 14 MeV neutrons would require a main shield around the PSNT chamber to reduce adverse effects of radiation damage to the pulsed power equipment. Shielding would consist of hydrogenous material such as borated paraffin or polyethylene. The neutron yield of 10^{15} neutrons per second equates to a neutron flux of 8.8×10^{13} neutrons per second per steradian. The primary borated hydrogenous shield is located at a distance of 15cm from the pinch which provides and incident flux at the shield of 3.9×10^{11} n/cm^2/sec. Using a calculated shielding thicknesses of 60cm of primary shielding reduces the neutron flux 9.3×10^8 n/cm^2/sec emitted from the primary shield. The secondary neutron shield for housing the DPF is 60cm of high density concrete located at a distance of 3.3 meters from the primary shield. The incident flux on the secondary shield is 9.3×10^3 n/cm^2/sec and the neutron flux outside of the shield is approximately 1.0 n/cm^2/sec with an average energy of approximately 200 KeV. This represents a neutron dose of 0.0115 millirad per hour.

d. Pulsed Power Components

Pulsed power components have a finite lifetime and will require periodic maintenance and overhaul. The maintenance will be conducted during the two days when the PSNT systems are not operating.

3. Layout of DPF Facility

The 10m x 22m space for the DPF development facility is shown in Figure IV-5. The 220 m^2 area, which will occupy ~1/2 of one of the Nike missile site bunkers, will be divided into a well-shielded production area, a maintenance and set-up area, and a storage area for the incoming inventory of replacement parts. The 4m x 5m shielded control area is adjacent to the main DPF room. A conceptualized production unit is shown in Figure IV-5 in the western most vault. Space requirements for the production unit are substantially less than for the development activity.

4. Safety

High voltage, high current hazards require numerous safety interlocks and well trained personnel. The DPF facility will be constructed in accordance with OSHA and EPA guidelines.

Tritium use in the facility in the PSNT devices requires radiation safety procedures for handling and possible releases. The PSNT is being designed to prevent such releases by

developing a completely sealed system. After neutron irradiation and activation of the materials in the PSNT facility, the entire PSNT will be remotely removed and taken to the hot cell areas for harvesting of the radionuclides produced and salvaging of the remaining D-T gas mixture.

Layered radiation shielding will be constructed to comply with DOE's ALARA (As low as reasonably achievable) policy. The 14 MeV neutrons will be thermalized and captured in hydrogenized materials containing boron or some other substance with a high neutron capture cross section. Lead shielding will be provided to attenuate gamma-radiation associated with the activations.

5. Dense Plasma Focus Components

The DPF device consists of a number of separately identifiable components with the following specifications.

a. High Voltage Power Supply

The high voltage power supply must be highly efficient and highly reliable. The power supply must be able to quick charge the capacitor banks in a second or less. It should operate on 3 phase, 240 or 480 VAC. The high voltage power supply will be designed to be able to charge several systems at one second intervals.

b. Pulsed Sealed Neutron Tube

The pulsed sealed neutron tube will be constructed from materials of high integrity to prevent rupture of the tube even in case of failure. Materials will be selected to make product whenever possible. High voltage integrity of the tube, for the expected lifetime of four days or ~35,000 shots before harvesting of radionuclides, is a requirement. Initially, for the D-D development, the tube will be made of a stainless steel cylinder with stainless steel conflat flanges for ease of assembly and repair. Other construction materials will be tested to make product. After testing and development, a sealed tube will be used for the D-T development.

c. Capacitor Bank

The capacitor bank will have the following specifications: 1 MJ, 4 MA, one pulse per 10 seconds or 0.1 Hz, with a three-five μs rise time. The capacitor bank will include capacitors and the transmission lines to the plasma focus. Capacitors and components should be stable to 10^6 shots or better. For a weekly shot rate of ~35,000, this would require capacitor bank overhaul every 25-30 weeks. The individual capacitors should be easily replaceable in the capacitor bank.

d. Main Pulsed Power Switches

The main pulsed-power switches would be a high-pressure rail switch. These switches may require significant maintenance after 100,000 shots. For a weekly shot rate of ~35,000, this would require pulsed-power switch maintenance every three weeks or so. In the future, solid state switches may be employed as their current carrying capabilities and reliability increase in the future. The solid state switches would be essentially maintenance free.

e. D-T Gas Handling

D-T gas handling will utilize sorption pumps. These gas supplies will set operating pressures for the plasma focus, permit dynamic gas cleaning, and provide D-T gas reclamation, either at the end of a run or in the event of a system failure. With this approach for the D-T gas handling, the probability of a possible tritium release should be acceptably small. This type of system has been used extensively in the manufacture of pulsed sealed neutron tubes by Halliburton Services which produces neutron oil well logging systems for the petrochemical industry. Several thousand of these units are in operation in Texas and throughout the United States and have been demonstrated to be inherently safe. These systems are routinely licensed by the Texas Department of Health Bureau of Radiation Safety.

f. Control Electronics

The control system will provide charging, firing, and failure detection. The control electronics will switch the main power supply, detect completed charge of capacitor banks, and issue the trigger signal that is amplified to fire the main pulsed-power switches. After firing, the control electronics will recycle the switch gases for the pulsed-power switches and reset the capacitor bank in preparation for the next charging cycle. The control system will also monitor the cooling/heating of the plasma.

g. Diagnostics

Shot diagnostics would determine the neutron yield per shot and the integral neutron over a specified number of shots. The neutron yield per shot determination is necessary to assess operations, gas recycling, and the possibility of tube failure. The monitors for the pulsed-power system performance provide a redundant indication for tube failure as well as other components that will eventually fail. The facility should have a number of redundant neutron detection systems initially, all consistent with one another in terms of neutron yield per shot. The facility should initially have two silver activation detectors, two lead isomer detectors, and three neutron time-of-flight detectors located at flight paths of ~2 m, ~6 m, and ~30 m. In addition, fission track detection should also be available for periodic checking of detector calibrations. The fission tracks should be counted with an automatic counting system.

h. Ancillary Systems

Ancillary gas handling should be available for the main pulsed-power switches. At a shot rate of 0.1Hz, the power input will be ~100kW. This power will be reduced to heat in various components that will require either passive or active cooling, depending on location. This cooling requirement, while a bit of a challenge in the PSNT itself, is relatively straightforward. However, if our shot rate must increase to ~0.5Hz, then the power input will rise to ~500kW, and the complexity of the cooling system will be greater.

General temperature and humidity control are required to support the voltage controls that are incorporated into the pulsed-power supply design. The design goal for the production machine is to use air insulation for the high-voltage stand-off control, rather than transformer oil for example.

6. Target Systems

The geometry of the plasma focus anode will be modified to contain the sample of material that will be transmutated to the radioisotope of interest. The key design issues are that the material to be irradiated must be protected from the plasma discharge, the sample must be located as close to the plasma pinch as practical to enhance the neutron flux density, and the average performance of the plasma focus must not be degraded. The montecarlo code, MCNP, will be use extensively to study the design parameters.

7. Pulsed Sealed Neutron Tube Development

The pulsed sealed neutron tube (PSNT) will be developed over a period of two to three years. The first major task is to complete the scaling of the plasma focus machine to a neutron yield of greater than 10^{13} neutrons/pulse (D-D), or to establish that this scaling will not be practical so an alternative plan can be implemented. During the time of this task, a prototype sealed tube for running D-D will be designed and fabricated for tests on the LANL 750kJ capacitor bank. The second major task is to specify, fabricate, and life test a sealed tube that will run with deuterium to determine yield reliability, tube gas containment, and the gas handling system. The third major task is to build a sealed system for D-T operations from suitable materials to provide final confirmations of earlier results.

C. Stable Isotopes and Enrichment Facilities

The future availability of enriched stable isotopes is now becoming a matter of serious concern to the Nuclear Medicine industry, especially since the beginning of this decade when funding shortfalls for isotope separations became painfully obvious. The industry has finally begun to recognize that production of radionuclides for both established clinical applications and research products for the future could be in jeopardy, if the U.S. supply of enriched stable isotopes continues to decline. The Calutrons at Oak Ridge National Laboratory have been non-operational (standby) on at least two separate (extended) occasions since the mid

1980's, with the most recent standby mode lasting from mid 1991 to early 1995. Commercial production of several radionuclides such as; gallium-67, indium-111 and iodine-123 could not exist without the use of highly enriched stable isotopes to maximize the radionuclidic purity of the final product. For thallium-201 production, it could never have developed beyond the research stage without enriched thallium-203. Production of thallium-201 today would require at least two dozen additional commercial cyclotrons to meet the clinical demand in the U.S. alone. Despite the estimated $20,000,000 commercial expenditure for enriched thallium-203 over the past two decades (as feedstock for thallium-201), it's value in reduction of production costs alone exceeds $200,000,000. But, the real value of enriched thallium-203 is not cost reduction alone, its also because it was available in the first place, and enhanced the production and availability of thallium-201.

Availability of new radionuclides in the 21st century is highly dependent on access to a ready supply of economical enriched stable isotopes. The NBTF radionuclide production effort must be supported by ongoing research and development efforts in the stable isotope enrichment/separation field using advanced technology as well as support from the calutron facility at ORNL. The proposed Association will devote a considerable part of its efforts and assets toward advanced research techniques for enrichment or depletion of stable isotopes using state-of-the-art laser technology. Customized enrichment of stable isotopes (i.e. enrichment or depletion of one or more of the elements members) must be available at a relatively inexpensive cost if useful quantities of new and viable radionuclides are to enter the research and clinical marketplace in the next century. Technology to pre-enrich some of the low abundance isotopes or to reduce an unwanted isotope of an element by one technique prior to enrichment or separation by another technique will also be a research priority. The availability of pre-enriched tellurium-123 (to 3% or 4%) accompanied by a similar reduction of tellurium-124, to be used as feed material for subsequent calutron enrichment, would allow any of the 12 MeV (or larger) PET cyclotrons to produce clinical quantities of ultra high purity iodine-123 for regional distribution.

1. Stable Isotope Separation and Enrichment

A portion of this project definition study included assessment of the status of the availability and potential technology for the production of separated and enriched stable isotopes. A broad-ranging analysis is also provided in the recent report, *Isotopes for Medicine and the Life Sciences*, produced by a committee of the Institute of Medicine (S.J. Adelstein and F.J. Manning, eds., National Academy Press, 1994). Of particular importance to the NBTF effort is the availability of stable isotopes used for accelerator targets.

> *The availability of stable isotopic target materials is crucial to the production of both research and commercial quantity radioisotopes to the extent that stable isotope availability can be the limiting factor in the economical production of certain radioisotopes.*

Stable isotopes form the starting materials for accelerator-based production of radioisotopes

and for neutron reactions on targets in nuclear reactors (as opposed to nuclear fission). In addition, as aptly covered in the IOM report cited above, there exist a large number of applications of specific stable isotopes as tracers in medical and life sciences research and as probes in chemistry and physics studies.

The fundamental problem is that most elements of the periodic table exist in nature as a mixture of several isotopes. This is illustrated in Table V-6 where the distribution of naturally occurring elements (82) with a given number of stable isotopes (total of 252) is displayed. The tabulation does not include long lived isotopes which either exist in nature (for example ^{115}In) or have been produced in quantities adequate for radioisotope production (for example ^{99}Tc). Thus for the applications cited above, it is necessary to extract one particular isotope of an element from a mixture of naturally-occurring isotopes of that element (separation) or to at least increase a particular isotope's percentage in the resulting product (enrichment). In practice, enrichment (not complete separation) is most often achieved. In most cases when producing radioisotopes from stable isotopes, the higher the level of enrichment, the more economical the production, and the resulting product contains fewer unwanted radioactive byproducts and other contaminants.

The wartime Manhattan Project produced the first separated isotopes in quantity for research and bomb production using electromagnetic separation (the calutrons) and gaseous diffusion. Other methods, including gaseous centrifugation, are practiced in the defense establishments of several countries.

The U.S. stockpile, held by the Department of Energy at Oak Ridge National Laboratory (ORNL), is declining as stocks of stable isotopes are sold off. ORNL's sixty calutrons have for several years been in a non-producing, standby mode and the force of skilled operators has been depleted by retirement. In November 1994, DOE Isotope Production and Distribution Program personnel expected some of the calutrons to be operational in 1995 to fulfill a contract for the production of ^{203}Tl (IPPD, 1994). Other DOE facilities which have some capability for stable isotope separation using other technologies are also inactive (LANL and Mound Laboratories). A few commercial companies produce enriched stable isotopes of light elements (e.g., ^{18}O for ^{18}F production for PET studies). Legislatively-mandated pricing policies for DOE stable isotopes and aggressive marketing by Russian entrepreneurs has cut DOE's market share from about 90% in 1990 to less than 60% in 1992 (Arthur Andersen & Co., 1993).

> *All authorities agree that the unsteady nature of the stable isotope supply is a threat to the future of nuclear medicine and allied fields that require stable isotopes.*

2. New Separation Technologies.

Different methods and technologies have been proposed to provide stable isotope separation and enrichment. Among these potential methods are several mechanical processes based upon radial pressure gradients, differential diffusion, differential centrifugation, and arc

plasma centrifugation of fully ionized plasma containing a mixture of ions of different isotopes (e.g., Eerkens, 1989; Ikehata et al., 1989; Hirshenfeld et al., 1989; Ikehata et al., 1992). Also, laser-based methods have been developed, which use atomic ionization and

Table V-6
Number of stable isotopes for naturally occurring elements.

1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
Be	H	O	S	Ca	Kr	Mo	Xe		Sn
F	He	Ne	Fe	Ti	Pd	Ru			
Na	Li	Mg	Zn	Ni	Gd	Cd			
Al	B	Si	Sr	Ge	Er	Ba			
P	C	Ar	Sm	Se		Dy			
Sc	N	Cr		Zr		Yb			
V	Cl	Ce		Te		Hg			
Mn	K	W		Nd					
Co	Cu	Pb		Hf					
As	Ga			Os					
Rb	Br			Pt					
Y	Ag								
Nb	Sb								
Rh	Eu								
In	Ir								
I	Tl								
Cs									
La									
Pr									
Tb									
Ho									
Tm									
Lu									
Ta									
Re									
Au									
Bi									

molecular dissociation (e.g., Letokhov, 1986). It has been claimed that for uranium isotope enrichment, laser induced activation of chemical reactions can be used (e.g., Eerkens patents, 1978-1993). The experimental verification of this so called chemical reaction by isotope selective laser activation (CRISLA) technique is being pursued at the University of Missouri (Kunze and Eerkens, 1995). All of these methods become more difficult for high-mass elements (e.g., molybdenum isotopes). Development of high-mass isotope separation methods were primarily driven by the requirements of the nuclear power industry for enriched uranium. There is, however, some commonality in methods for different high-mass elements.

A comparison of isotope separation methods developed for the enrichment of uranium is shown in Table V-7, which is derived from Eerkens' (1989) paper. One of the more important parameters to consider is the energy expenditure (kWh) per separative work unit (SWU). All mechanical methods are more expensive than laser induced methods from the perspective of energy expended. One should use caution in comparing the entries in Table V-7. The three mechanical methods have all produced large quantities of enriched uranium. None of the laser methods have been used in production facilities, but the first two have been developed to the point of pilot plant designs. Another method, the vacuum arc centrifugation (VAC) method (which was not included in Table V-7) has been recently improved (Ikehata, 1989 and Krishnan, 1993). The VAC is being developed under DOE support and represents a method useful for a wide range of isotopes. The cost relative to laser-driven methods for a specific isotope, remains to be assessed.

We propose a program of research on laser-based isotopic separation, as these methods appear to be most efficient and therefore adaptable to economical, commercial-scale production.

Laser-based methods of isotope separation include Atomic Vapor Laser Isotope Separation (AVLIS) (Davis et al., 1982), Molecular Laser Isotope Separation (Jensen et al., 1982), an MLIS variant Infrared Multiple Photon Dissociation (IRMPD) (Letokhov 1979; Grunwald 1978; Cantrell 1986; Lyman, 1987; Okada et al., 1990; Freund and Lyman, 1987; Oyama et al., 1988), and Chemical Reaction by Isotope Selective Laser Activation (CRISLA) (Eerkens patents, 1978-1993).

AVLIS is based on the three-step ionization of ^{235}U atoms by means of three pulses from dye lasers, which are pumped by copper-vapor lasers. This method was developed for uranium enrichment by AVCO-Exxon in the mid 70s and by the Lawrence Livermore National Laboratory in the late 70s and early 80s. It is only workable if an extremely sophisticated (and expensive) laser system is used. The AVLIS method may be suitable for more volatile metals, such as calcium and mercury.

Table V-7
Comparison of methods developed or suggested for the enrichment of Uranium.

Process Name	Key Separation Mechanism	Energy used for separation	kwh per SWU	% of world market
Mass Action Processes				
Jet process	Radial pressure gradients in jets	Mechanical	3000	--
Diffusion	Differential diffusion through porous walls	Mechanical	2500	90
Ultra-centrifuge	Differential centrifugation	Mechanical	50	10
Quantum processes				
AVLIS	Laser-driven ionization	Photonic	40	--
MLIS	Laser-driven dissociation	Photonic	30	--
CRISLA	Laser-catalyzed chemical reaction	Chemical	10	--

The MLIS method, developed for uranium enrichment by the Los Alamos National Laboratory (Jensen et al., 1982) from the mid 70s to the early 80s, requires infrared laser excitation followed by ultraviolet-laser dissociation of the vibrationally-excited UF_6 molecules. The MLIS method also requires cooling by supersonic expansion of a carrier gas containing UF_6 to simplify the infrared spectrum sufficiently to obtain high isotopic selectivity.

The IRMPD method uses one or more infrared lasers to photodissociate polyatomic molecules by multiple-photon excitation. Many papers have been published on this process. Several book-length reviews summarize this research (Letokhov 1979, Grunwald 1978, Cantrell 1986). One paper (Lyman, 1987) is a fairly recent review of its application to isotope separation. Laboratories in several countries have evaluated the AVLIS, MLIS, IRMPD, and in some cases the CRISLA methods and have concluded that the IRMPD method is superior for uranium isotope separation and for enrichment of some lighter isotopes. The German company, Uranit, recently completed about ten years of research and development on the method. They used the IRMPD method with several infrared lasers and made significant improvements in laser operation, enrichment efficiency, and aerodynamic

design over the Los Alamos MLIS method (Schweizer, 1990). Another German laboratory, Max Planck Institute for Quantum Optics, has developed an IRMPD method to the point of marketing analysis for separation of carbon isotopes (Fuss et al., 1994). Japanese researchers have developed IRMPD methods for tritium (Lyman, 1987 and references cited therein) and silicon enrichment (Aria et al., 1991). The Atomic Energy Corporation of South Africa has abandoned their successful jet process (Table V-7) in favor of a new IRMPD plant under construction for enrichment of uranium (Fouché, 1994).

The CRISLA method is similar to MLIS, being based on selective catalysis of chemical reactions induced by infrared laser light excitation of polyatomic molecules (usually a metal hexafluoride such as UF_6 ,SF_6, MoF_6 etc., containing the desired isotope) with a co-reactant. However, the details of this process have never been published, and the published spectroscopy is not consistent with the selective chemical reactions required (Lyman, 1987). The CRISLA method is being extensively investigated at the University of Missouri (Kunze and Eerkens, 1995) for the enrichment of molybdenum isotopes.

This review suggests that the IRMPD method may be cheaper and more applicable to high-mass isotope separation. In particular, selective, multiple-photon dissociation has been demonstrated for MoF_6 with light provided by CO_2 and para H_2 Raman lasers (Okada et al., 1990; Freund and Lyman, 1978; Oyama et al., 1988). However, this method has not been optimized and further work is needed to define how molybdenum isotopes can be extracted from dissociated molecules. Application of this method to other elements has been reviewed by Lyman (Lyman, 1987).

> ***AITI has initiated a research program to develop and optimize the MLIS method for isotope enrichment. AITI also proposes development of extraction methods for dissociated molecules of enriched isotopes intended for accelerator targets.***

Toward this end, AITI and UNT researchers initiated a research and development effort to produce a high powered laser source through coupled low power (inexpensive) lasers. This program, supported by an SBIR grant from the Office of Naval Research, recently demonstrated successful coupling of two low power lasers to produce a beam four times the power of each individual laser. We believe this technique may provide relatively inexpensive lasers of sufficient power to make laser-based separation, such as that described above, practical.

3. A Technical Approach

A typical scheme for implementation of a laser-selective, multiple-photon dissociation reaction of MoF_6 for molybdenum isotopes enrichment would consist of a powerful, tunable infrared laser system with wavelength in the absorption region of MoF_6 molecules contained in a reaction chamber with MoF_6 in the gas phase (e.g., Freund and Lyman, 1978; Oyama et al., 1988). Since only about one percent of the molecules of MoF_6 at room temperature exist in the ground state, the reaction chamber must be cooled (by liquid nitrogen, for example) to

increase the selectivity of the laser-induced excitation and dissociation reactions. It should be stressed that in some high mass isotope separation experiments, an additional infrared laser can be used (with wavelength slightly different from the wavelength of the main laser) or an additional UV laser (Lyman, 1987). The reason for the second laser is to improve isotopic selectivity. (In the MLIS process the second laser is ultraviolet.) The infrared dissociation process is a multiple-photon process. The energy required for dissociation of MoF_6 is 44 photons at the frequency of 752 cm-1, the frequency of the strong ν_3 infrared absorption band. Absorbing that much energy requires high intensity. Unfortunately, the high intensity also broadens the infrared excitation into other isotopes and tends to destroy the isotopic selectivity of the dissociation process. This can be at least partially overcome by using an initial lower intensity laser pulse to vibrationally excite one isotopic form of the molecule and to use a second, higher-intensity laser at a slightly lower frequency to dissociate the vibrationally excited molecules. The best laser candidate for this process is the CO_2 laser shifted to the 13μm region by para-hydrogen or ortho-deuterium (Okada et al., 1990; Oyama et al., 1988). The selective laser-induced photodissociation of MoF_6 molecules can be described by the following equation:

$$ {}_{n}MoF_6 + h_j\nu \longrightarrow {}_{j}MoF_5 + F + {}_{n-j}MoF_6 $$

Where: n = number of molybdenum isotopes in natural abundance; h = Planck's constant; ${}_j\nu$ = light frequency related to the absorption line of the particular isotope. ${}_jMoF_5$ is in the solid phase which contains the molybdenum isotope of interest. ${}_{n-j}MoF_6$ is unexcited molybdenum hexaflouride. The ${}_jMoF_5$, which contains the molybdenum isotope of interest, condenses to solid particles and may be collected on a filter. The ${}_{n-j}MoF_6$ is unreacted molybdenum hexafluoride. It remains in the gas phase.

We have worked out many of the details of the chemical, physical, optical, and laser requirements of such a system. This description is meant to serve as an example of the kind of research and development effort needed in the area of stable isotope separation.

4. Supporting Expertise and Facilities

The IOM report, *Isotopes for Medicine and the Life Sciences*, which was cited earlier, points out the crucial need for detection instrumentation:

> *"The committee found this lack of detection instrumentation one of the most important impediments to the use of stable isotopes."*

The IOM report also acknowledges that, "Accelerator Mass Spectrometry has been shown to be several orders of magnitude more sensitive than counting radioactivity for the detection of certain long lived radionuclides."

AITI will look to other members of the UNT/NTRI-led group for support research and development — and provide analytical services for researchers — in the area of detection instrumentation. Currently, UNT's Ion Beam Modification and Analysis Laboratory (IBMAL) operates five particle accelerators and is the world's leader in atomic mass spectrometry (AMS) of stable isotopes. They have perfected the technology to detect uniquely any element in the periodic table except indium,(which has isobaric interferences) at the parts-per-billion level (one part in 10^9) and is expected to improve the detection limit to parts-per-trillion (on part in 10^{12}) in the near future. Currently, the group is exploring new techniques to discriminate isobars — namely isotopes of different elements with the same atomic mass but different atomic number (different Z). The AMS capability, plus a variety of other accelerator-based analytical capabilities (particle-induced X-ray emission [PIXE], Rutherford backscattering, proton microbeam, nuclear reaction analysis [NRA], etc.) and other state-of-the-art capabilities available in UNT's Center for Materials Characterization, will provide valuable support to the AITI's research program and in quality control of its research isotope products.

VI. Operations and Financial Plans

Sources and application of funds over a five-year period are shown in Table VI-1. The major source of funds are from the private placement sale of securities of the Corporation and the sale of Industrial Revenue Bonds totaling $19.54 million. The major application of funds is devoted to the manufacture of products, development of facilities, and purchase of capital facilities and processing equipment. The capital expenditures required for radioisotope production using the linac is approximately $18 million which includes the linac, beam transport, radioisotope production and processing facility and associated equipment. The ISOGEN facility, stable isotope facility and regionally operated ISOGEN systems requires a investment of $23.46 million totaling $41.46 million over a period of five years to seven years. $6.4 million is provided as excess working capital from operations during that period. The projected revenue and income from operations of the linac radioisotope production facility is shown in Table VI-2. The proforma operations due to all divisions of the corporation is shown in Table VI-3.

The primary purposes of the Advanced Isotope Technologies facilities are to provide manufacturing and marketing of its proprietary products, the production of standard radioisotopes for nuclear medicine, radiochemistry, and radiopharmaceuticals, as well as industrial tracers used in the semiconductor, petrochemical, and electric power industries. Annual product sales and isotope production is expected to reach a level of $90 million within five years. Revenue will also be generated through research contracts and research development contracts with the Department of Energy, the National Science Foundation, industrial companies and various other state and federal agencies. It is anticipated that this research and development revenue will approach $2 million annually within five years of receiving financial backing to start the project.

The business plan and proforma operations of AITI are proprietary and confidential and may not be distributed without the expressed written consent of the Company. A copy of the detailed business plans may be obtained by written request to George A. Keyworth, Chairman and CEO of AITI.

Table VI-1
ADVANCED ISOTOPE TECHNOLOGIES, INC.
SOURCE AND APPLICATION OF FUNDS
(5 Years)

Source of Funds (1000)		
Private Placement Equity		$ 10,540
Bridge Equity		300
Convertible Debenture		3,000
Revenue Bond	15,000	
Interest Income		3,927
Net Income From Operation		18,118
Total	**$ 50,885**	
Application of Funds (1000)		
Cost of Sale of Securities	$ 1,342	
Cost of Sale of Revenue Bonds		600
Interest Expense		780
Bridge Financing	300	
Capital Facilities, Denton	18,000	
Regional Facilities	23,463	
Excess Working Capital		6,400
Total	**$ 50,885**	

Table VI-2
LINAC RADIOISOTOPE PRODUCTION PROFORMA

	Year 1	Year 2	Year 3	Year 4	Year 5
1. Income	0	500	5,150	7,969	11,964
2. Cost	505	1,490	4,897	7,210	8,971
3. Net Income	(505)	(990)	253	759	2,993
4. Capital Investment	3,512	8,651	14,300	8,500	8,500
5. Opening Cash	0	25,443	18,042	7,208	4,809
6. Ending Cash	25,443	18,042	7,208	4,809	7,652
7. Lease Expense	0	300	300	300	300
8. Debt Service	0	135	500	500	500
9. Beam Costs	0	90	1,100	1,808	2,250
10. Personnel FTE	5	12	22	34	35

Amortization of the debt associated with completion of the linac and construction of radioisotope processing facilitates is included in the financial operations under items 7, 8, and 9. Items 7,8, and 9 are included in the Cost item (#2).

* Items 5 & 6 include income and investment from all AITI operations.

Table VI-3

ADVANCED ISOTOPE TECHNOLOGIES, INC						
PROFORMA OPERATIONS ALL DIVISIONS						
(x $1000)						
YEAR	1995	1996	1997	1998	1999	2000
Total revenue	2407	9300	26500	44369	65864	96400
Total manufacturing cost	1947	5075	14210	23411	34568	50040
Total margin	$460	$4,225	$12,290	$20,958	$31,296	$46,360
Research and development cost	135	725	1375	2750	4500	5500
Marketing cost	90	400	1090	2050	3250	4600
G & A cost	148	325	750	1400	2250	3250
Amortization Of capital facilities	0	300	400	805	950	1005
Accelerator lease	0	700	2290	2650	2650	2650
Product liability insurance	0	350	900	1620	2900	3200
Total cost	$373	$2,800	$6,805	$11,275	$16,500	$20,205
Operations profit before tax	87	1425	5485	9683	14796	26155
Interest expense @ 6.5% On ind rev bonds	390	675	975	975	975	975
Interest expense @ 6.5% On conv. Debent.	195	195	195	195	195	195
Interest income @ 6% on ave. Cash Balance	1527	1071	397	228	385	1034
Total profit including interest income	$1,029	$1,626	$4,712	$8,741	$14,011	$26,019
Profit after tax (assume 35% rate)	$669	$1,057	$3,063	$5,681	$9,107	$16,912
Cash flow:						
Opening cash	0	25443	17849	6611	3793	6400
Equity common shares	10540	0				
Equity convertible preferred	3000	0	0			
Industrial revenue bonds	15000	0	0			
Profit (loss)	415	1057	3063	5681	9107	16912
Capital facilities	3512	8651	14300	8500	6500	6500
Balance	$25,443	$17,849	$6,611	$3,793	$6,400	$16,812
Average cash balance	$25,443	$17,849	$6,611	$3,793	$6,400	$16,812

VII. References

Arai, S., S. Nakahashi, and Y. Iizuka 1993 Isotope-selective infrared multiple photon decomposition of Si2F6 and its application to silicon isotope separation. New Functionality Materials, Vol. C, Synthetic Process and Control of Functionality Materials, T. Tsuruta, M. Doyama, M. Seno (editors), Elsevier Science Publishers B. V.

Billen, James H. *et al*, "A New RF Structure for Intermediate-Velocity Particles", LANL Report LA-UR-94-2801

Brzosko, J.S., Nardi, V. and C. Powell, "$^{12}C + D$, $^{14}N + D$, and $^{14}N + {}^{3}He$ Nuclear Reactions in the Plasma Focus Pinch," 19th International Conference on Plasma Science at Tampa, Florida, 1992.

IPDP, 1994. Private discussions by J. Beaver and W. Courtney with DOE IP&DP personnel at the Thirteenth International Conference on the Applications of Accelerators in Research & Industry, Denton, TX.

Cantrell, C. D. 1986 Multiple-Photon Excitation and Dissociation, Springer-Verlag, Heidelberg.

Davis, J.I., J.Z. Holtz, and M.L. Spaeth 1982 Status and prospects for lasers in isotope separation. *Laser Focus, 18*: 49-54

Eerkens, J.W. 1978 High-Mass Isotope Separation Process and Arrangement, US Patent Number 4,082,633

Eerkens, J.W. 1991 High-Mass Isotope Separation Arrangement, US Patent Number 5,015,348

Eerkens, J.W. 1992 Isotope Separation Process, US Patent Number 5,108,566

Eerkens, J.W. 1992 High-Mass Isotope Separation Arrangement, US Patent Number 5,110,430

Eerkens, J.W. 1993 Isotope Separation Process, US Patent Number 5,221,446

Eerkens, J.W. 1989 CRISLA aims to reduce costs. *Nuclear Engineering International, 34*: 48

Filippov, N.V., "Current Structure of a Plasma Focus During Generation of Fast Particles," JETP Letters, Vol 31, No. 2, 20 January 1980, pp. 119-124.

Fouché, Karel F. 1994 Atomic Energy Corporation, South Africa, private communication to John L. Lyman.

Freeman, B.L., Morgan, I.L., Chrien, R. and K. Sowder, "Current Progress with a 500 kJ Plasma Focus," 20th International Conference on Plasma Science in Vancover, Canada 1993.

Freund, S.M., and J.L. Lyman 1978 Multiple-photon isotope separation in MoF_6. *Chemical Physics Letters, 55*: 435-37

Fuss, W. 1994 IR multiphoton absorption and isotopically selective dissociation of CHClF2 in a Herriott multipass cell. Z. Phys. D: At., Mol. Clusters 29, 391.

Grunwald, E 1978 Megawatt Infrared Laser Chemistry. Wiley, New York.

Gullickson, R.L., and H. Sahlin, " Activtion Measurements of High Energy Deuterons in the Plasma Focus Device," Lawrence Livermore Laboratory Report UCRL-77173, December 4, 1975.

Jager, U. and H. Herold, "Fast Ion Kinetics and Fusion Reaction Mechanism in the Plasma Focus," Nuclear Fusion, Val 27, #3 (1987), pp 407-423.

Jensen, R. J., O. P. Judd, and J. A. Sullivan 1982 Separating Isotopes with Lasers. Los Alamos Sci. 3, 2.

Hirshenfeld, J.L., A. Levin, and O. Danziger 1989 Vacuum arcs for plasma centrifuge isotope enrichment. *IEEE Transactions on Plasma Science*, 17: 5

Ikehata, T, K. Oohashi, N.Y. Sato, T. Tanabe and H. Mase 1992 Plasma centrifige for separation of metal elements and isotopes. *Nuclear Imstruments and Methods in Physics Research, B70*: 26-32

Ikehata, T., M. Suzuki, T.Tanabe, and H. Mase 1989 Centrifugal mass separation in rotating plasmas oduced by a coaxial plasma gun. *Appl. Phys. Lett. 65*: 1281-91

Krishnan, K. 1993. The Vacuum Arc Centrifuge. Presentation to the Biomedical Isotopes Committee, Institute of Medicine, National Academy of Sciences, Washington, D.C., November 19, 1993.

Kunze, J.F. and J.W. Eerkens 1995. University of Missouri, Columbia, MO, private communication to R. Schafer and W. Courtney.

Letokhov, V.S. 1986 Laser induced processes in spectroscopy, isotope separation, and photochemistry. *Sov. Phys. Usp., 29*: 70-81

Lyman, J, 1987 Laser induced molecular dissociation. In L.J. Radziemski, L.J., R.W. Solarz, and J.A. Paisner (eds.), *Laser Spectroscopy and its Applications*, Marcel Dekker, Inc., NY, pp. 000-505.

Mathur, J.W., Bottoms, P.J., Carpenter, J.P, Ware, K.D., and A.H. Williams, "Recent Studies of Dense Plasma Focus", Plasma Physics and Controlled Nuclear Fusion Research Conference, IAEA-CN-28/D5, p. 561-572 (1970).

Mills, S.J, Nortier, F.M., Rautenbach, W.L., Smit, G.F. and Steyn, G.F 1991 A multi-purpose target station for radioisotope production at medium energies. 12th Int. Conf. on Cyclotrons and their Applications.

Okada, Y., S. Kato, S. Satoka and K Takeuchi 1990 Laser isotope separation of heavy elements by infrared multiphoton dissociation of metal alkoxides. *Spectrochemic Acta, 46 A*: 643-646

Oyama, T., S. Satooka, S. Kato, K. Midorikawa, H. Tashiro and K. Takeuchi 1988 Isotopically selective infrared multiple-photon dissociation of MoF_6 by an H_2-Raman laser. *Laser Chem., 8*: 235-42

Proudfoot, Gary, AEA Technology, *private communication*, 1995.

Schweizer, Gerhardt 1990 Uranit GmbH, Jülich, Germany, private communication to John L. Lyman.

Steyn, G.F. et al 1992 *Nucl. Instr. Meth., A136*: 128-133.

Swenson, Donald A., "RF-Focused Drift Tube Linac Structure", 17th Int'l Linac Conf., LINAC'94, Aug. 21-26, 1994, Tsukuba, Ibarki, Japan. *To be published.*

Ware, K.D., Williams, A.H. and R.W. Park "Operation of a 720 kJ, 60 kV Dense Plasma Focus, Bull. Am. Phys. Soc. September 1973, Series II, Vol. 18 #9 1364.

Young, Lloyd M., "An 8-Meter-Long Coupled Cavity RFQ Linac", LANL Report LA-UR-94-905, 1994.

Zucker, D., Bostick, W., Gullickson, R. Lone, J., Luce, J. and H. Sahlin, " The Design of a Repetitively Pulsed Magujoule Dense-Plasma Focus," Laurence Livermore Laboratory Report UCRL - 51872, August 1, 1975.

APPENDIX IV

ADVANCED MEDICAL IMAGING CENTER SUPPORTING THE NATIONAL BIOMEDICAL TRACER FACILITY

Basic Proposal

The faculty of the Radiological Sciences program of the University of Texas Southwestern Medical Center (UTSMC) propose to establish an Advanced Medical Imaging Center in association with the National Biomedical Tracer Facility (NBTF) to advance the state-of-the-art in medical imaging.

> ***The proposed imaging center will be located adjacent to the proposed National Biomedical Tracer Facility (NBTF) in North Central Texas, but will be financed and operated independently of the NBTF and the commercial production facility.***

The imaging facilities will include both anatomic (CT) and functional (PET and SPECT) imaging devices specialized for small animal imaging at high resolution and sensitivity. A special focus of the imaging center will be the design, development, and building of advanced prototype imaging devices for special applications. The Advanced Medical Imaging Center will contain animal care facilities, and later, human clinical facilities to accommodate preclinical and clinical research. The imaging center could ultimately serve as a Southwestern regional imaging facility to provide needed medical services, a pool of potential research subjects, and a clinical revenue stream in support of its operations.

> ***The Denton imaging facility, located adjacent to the NBTF, will have access to a unique source of radioisotopes with a wide range of chemical/biological properties, energies, and half-lives that will enable research that otherwise could not be done at any existing center in the U.S.***

The Advanced Medical Imaging Center will be managed by personnel of the University of Texas Southwestern Medical Center (UTSMC) at Dallas under the umbrella of UTSMC and the NBTF Association, and in association with the NBTF. Like the NBTF, the imaging center's facilities will be open to Association members and other users for basic and preclinical research.

Development of the imaging center will be staged — first located in existing facilities with small animal support facilities in Dallas, later augmented in a specially designed facility at the Denton site. Separate financing for the Advanced Medical Imaging Center will be sought

from the state, federal agencies, and the private sector.

The Radiological Sciences program at UT Southwestern at Dallas is heavily engaged in research and development of advanced medical imaging technologies, as well as basic, preclinical, and clinical research on nuclear medicine imaging and therapeutic agents. This interest on the part of UTSMC researchers and physicians is responsible for the proposal to develop a basic/preclinical experimental imaging unit adjacent to the NBTF at the Denton site.

Background

Historically, the medical community has been a major innovator and user of radioisotopes, both in research and in applications to health care. This proposal for a National Biomedical Tracer Facility addresses the production of both stable and radioactive isotopes to satisfy existing and developing needs in biomedical research and practice. However, raw radioisotopes produced in a particle accelerator or a nuclear reactor often must be transformed considerably and linked with a biomolecule to target a specific function and to be safe and suitable for nuclear medicine applications.

Radionuclides created through particle accelerator technology, such as that of the proposed NBTF, are seldom produced in a suitable chemical form for biomedical applications, particularly nuclear medicine applications. Therefore, a considerable amount of chemical and biological processing is required in the production of a radiopharmaceutical product.

After the production of a desired radionuclide with appropriate isotopic purity, it must be converted into a suitable salt and formulated in a medium suitable for biological evaluations. In other cases, the radionuclide has to be complexed or chelated with appropriate ligands such that the radiolabeled product has the affinity and selectivity to precisely target the desired organ or diseased tissue. A pharmaceutical product used in human medicine must also have appropriate pharmacokinetic characteristics to ensure that it enters the target tissue, binds strongly enough to its molecular target or lingers long enough at the target to be detected by imaging machines outside the body.

Research and development to achieve these requirements is highly complex. Depending on the radioelement under study, appropriate ligands, radiolabeling techniques and formulations suitable for biological evaluations must be developed and evaluated. Highly advanced analytical methods must be used to test potential new pharmacological agents for radiochemical purity, stability and pharmaceutical quality. Finally, prospective imaging agents must be tested *in vivo* — first in small animals, then in human subjects — to assess their capacity to delineate the specific physiological processes which they are intended to target.

We propose to address the manifold needs of advanced research and education in radiochemistry, radiopharmaceutical development, and in preclinical evaluations of new imaging agents and technologies.

Research and education in radiochemistry, radiopharmaceutical research and applications, and radiopharmacy (formulation and product delivery) will be provided at collaborating institutions of the proposed NBTF Association, including UTSMC, the University of New Mexico (UNM), the University of North Texas (UNT), and the University of Oklahoma (OU). It is an aim of this proposal to enhance these activities. To this end, we describe here an experimental imaging facility, co-located with the NBTF and dedicated to research and education in radiochemistry, radiopharmacy, and nuclear medicine imaging.

Specific Aims of the Proposed Advanced Medical Imaging Center

The proposed imaging facility has three specific aims related to imaging agents and therapy. First, it will be used for developing new imaging applications for specialty radioisotopes. Second, it will support preclinical research on imaging agents and radiopharmaceuticals. Third, it will support research studies on biodistribution and dosimetry for radioimmunotherapy and other therapeutic applications.

Further, it will develop new functional imaging technologies that provide for increased spatial resolution, functional specificity, and compatibility with simultaneous anatomical imaging.

Current Paradigms in Nuclear Medicine Practice

Nuclear Medicine is the clinical specialty that uses radionuclides for imaging the ongoing functioning of organs, tissues and cells to identify disease states. The discipline is based on two paradigms. First, nuclear medicine physicians use radiopharmaceuticals to detect abnormalities in function. Second, nuclear medicine physicians use anatomical imaging to localize functional abnormalities within organs and tissues.

A major advantage of nuclear medicine technology is the ability to often identify disease at an earlier time, with greater specificity and with higher sensitivity, than methods targeted at anatomic and structural abnormalities alone. Then, by combining anatomical and functional imaging, the physician can localize the abnormality within a specific structure, within the organ and anatomic site (Nunally and Antich , 1991). The resulting information has both diagnostic and prognostic power.

Current technology is based on devices optimized either for Tc-99m imaging, or for positron emitters; and on pharmaceuticals tagged with these radionuclides.

A Paradigm Shift

Medical imaging cameras now in use follow basic designs that originated in the 1960s. These cameras are sensitive to specific energies, around the 140 keV gamma emission of technetium-99m, and the selection of specific isotopes has been driven by the camera design and the desired half-life. Currently, technetium-99m accounts for the bulk of the procedures used in nuclear medicine. However, technetium chemistry, while rich, is not ideal for labeling biomolecules, and its six-hour half-life and emission energy are by no means appropriate for all potential applications. Moreover, decay modes involving higher photon energies B^+ or multiple photon emission will result in higher sensitivity, sharper resolution, and noise free images. These properties may well be necessary for further progress of this field.

Research and education are necessary to bring a paradigm shift in nuclear medicine that will advance imaging and therapy. *Research* is needed to identify the most desirable radioisotopes in terms of their chemistry, half-life, and energy of emission for specific applications. The results of such research can then be applied to labeling biomedical probes with the isotopes of choice and designing new camera technologies with enhanced resolution and sensitivity. Research also can lead to lower costs for radioisotope production and can help to achieve the higher specific activities needed for some applications such as molecular radiotherapy. *Education* is needed to achieve a paradigm shift within nuclear medicine if the technology is to reach its ultimate potential. Ultimately, patient care will improve as the result of more effective research and development catalyzed by a new paradigm.

An economic argument opposes the paradigm shift we suggest. The thousands of existing imaging cameras (optimized for the 140 keV gamma emission of technetium-99m) represent a tremendous capital investment. Nevertheless, even these cameras can be applied to imaging a broader range of energies. Further, research and development can improve existing technology, as well as lead to new technology. Moreover, powerful new applications such as molecular nuclear medicine will inevitably drive the creation and adoption of new technology.

Potential of Therapeutic Nuclear Medicine

Therapeutic nuclear medicine, while not currently a major component of everyday medical practice, is a developing area with highly specialized requirements, particularly in

radioimmunotherapy. Research and development of methods of therapy based on the delivery of highly selective carriers of radioactive isotopes is currently underway, and applications are expected to accelerate rapidly in the next decade.

The development of therapeutic nuclear medicine will involve methods that require radioisotopes different from those used in imaging.

A point of strength of the NBTF in support of nuclear imaging and therapy R&D will be the availability of a wide spectrum of isotopes with different decay schemes. Such isotopes will permit researchers to follow the fate of potential therapeutic agents *in vivo* and thus optimize their therapeutic effectiveness. Biological evaluation of new imaging agents and potential therapeutic agents requires gathering data on the pharmacokinetics and biodistribution of such probes through animal imaging studies that will be done at the proposed imaging center.

Diagnostic nuclear medicine is a well established diagnostic methodology, but the technology holds great promise to further improve the practice of medicine. Currently, on a cost-per-study basis, the SPECT technique is not only quite powerful, but also intrinsically less expensive than other technologies. New radiopharmaceuticals — when fully developed — are expected to improve diagnosis and decision making. Increased sensitivity and specificity of improved radiopharmaceutical agents can better inform the physician of the stage of a disease and help to indicate rational choices among available treatment options. In both imaging and therapy, new advances are underway, aided especially by the powerful techniques of molecular biology and bioengineering (Reba, 1992).

The proposed North Texas center brings together a unique combination of resources for nuclear medicine research and development: NBTF-produced research isotopes, the experimental imaging center, and great expertise in both molecular and nuclear medicine at UTSMC.

The rapid and definitive advances in molecular biology that permeate all branches of biomedical science have catalyzed the development of *molecular nuclear medicine*, which is developing rapidly in the U.S. and abroad. The discovery and identification of highly specific, disease-related markers on the cytoplasmic or nuclear membranes of cells has enabled development of highly specific molecular probes. Such probes include antibodies, oligonucleotides, peptides, and even carbohydrates. This important developmental effort is largely based on nuclear medicine technology, because no other imaging methods have comparable sensitivity. But even more sensitive technology is needed.

Although significant advances have improved nuclear medical technology over the decades since its inception, the sensitivity and resolution of current devices needs improvement. Likewise a wider range of specific agents is needed in the radiopharmaceutical armamentarium.

Development of New Imaging Agents and Technologies

In order for Nuclear Medicine to broaden its current scope, new imaging agents and methods must be developed and tested. To promote new advances in these two areas, we propose to develop a basic/preclinical imaging unit available to collaborating institutions. The specific aim of this unit will be (1) research and development directed at improving diagnosis and therapy, and (2) an educational program to promote the understanding of radioisotope needs and uses in biomedicine.

The close proximity of the proposed unit to the isotope production facility at the NBTF is dictated by the need for availability of radioisotopes with a wide range of energies and half-lives, including their production, separation, incorporation into radiochemicals, and safe disposal and waste management. Close proximity is also needed for this facility to most effectively support research, education, and training at the NBTF.

Staging the Proposed Imaging Facility

Initially, the unit will be housed in existing facilities at the University of Texas Southwestern Medical Center at Dallas, under the aegis of its Department of Radiology, the Nuclear Medicine Center and the Advanced Radiological Sciences Division. A close association with UT Southwestern provides access to the expertise available there in biomedicine and molecular bioengineering. However, the unit will be available to house and support not only the R&D activities of the regional associates of the NBTF in the areas of radiopharmacology and imaging but also the educational and training programs associated with the NBTF program. Funds to support these activities will be sought from federal and state agencies and the private sector.

> ***To reiterate, the proposed Advanced Medical Imaging Center will be separately financed and operated, independently of the proposed NBTF and the commercial production facility.***

This laboratory will include both anatomic (CT) and functional (PET and SPECT) imaging devices specialized for small animal imaging at the high resolution and sensitivity necessary for this purpose. These specialized devices, currently being constructed and tested at UT Southwestern and further developed by a corporate affiliate, are used to facilitate the translation of new radionuclide agents from the research environment to clinical applications (cf. Hichwa, 1994). Correlative MR imaging and spectroscopy will be supported by existing facilities at the Rogers Magnetic Resonance Center at UT Southwestern in Dallas.

The Advanced Medical Imaging Center will be developed in a staged fashion, after a careful assessment of existing and developing needs. Initially, the center will begin in currently

existing space in Dallas and will be equipped with PET and SPECT units specialized for imaging models of specific diseases in animals (Hahn et al., 1993), as well as by standard gamma cameras.

> ***While we envisage acquiring state-of-the-art, commercially available equipment as needed, we plan a major focus on designing, developing, and building new and prototype devices for specific applications.***

The UT Southwestern principals contributing to this proposal are in the forefront of developing the next generation imaging technology (e.g., Antich et al., 1990; Kulkarni et al., 1993; Anderson et al., 1993; Prior et al., 1993; Kulkarni et al., 1994). They have demonstrated that nuclear imaging devices built with plastic scintillating optical fibers can be used to image radionuclides with a wide range of energies, including I-125 with low energy photons (25-35 kev) and positron emitters. A prototype small animal imaging camera has been built and is operating at UTSMC. It incorporates arrays of 1 mm diameter plastic scintillating optical fibers and position sensitive photomultipliers (Anderson, et al., 1993).

The feasibility of *high resolution imaging* using this new technology was demonstrated by the study of rat brain blood flow using I-125 IMP (iodoamphetamine) and I-125 labeled folic acid to image folate receptor +ve (IGROV) tumor in a nude mouse in single photon emission computed tomographic mode (Kulkarni et al., 1994). Rat brain blood flow was demonstrated in PET mode using Cu-64 labeled PTSM (Kulkarni et al., 1993). These studies were possible because these devices achieve millimeter and sub-millimeter resolution, while maintaining high sensitivity.

New imaging units currently in the design-review stage in the laboratories of UT Southwestern include:

1. A cylindrical imaging unit (30 cm I.D. x 35 cm long), with integrated anatomic (CT, with external radioactive sources) and SPECT capabilities. This unit is not commercially available and will have numerous specific applications — for example in Oncology, as it allows whole-body imaging, and

2. A high resolution, high sensitivity PET camera with the same dimensions as above, based on fiber optic detectors and integrated with a magnetic resonance imaging device within which it will be inserted.

> ***The simultaneous acquisition of both functional and anatomical imaging data will offer an unprecedented degree of spatial and temporal correlation among different studies of anatomy and function.***

Radiochemistry laboratories will be included in the Denton facility to support and integrate the efforts of the NBTF with that of the imaging center. The radiochemistry laboratories at the Denton site will be complementary to the existing facility in the Department of Radiology at UTSMC in Dallas, which is directed by Professor P.V. Kulkarni. Dr. Kulkarni has strong credentials in radiochemistry R&D (e.g., Goomer et al. 1992; Das et al., 1992; Goomer et al., 1994). These facilities will be augmented by the UNT facilities of the Department of Chemistry at UNT in Denton, where Professor A.P. Marchand has both a strong interest and specific expertise in this area. The collaboration with the strong programs in radiopharmacy and radiopharmaceutical R&D at the OU and UNM Colleges of Pharmacy will enhance this effort and give it unique breadth and growth potential.

Ultimately, we envisage broadening the scope of the Advanced Medical Imaging Center with a clinical facility, in which radioactive agents will be used in human studies. Different radionuclides offer different advantages for this purpose, based on decay times, energies, nature of the emitted radiation, as mentioned previously. The Advanced Medical Imaging Center will support the initial dosimetric and biodistribution studies of new radiopharmaceuticals, as well as the objective assessment of efficacy and safety during treatment.

References

Anderson, J.A., J. Fernando, T. Nguyen, J.O. Prior, A. Constantinescu, R.W. Parkey, P.P. Antich, R.C. Chaney, H. Hammack, and E.J. Fenyves 1993 Constructing a small laboratory animal imaging device based on scintillating fibers. *Scintillating Fiber Technology and Applications, Proc. SPIE,* 2007: 125-131.

Antich, P., M. Atac, R. Chaney, D. Chrisman, D. Cline, E. Fenyves, and J. Park 1990 Development of a high resolution scintillating fiber gamma ray telescope. *Nuclear Instrumentation and Methods*, A297: 514-520.

Das, C., P.V. Kulkarni, A. Constantinescu, P.P. Antich, F.R. Blattner, and P.R. Tucker 1992 Recombinant antibody-metallothionein: Design and evaluation for radioimmunoimaging. *Proc. Natl. Acad. Sci.*, 89: 9749-53.

Goomer, N.C., P.V. Kulkarni, A. Constantinescu, P.P. Antich, R.W. Parkey, and J.R. Corbett. 1992 Synthesis and evaluation of technetium-99m monocationic mixed ligand complexes of phenyl substituted/condensed tetradentate Schiff's bases and trimethylphosphine. *Nuclear Medicine and Biology*, 19(6): 679-684.

Goomer, N.C., P.V. Kulkarni, A. Constantinescu, P.P. Antich, R.W. Parkey, and J.R. Corbett. 1994 Synthesis and evaluation of a new class of technetium-99m monocationic radiotracers from dithienyldiazalkanes. *Nuclear Medicine and Biology,* 21(4): 657-662.

Hahn, E.W., P. Peschke, R.P. Mason, E.E. Babcock, and P.P. Antich 1993 Isolated tumor growth in a surgically formed skin pedicle in the rat: A new tumor model for NMR studies. *Magnetic Resonance Imaging*, 11: 1007-1017.

Hichwa, R. 1994 Are animal scanners really necessary for PET? Editorial, *Journal of Nuclear Medicine.*

Kulkarni P.V., J.A. Anderson, P.P. Antich, J.O. Prior, Y. Zhang, J. Fernando, A. Constantinescu, N.C. Goomer, and R.W. Parkey 1993 New approaches in medical imaging using plastic scintillating detectors. *Nuclear Instrumentation and Methods in Physical Research*, B79: 921-925.

Kulkarni, P.V., P.P. Antich, A. Constantinescu, J.A. Anderson, J.L. Fernando, J. Prior, T. Nguyen, R.W. Parkey, S.D Weitman, B.A. Kamen, R.C. Chaney, and B.A. Fenyves BA 1994 Imaging of folate receptors with I-125 labeled folate using small animal imaging system built with plastic scintillating optical fibers. *Proc. SPIE*, 2281: 71-81.

Nunnally, R.L. and P.P. Antich 1991 New directions in medical imaging of cancer, magnetic resonance methods and single photon emission computed tomography. *Cancer*, 67: 1271-1277.

Prior, J.O., P.P. Antich, J. Fernando, J.A. Anderson, P.V. Kulkarni, R.W. Parkey, R.C. Chaney, and E.J. Fenyves 1993 Imaging strategies with scintillating fiber detectors: Issues and preliminary results: Scintillating fiber technology and applications. *Proc. SPIE,* 2007: 116-124.

Reba R.C. (ed.) 1992 *Proceedings of a Workshop on Molecular Nuclear Medicine*, U.S. Department of Energy, Medical Applications and Biophysical Research Division, Office of Health and Environmental Research.

Patents

1. E. Fenyves, D. Cline, M. Atac and P.P. Antich: High Resolution Gamma Ray Detectors for Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT), Patent No. 5,103,098, issued 7 April 1992.

2. P.P. Antich, R. Parkey and J. Anderson: Position Sensitive Gamma-Ray Detector, South Africa Patent No. 92/8298 issued 28 July 1993.

3. J. Anderson and P.P. Antich: Position Sensitive Radiation Detector, Patent No. 5,334,839, issued 2 August 1994.

4. C. Chaney, E. J. Fenyves, P. P. Antich, and H. Hammack: Method and Apparatus for Determining and Utilizing Cross-talk Adjusted Scintillating Fibers, Patent No. 5,374,824, issued 20 December 1994.

APPENDIX V

UNT FACILITIES SUPPORTING THE NATIONAL BIOMEDICAL TRACER FACILITY

THE ROBERT B. TOULOUSE SCHOOL OF GRADUATE STUDIES

The Board of Regents of the University of North Texas renamed the Graduate School the Robert B. Toulouse School of Graduate Studies when Dr. Toulouse retired from the university in 1990. His contributions to graduate education made the honor richly deserved. Dr. Toulouse served as graduate dean from 1954 to 1982 when he was named provost and vice president for academic affairs.

During Dr. Toulouse's tenure as graduate dean, almost every graduate program currently authorized at UNT was established. His leadership role in the establishment of these programs helped to make UNT the most comprehensive graduate institution in the North Texas region and one of the three largest graduate institutions in the state. In addition, graduate student enrollment grew from approximately 300 students to more than 5,500 — representing almost a third of UNT's total enrollment. Toulouse also provided the leadership in establishing the Federation of North Texas Area Universities in 1968.

Dr. Toulouse's efforts also had an extraordinary effect on the development of research at the university. As dean, he pursued a goal of enhancing research across the entire campus, involving as many professors as possible to build a strong base for attracting external funding. His insight and good judgment in managing the university's limited resources for research led to major increases in the quality and impact of research at UNT. In this, he laid the foundation for the explosive increase in external research funding of the 1980s.

OVERVIEW OF THE UNIVERSITY

The University of North Texas, with an enrollment of about 26,000 students, is the fourth-largest institution in Texas. UNT is recognized as a comprehensive teaching and research institution and as a leader in the performance of many public services, to include assisting in the economic diversification of the Dallas-Fort Worth metropolitan area and the state of Texas. UNT was recommended by the Select Committee on Higher Education in 1986 for designation by the state as "an emerging national research university" and was designated by the Carnegie Foundation for the Advancement of Teaching in 1976, 1987 and 1994 as a "Class I Doctorate-Granting Institution." Further national recognition came in 1988 when U.S. Secretary of Education William Bennett cited UNT for its innovative approach to undergraduate education in the Classic Learning Core, an integrated liberal arts curriculum similar to those usually found only in small, private colleges. In 1992, UNT was elected to full membership in the National Association of State Universities and Land-Grant

Colleges. Since its founding in 1890, North Texas has awarded more than 135,000 bachelor's, master's and doctoral degrees. It has offered master's degrees since 1935 and doctoral degrees since 1950. UNT has about 63,000 active alumni in the Dallas-Fort Worth region and another 30,000 active alumni reside elsewhere.

UNT is located in the city of Denton, easily accessible via interstate highway from Dallas (37 miles) and Fort Worth (35 miles). The university campus is composed of 116 structures on 455 acres.

ACADEMIC AND RESEARCH PROGRAMS

- UNT is the most comprehensive graduate and research university in the region, with 138 undergraduate and graduate majors. Approximately 25 percent of the student body is graduate students.
- UNT has nationally accredited professional programs in business, chemistry, clinical and counseling psychology, computer sciences, counselor education, hotel and restaurant management, interior design, journalism, library sciences, medical technology, music, public administration, recreation and leisure studies, rehabilitation studies, social work, speech-language pathology and audiology and the child development laboratory.
- The College of Business Administration is one of the largest in the nation as well as the most comprehensive in the region, with an undergraduate enrollment of almost 5,000 students and more than 900 master's and doctoral students. The accounting department enjoys "preferred" status among major corporations, with special strength in oil and gas accounting.
- UNT has the highest teacher education admission and exit standards in the state and among the highest in the nation. Its Quality Assurance Program guarantees the performance of UNT graduates of the teacher education program.
- UNT constitutes one of the largest centers of instructional computing in the nation, encompassing computer sciences — one of the first such programs to be nationally accredited — computer education and cognitive systems, business computer information systems, and library and information sciences.
- The innovative hospitality management degree program is the only one of its kind in the North Texas region; a master's program was initiated in 1989.
- The UNT College of Music is the second largest in the nation and is internationally known for the One O'Clock Lab Band, UNT Symphony, A Cappella Choir, and Center for Experimental Music and Intermedia. In 1986 the college received the Yamaha Award.
- The UNT School of Visual Arts is one of the most comprehensive in the region and one of the largest in the country with a faculty of international stature.
- UNT assists Texas in fostering economic diversification through the University Center for Economic Development and Research, the Professional Development Institute (PDI) training program in accounting and business computer information systems, the Information Systems Research Center, the Institute for Petroleum Accounting, and such science and technology research as the study of turbulence around airfoils, airline gate

scheduling, the creation of fuel from municipal waste products and improved processes for the cement and lime industries.

- UNT regularly provides continuing education to audiences ranging from accountants to municipal clerks to electronics workers and plays host to conferences with as many as 5,000 participants with support provided by the Office of Continuing Education and Conference Management. The Radisson Hotel at UNT, as well as campus facilities, are available for public use.
- The University of North Texas is a true regional university, serving commuting and resident students. Approximately 3,200 students lived in campus residence halls in fall 1994.

SCIENCE, TECHNOLOGY, AND RESEARCH

- Externally funded projects totaled more than $20 million for 1994-95, with further growth expected in the future.
- The state-of-the-art Science Research Building is dedicated solely to research.
- North Texas has widely recognized strengths in the physical and mathematical sciences, including single atom and small accelerator physics, organometallic chemistry and mathematical image processing.
- Biochemistry, which is shared with UNT's sister institution, the University of North Texas Health Science Center at Fort Worth, is well-known for research into critical human health problems.
- The engineering technology program was instrumental in the site selection for the regional Boeing Electronics and Texas Instruments plants.
- The problem-solving approach of the Institute of Applied Sciences helps Texas address its water quality needs.
- Research on how neural networks process and store information is a pioneering effort of the Center for Network Neuroscience.
- UNT is the site of the Texas Academy of Mathematics and Science, a program for early college admission of students drawn from among outstanding high school sophomores; the academy is a nationally unique model of integrating academy and regular university students.

THE UNIVERSITY'S MISSION

The University of North Texas is the largest and most comprehensive research and doctoral degree-granting institution in North Texas. The university is committed to excellence in teaching and the discovery and application of knowledge through research and creative activities. As a metropolitan university, the institution is dedicated to continued growth as a leader in the Dallas-Fort Worth-Denton area; the Metroplex; and state, national and international education communities.

The university:

- conducts high-quality instruction, scholarship and service by:
  - fostering excellence and innovation in teaching and learning;

  - supporting research and creative activities that advance knowledge, strengthen undergraduate and graduate programs, and promote the application of knowledge for the benefit of society; and
  - accepting a primary leadership role in addressing community needs of the Metroplex region and the state;
- maintains a community founded on free and open inquiry, academic integrity and the examination of values;
- nurtures development of students by providing continuing opportunities for intellectual, physical, emotional, social and career growth;
- stresses understanding and appreciation of the historical, intellectual, technological, scientific and cultural nature of the search for knowledge;
- promotes the advancement of the arts; and
- supports a culturally diverse environment and advocates mutual respect for all members of the university community as they strive for excellence.

The university fosters its relationship with the University of North Texas Health Science Center at Fort Worth and cultivates partnerships with elementary and secondary schools, community colleges, other universities, businesses, government agencies and nonprofit organizations to improve the quality of education and community life.

APPENDIX VI

SANDIA REACTOR FACILITIES SUPPORTING THE NATIONAL BIOMEDICAL TRACER FACILITY

OVERVIEW

The DOE Isotope Production and Distribution Program (IPDP) selected the Reactor Engineering Technology Center at Sandia National Laboratories for production of radioisotopes for nuclear medicine pending completion of the National Environmental Policy Act (NEPA) process and approval of a detailed resource-loaded schedule. The facilities selected are the Annular Core Research Reactor (ACRR) and the Hot Cell Facility (HCF) at Sandia National Laboratories Technical Area-V, located on DOE land about four miles south of Albuquerque, New Mexico, on Kirtland Air Force Base. The Sandia Pulse Reactor III (SPR III), which is operated in the same technical area, can also be used without modifications to produce research quantities of radioisotopes.

Sandia National Laboratories is a Department of Energy multiprogram national laboratory employing about 8,500 people, including nearly 4,000 technical professionals, and having an annual budget of approximately $1.4 billion. Its mission is to provide scientific and engineering solutions to meet national needs in nuclear weapons and related defense systems, energy security, and environmental integrity, and to address emerging national challenges for both government and industry.

Sandia's core competencies are found in its research foundations and integrated capabilities. Its research foundations are: engineered materials and processes, microelectronics and photonics, computational and information sciences, and engineering sciences. Its integrated capabilities are: advanced manufacturing technology, advanced information technology, electronics technology, and pulsed power technology. Sandia's nuclear technology and nuclear facilities are part of the engineering sciences research foundation.

Sandia and NBTF Collaboration

Sandia and the NBTF consortium that produced this proposal have agreed, under a *Memorandum of Understanding*, to cooperate and provide mutual support in research, development, testing, production, and supply of radioactive and stable isotopes and related areas, including detection, imaging, radiopharmaceuticals development, automation of separation and manufacturing processes, information technology, hazards analysis, facility operations, and environment, safety, and health issues. Under this agreement the parties will

provide to each other such quantities of research and other radioisotopes requested by the other party, consistent with the primary missions of the respective organizations.

REACTOR SYSTEMS

Sandia Annular Core Research Reactor and Sandia Pulse Reactor III

Sandia's Annular Core Research Reactor (if conversion approval is received) and SPR III can provide reactor-produced radioisotopes, and the North Texas NBTF Consortium can provide accelerator-produced radioisotopes. Through this agreement the national interest will be served effectively. Other members of the North Texas NBTF Consortium can also access the technologies of Sandia National Laboratories. Sandia can benefit from the experience and capabilities of the North Texas Research Institute and the other Consortium members in identifying and addressing problems in medicine, agriculture, manufacturing, energy, and the environment through the application of the technology of radioactive materials.

The SPR III reactor is operating and does not require modifications to produce radioisotopes. Modifications to the ACRR reactor and Hot Cell Facility, and start-up, will require approximately 18 months. Production of radioisotopes from the fission process will begin at that time; however, FDA approval may require up to six additional months. Molybdenum-99 suitable for medical use should be available from Sandia by October, 1996. It is possible that Sandia will be asked to implement a plan to provide emergency backup to Nordion of Canada for supply of molybdenum-99. In that event raw molybdenum-99, and possibly iodine-131, and xenon-133, could be available from Sandia as early as October 1995. Implementation of the emergency backup plan would introduce some delays in Sandia's preparations for production of finished molybdenum-99.

On completion of facility modifications at Sandia molybdenum-99, xenon-133, and iodine-131 will be harvested from the fission process, and iodine-125 will be produced by activation of xenon-124. Irradiated targets will be transported to the Hot Cell Facility in an adjacent building for processing to extract the desirable fission products. The facility will be capable of exceeding the U.S. demand for molybdenum-99 should this become necessary.

Because the fissioning of uranium is a random process, the fission reaction used to generate molybdenum-99 produces a number of other isotopes. Figure 1 shows the percentage fission yield from thermal fission of uranium-235. The yield curve has two peaks: the first occurring at mass numbers from 90 to 100, and the second from 135 to 145. Table 1 and Table 2 list the radioisotopes and elements with activities greater than 1 curie produced in a 20-kilowatt target after a seven-day irradiation in ACRR.

Figure 1 Percentage Yield from Thermal Fission of ^{235}U

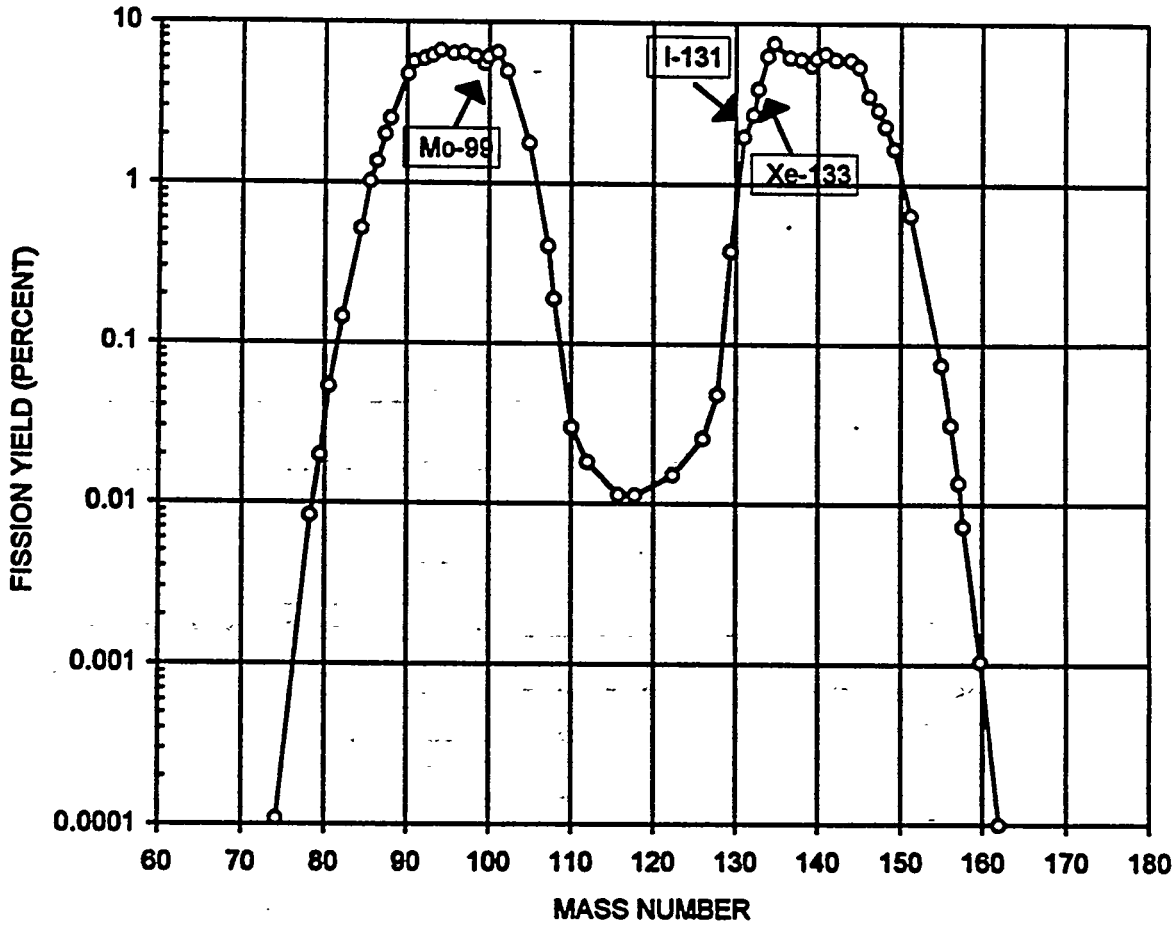


Table 1 Isotopic Decay (Curies) from Target Element
Target irradiated 7 days at 20 kW
Specified are all isotopes >1 curie one hour or later after removal from the reactor

Isotope	0-sec	10-min	30-min	1-hour	2-hour	6-hour	12-hour	1-day	2-day	4-day	7-day	14-day	30-day	120-day	1-year
AS 77	1.40E+00	1.39E+00	1.39E+00	1.38E+00	1.37E+00	1.30E+00	1.20E+00	1.00E+00	6.74E-01	2.90E-01	8.03E-02	4.00E-03	4.19E-06	7.35E-23	0.00E+00
GE 78	3.03E+00	2.80E+00	2.39E+00	1.88E+00	1.17E+00	1.72E-01	9.79E-03	3.16E-05	3.29E-10	3.56E-20	4.24E-35	0.00E+00	0.00E+00	0.00E+00	0.00E+00
AS 78	3.07E+00	3.06E+00	2.98E+00	2.81E+00	2.32E+00	6.99E-01	7.32E-02	4.94E-04	1.28E-08	4.84E-18	2.52E-32	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SE 83	3.31E+01	2.45E+01	1.32E+01	5.26E+00	9.29E-01	5.09E-04	7.77E-09	1.91E-18	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
BR 83	8.94E+01	8.71E+01	8.07E+01	7.10E+01	5.37E+01	1.69E+01	2.96E+00	9.13E-02	8.66E-05	7.79E-11	6.65E-20	0.00E+00	0.00E+00	0.00E+00	0.00E+00
KR 83M	8.94E+01	8.94E+01	8.87E+01	8.65E+01	7.86E+01	3.89E+01	9.22E+00	3.53E-01	3.65E-04	3.32E-10	2.84E-19	0.00E+00	0.00E+00	0.00E+00	0.00E+00
BR 84	1.69E+02	1.49E+02	9.77E+01	5.08E+01	1.37E+01	7.34E-02	2.87E-05	4.39E-12	1.03E-25	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
KR 85M	2.13E+02	2.10E+02	1.99E+02	1.85E+02	1.58E+02	8.51E+01	3.37E+01	5.26E+00	1.28E-01	7.65E-05	1.11E-09	5.74E-21	0.00E+00	0.00E+00	0.00E+00
KR 87	4.31E+02	3.98E+02	3.32E+02	2.53E+02	1.47E+02	1.86E+01	6.29E-01	9.07E-04	1.89E-09	8.21E-21	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
KR 88	6.08E+02	5.84E+02	5.36E+02	4.76E+02	3.73E+02	1.41E+02	3.25E+01	1.73E+00	4.95E-03	4.02E-08	9.32E-18	1.43E-33	0.00E+00	0.00E+00	0.00E+00
RB 88	6.13E+02	6.07E+02	5.91E+02	5.26E+02	4.16E+02	1.57E+02	3.63E+01	1.94E+00	5.53E-03	4.49E-08	1.04E-17	1.60E-33	0.00E+00	0.00E+00	0.00E+00
RB 89	8.04E+02	6.17E+02	2.57E+02	6.55E+01	4.24E+00	7.50E-05	5.56E-12	3.06E-26	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SR 89	7.37E+01	7.37E+01	7.36E+01	7.36E+01	7.36E+01	7.34E+01	7.34E+01	7.29E+01	7.19E+01	6.99E+01	6.71E+01	6.10E+01	4.89E+01	1.42E+01	4.91E-01
SR 91	9.80E+02	9.69E+02	9.46E+02	9.12E+02	8.48E+02	5.33E+02	4.09E+02	1.70E+02	2.96E+01	8.91E-01	4.66E-03	2.21E-08	1.50E-20	0.00E+00	0.00E+00
Y 91	7.15E+01	7.16E+01	7.17E+01	7.19E+01	7.23E+01	7.37E+01	7.51E+01	7.84E+01	7.85E+01	7.48E+01	7.23E+01	6.65E+01	5.50E+01	1.89E+01	1.04E+00
Y 91M	5.68E+02	5.68E+02	5.65E+02	5.56E+02	5.29E+02	4.02E+02	2.60E+02	1.09E+02	1.98E+01	6.96E-01	2.96E-03	1.41E-08	9.55E-21	0.00E+00	0.00E+00
SR 92	1.00E+03	9.81E+02	9.83E+02	7.77E+02	6.01E+02	2.18E+02	4.66E+01	2.19E+00	4.96E-03	2.19E-08	2.19E-18	4.86E-36	0.00E+00	0.00E+00	0.00E+00
Y 92	1.00E+03	1.00E+03	9.98E+02	9.82E+02	9.29E+02	6.16E+02	2.56E+02	3.19E+01	3.38E-01	2.91E-06	2.19E-11	1.12E-25	0.00E+00	0.00E+00	0.00E+00
SR 93	1.06E+03	4.26E+02	6.71E+01	4.19E+00	1.64E-02	3.81E-12	1.35E-26	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Y 93	1.08E+03	1.08E+03	1.06E+03	1.02E+03	9.55E+02	7.26E+02	4.91E+02	2.11E+02	4.06E+01	1.51E+00	1.08E-02	1.06E-07	3.80E-19	0.00E+00	0.00E+00
Y 94	1.05E+03	7.77E+02	3.76E+02	1.27E+02	1.43E+01	2.37E-03	5.02E-09	2.25E-20	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Y 95	1.07E+03	5.71E+02	1.53E+02	2.10E+01	4.01E-01	5.29E-08	2.52E-18	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ZR 95	7.83E+01	7.84E+01	7.84E+01	7.84E+01	7.84E+01	7.82E+01	7.80E+01	7.76E+01	7.67E+01	7.51E+01	7.27E+01	6.74E+01	5.67E+01	2.14E+01	1.50E+00
NB 95	5.21E+00	5.22E+00	5.24E+00	5.27E+00	5.33E+00	5.57E+00	5.92E+00	6.63E+00	8.00E+00	1.06E+01	1.43E+01	2.14E+01	3.23E+01	3.16E+01	3.20E+00
ZR 97	9.79E+02	9.73E+02	9.60E+02	9.40E+02	9.02E+02	7.96E+02	6.99E+02	3.96E+02	1.37E+02	1.91E+01	9.97E-01	1.91E-03	1.47E-10	0.00E+00	0.00E+00
NB 97	9.83E+02	9.82E+02	9.78E+02	9.70E+02	9.46E+02	9.19E+02	8.43E+02	3.69E+02	1.37E+02	1.92E+01	1.00E+00	1.02E-03	1.58E-10	0.00E+00	0.00E+00
NB 97M	9.28E+02	9.21E+02	9.09E+02	8.91E+02	8.55E+02	7.25E+02	5.87E+02	3.47E+02	1.30E+02	1.81E+01	9.44E-01	9.80E-04	1.38E-10	0.00E+00	0.00E+00
MO 99	8.35E+02	8.34E+02	8.31E+02	8.27E+02	8.19E+02	7.84E+02	7.37E+02	6.49E+02	5.05E+02	3.05E+02	1.43E+02	2.45E+01	4.34E-01	6.11E-11	0.00E+00
TC 99M	7.31E+02	7.31E+02	7.31E+02	7.31E+02	7.30E+02	7.19E+02	6.91E+02	6.21E+02	4.86E+02	2.94E+02	1.38E+02	2.36E+01	4.19E-01	5.89E-11	0.00E+00
MO101	8.45E+02	5.31E+02	2.06E+02	4.96E+01	2.89E+00	3.30E-05	1.29E-12	1.91E-27	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
TC101	8.45E+02	7.76E+02	4.91E+02	1.85E+02	1.80E+01	4.76E-04	2.87E-11	5.80E-26	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
MO102	7.03E+02	3.85E+02	1.11E+02	1.70E+01	4.01E-01	1.24E-07	2.14E-17	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
TC102	7.03E+02	3.88E+02	1.11E+02	1.71E+01	4.04E-01	1.25E-07	2.16E-17	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
RU103	6.12E+01	6.12E+01	6.11E+01	6.11E+01	6.11E+01	6.09E+01	6.06E+01	6.01E+01	5.91E+01	5.70E+01	5.41E+01	4.78E+01	3.60E+01	7.36E+00	9.72E-02
RH103M	5.51E+01	5.51E+01	5.51E+01	5.51E+01	5.50E+01	5.49E+01	5.47E+01	5.42E+01	5.32E+01	5.14E+01	4.87E+01	4.31E+01	3.25E+01	6.64E+00	8.76E-02
TC104	3.09E+02	2.30E+02	1.08E+02	3.44E+01	3.50E+00	3.75E-04	4.17E-10	5.14E-22	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
TC105	1.71E+02	8.01E+01	1.42E+01	1.05E+00	5.82E-03	5.42E-12	1.54E-25	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
RU105	1.71E+02	1.70E+02	1.63E+02	1.52E+02	1.30E+02	6.94E+01	2.72E+01	4.19E+00	9.84E-02	5.47E-06	7.16E-10	2.90E-21	0.00E+00	0.00E+00	0.00E+00
RH105	1.47E+02	1.48E+02	1.48E+02	1.48E+02	1.48E+02	1.44E+02	1.33E+02	1.07E+02	6.75E+01	2.63E+01	6.42E+00	2.38E-01	1.28E-04	5.25E-23	0.00E+00
RH107	2.92E+01	2.55E+01	1.42E+01	5.48E+00	9.07E-01	3.79E-04	3.83E-09	3.94E-19	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
PD109	5.92E+00	5.90E+00	5.91E+00	5.86E+00	5.39E+00	4.39E+00	3.21E+00	1.73E+00	5.04E-01	4.25E-02	1.04E-03	1.83E-07	4.72E-16	0.00E+00	0.00E+00
AG109M	5.92E+00	5.90E+00	5.91E+00	5.86E+00	5.39E+00	4.39E+00	3.22E+00	1.73E+00	5.04E-01	4.25E-02	1.04E-03	1.83E-07	1.10E-15	5.50E-16	3.91E-16
AG111	1.74E+00	1.75E+00	1.75E+00	1.75E+00	1.74E+00	1.71E+00	1.67E+00	1.60E+00	1.46E+00	1.21E+00	9.14E-01	4.77E-01	1.09E-01	2.49E-05	3.06E-15
AG113	2.14E+00	2.10E+00	2.01E+00	1.86E+00	1.65E+00	9.79E-01	4.47E-01	9.30E-02	4.03E-03	7.57E-06	6.15E-10	1.77E-19	0.00E+00	0.00E+00	0.00E+00

Isotope	0-sec	10-min	30-min	1-hour	2-hour	6-hour	12-hour	1-day	2-day	4-day	7-day	14-day	30-day	120-day	1-year
CD115	1.62E+00	1.62E+00	1.62E+00	1.61E+00	1.59E+00	1.51E+00	1.40E+00	1.20E+00	8.76E-01	4.70E-01	1.95E-01	2.10E-02	1.44E-04	9.99E-17	0.00E+00
IN115M	1.62E+00	1.62E+00	1.62E+00	1.62E+00	1.62E+00	1.58E+00	1.50E+00	1.30E+00	9.53E-01	5.11E-01	2.01E-01	2.28E-02	1.58E-04	2.02E-07	4.47E-09
CD117	1.36E+00	1.31E+00	1.20E+00	1.05E+00	8.02E-01	2.76E-01	5.57E-02	2.27E-03	3.78E-06	1.05E-11	4.95E-20	0.00E+00	0.00E+00	0.00E+00	0.00E+00
IN117	1.25E+00	1.25E+00	1.24E+00	1.21E+00	1.11E+00	6.06E-01	1.90E-01	1.12E-02	5.91E-05	2.84E-09	1.30E-15	1.74E-30	0.00E+00	0.00E+00	0.00E+00
IN117M	1.58E+00	1.58E+00	1.57E+00	1.53E+00	1.40E+00	7.43E-01	2.12E-01	1.32E-02	6.96E-05	2.48E-09	1.00E-15	1.34E-30	0.00E+00	0.00E+00	0.00E+00
CD118	2.33E+00	2.04E+00	1.55E+00	1.02E+00	4.47E-01	1.64E-02	1.15E-04	5.63E-09	1.36E-17	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
IN118	2.33E+00	2.04E+00	1.55E+00	1.02E+00	4.48E-01	1.64E-02	1.15E-04	5.64E-09	1.36E-17	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SN121	2.43E+00	2.42E+00	2.40E+00	2.37E+00	2.31E+00	2.09E+00	1.79E+00	1.31E+00	7.02E-01	2.03E-01	3.15E-02	4.09E-04	1.99E-08	0.00E+00	0.00E+00
SN127	1.52E+01	1.44E+01	1.29E+01	1.09E+01	7.96E+00	2.10E+00	2.90E-01	5.52E-03	2.00E-06	2.64E-13	1.26E-23	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SB127	1.68E+01	1.68E+01	1.68E+01	1.68E+01	1.67E+01	1.64E+01	1.57E+01	1.44E+01	1.20E+01	8.36E+00	4.87E+00	1.38E+00	7.75E-02	7.10E-09	4.71E-28
TE127	1.46E+01	1.46E+01	1.46E+01	1.46E+01	1.46E+01	1.45E+01	1.43E+01	1.35E+01	1.15E+01	8.11E+00	4.79E+00	1.45E+00	1.95E-01	6.94E-02	1.44E-02
SN128	5.81E+01	5.17E+01	4.09E+01	2.87E+01	1.42E+01	8.47E-01	1.23E-02	2.61E-06	1.18E-13	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SB128	2.19E+00	2.16E+00	2.10E+00	2.03E+00	1.89E+00	1.36E+00	9.69E-01	3.45E-01	5.45E-02	1.36E-03	5.34E-06	1.31E-11	1.94E-24	0.00E+00	0.00E+00
SB128M	5.96E+01	5.71E+01	4.91E+01	3.47E+01	1.72E+01	1.03E+00	1.50E-02	3.17E-06	1.43E-13	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SB129	1.10E+02	1.08E+02	1.03E+02	9.49E+01	8.08E+01	4.25E+01	1.62E+01	2.37E+00	5.03E-02	2.27E-05	2.19E-10	4.27E-22	0.00E+00	0.00E+00	0.00E+00
TE129	9.90E+01	9.87E+01	9.77E+01	9.49E+01	8.69E+01	5.10E+01	2.07E+01	4.23E+00	1.43E+00	1.32E+00	1.24E+00	1.07E+00	7.70E-01	1.20E-01	7.64E-04
TE129M	2.12E+00	2.12E+00	2.12E+00	2.13E+00	2.14E+00	2.16E+00	2.16E+00	2.15E+00	2.11E+00	2.02E+00	1.90E+00	1.65E+00	1.19E+00	1.95E-01	1.17E-03
SB131	4.25E+02	3.20E+02	1.75E+02	7.09E+01	1.16E+01	9.40E-03	1.63E-07	6.15E-17	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
TE131	4.29E+02	4.11E+02	3.34E+02	2.10E+02	6.95E+01	1.19E+01	1.02E+01	7.72E+00	4.43E+00	1.46E+00	2.77E-01	5.71E-03	8.01E-07	1.70E-28	0.00E+00
TE131M	5.83E+01	5.92E+01	5.99E+01	5.83E+01	5.70E+01	5.20E+01	4.53E+01	3.43E+01	1.97E+01	6.50E+00	1.23E+00	2.54E-02	3.56E-06	7.54E-28	0.00E+00
I131	2.09E+02	2.09E+02	2.10E+02	2.10E+02	2.10E+02	2.07E+02	2.04E+02	1.97E+02	1.83E+02	1.56E+02	1.21E+02	6.63E+01	1.67E+01	7.13E-03	4.69E-12
TE132	5.51E+02	5.51E+02	5.49E+02	5.47E+02	5.42E+02	5.23E+02	4.96E+02	4.46E+02	3.60E+02	2.36E+02	1.24E+02	2.81E+01	9.33E-01	4.61E-09	0.00E+00
I132	5.54E+02	5.54E+02	5.54E+02	5.53E+02	5.51E+02	5.37E+02	5.11E+02	4.59E+02	3.72E+02	2.43E+02	1.28E+02	2.89E+01	9.61E-01	4.65E-09	0.00E+00
TE133	6.44E+02	4.41E+02	1.90E+02	6.26E+01	1.95E+01	9.29E-01	1.03E-02	1.26E-06	1.98E-14	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
TE133M	5.01E+02	4.42E+02	3.44E+02	2.36E+02	1.12E+02	5.54E+00	6.13E-02	7.90E-06	1.12E-13	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
I133	1.12E+03	1.12E+03	1.11E+03	1.10E+03	1.07E+03	9.42E+02	7.72E+02	5.17E+02	2.32E+02	4.70E+01	4.26E+00	1.89E-02	4.37E-08	0.00E+00	0.00E+00
XE133	5.95E+02	5.95E+02	5.96E+02	5.98E+02	5.90E+02	5.99E+02	6.09E+02	6.10E+02	5.80E+02	4.75E+02	3.27E+02	1.31E+02	1.99E+01	1.09E-04	9.14E-19
XE133M	2.70E+01	2.70E+01	2.70E+01	2.71E+01	2.71E+01	2.72E+01	2.70E+01	2.57E+01	2.15E+01	1.29E+01	5.23E+00	5.79E-01	3.96E-03	1.55E-15	0.00E+00
TE134	1.13E+03	9.58E+02	6.87E+02	4.19E+02	1.55E+02	2.99E+00	7.39E-03	4.82E-08	2.05E-19	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
I134	1.27E+03	1.25E+03	1.15E+03	9.47E+02	5.65E+02	3.80E+01	4.00E-01	3.23E-05	1.96E-13	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
I135	1.05E+03	1.04E+03	1.00E+03	9.49E+02	8.55E+02	5.62E+02	3.00E+02	8.51E+01	6.87E+00	4.48E-02	2.36E-05	5.29E-13	1.73E-30	0.00E+00	0.00E+00
XE135	2.05E+02	2.16E+02	2.37E+02	2.65E+02	3.12E+02	4.12E+02	4.11E+02	2.58E+02	5.95E+01	1.89E+00	8.21E-03	2.26E-08	4.32E-21	0.00E+00	0.00E+00
XE135M	1.90E+02	1.79E+02	1.66E+02	1.53E+02	1.37E+02	9.00E+01	4.90E+01	1.36E+01	1.10E+00	7.18E-03	3.79E-06	8.47E-14	2.77E-31	0.00E+00	0.00E+00
XE138	1.05E+03	6.43E+02	2.42E+02	5.57E+01	2.96E+00	2.36E-06	8.31E-13	2.69E-29	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CS138	1.13E+03	1.07E+03	8.35E+02	4.94E+02	1.45E+02	9.43E-01	3.63E-04	6.75E-11	2.33E-24	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CS139	1.07E+03	5.42E+02	1.24E+02	1.36E+01	1.63E-01	3.35E-09	9.93E-21	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
BA139	1.08E+03	1.08E+03	9.37E+02	7.39E+02	4.48E+02	5.99E+01	2.93E+00	7.02E-03	4.02E-08	1.32E-18	2.49E-34	0.00E+00	0.00E+00	0.00E+00	0.00E+00
BA140	3.29E+02	3.29E+02	3.29E+02	3.29E+02	3.29E+02	3.25E+02	3.20E+02	3.12E+02	2.95E+02	2.65E+02	2.25E+02	1.54E+02	6.48E+01	4.93E-01	8.33E-07
LA140	2.31E+02	2.32E+02	2.32E+02	2.33E+02	2.35E+02	2.41E+02	2.49E+02	2.61E+02	2.76E+02	2.77E+02	2.51E+02	1.77E+02	7.45E+01	5.69E-01	9.59E-07
BA141	9.90E+02	6.63E+02	3.20E+02	1.02E+02	1.05E+01	1.16E-03	1.36E-09	1.95E-21	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
LA141	9.83E+02	9.79E+02	9.50E+02	8.96E+02	7.49E+02	3.70E+02	1.29E+02	1.55E+01	2.25E-01	4.74E-06	1.45E-10	1.97E-23	0.00E+00	0.00E+00	0.00E+00
CE141	1.32E+02	1.32E+02	1.32E+02	1.32E+02	1.33E+02	1.34E+02	1.35E+02	1.34E+02	1.31E+02	1.26E+02	1.19E+02	1.02E+02	7.23E+01	1.06E+01	5.69E-02
LA142	9.98E+02	9.69E+02	8.72E+02	7.09E+02	4.54E+02	7.55E+01	5.12E+00	2.35E-02	4.95E-07	2.20E-16	2.06E-30	0.00E+00	0.00E+00	0.00E+00	0.00E+00
LA143	9.97E+02	6.11E+02	2.27E+02	5.14E+01	2.63E+00	1.92E-05	3.31E-13	1.09E-28	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CE143	9.62E+02	9.62E+02	9.58E+02	9.49E+02	9.29E+02	8.54E+02	7.53E+02	5.85E+02	3.54E+02	1.29E+02	2.84E+01	8.34E-01	2.62E-04	5.19E-24	0.00E+00
PR143	2.23E+02	2.24E+02	2.24E+02	2.25E+02	2.26E+02	2.32E+02	2.39E+02	2.50E+02	2.61E+02	2.57E+02	2.29E+02	1.63E+02	7.18E+01	7.23E-01	2.61E-06
CE144	1.54E+01	1.54E+01	1.54E+01	1.54E+01	1.54E+01	1.54E+01	1.54E+01	1.54E+01	1.53E+01	1.53E+01	1.52E+01	1.49E+01	1.43E+01	1.15E+01	6.33E+00
PR144	1.65E+01	1.62E+01	1.58E+01	1.55E+01	1.54E+01	1.54E+01	1.54E+01	1.54E+01	1.53E+01	1.53E+01	1.52E+01	1.49E+01	1.43E+01	1.15E+01	6.33E+00
PR145	6.54E+02	6.48E+02	6.24E+02	5.88E+02	5.24E+02	3.30E+02	1.64E+02	4.09E+01	2.54E+00	9.72E-03	2.31E-06	8.09E-15	3.79E-34	0.00E+00	0.00E+00

Isotope	0-sec	10-min	30-min	1-hour	2-hour	6-hour	12-hour	1-day	2-day	4-day	7-day	14-day	30-day	120-day	1-year
CE146	4.98E+02	3.08E+02	1.16E+02	2.69E+01	1.43E+00	1.17E-05	2.73E-13	1.49E-28	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
PR146	4.98E+02	4.72E+02	3.48E+02	1.79E+02	3.69E+01	4.03E-02	1.34E-06	1.48E-15	1.81E-33	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
PR147	3.81E+02	2.36E+02	7.49E+01	1.33E+01	4.14E-01	3.95E-07	3.69E-16	3.08E-34	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ND147	1.35E+02	1.35E+02	1.35E+02	1.35E+02	1.35E+02	1.33E+02	1.31E+02	1.27E+02	1.20E+02	1.05E+02	8.74E+01	5.84E+01	2.07E+01	7.34E-02	1.55E-08
ND149	1.62E+02	1.73E+02	1.52E+02	1.24E+02	8.33E+01	1.69E+01	1.52E+00	1.24E-02	9.25E-07	3.67E-15	1.09E-27	0.00E+00	0.00E+00	0.00E+00	0.00E+00
PM149	1.58E+02	1.58E+02	1.58E+02	1.58E+02	1.57E+02	1.51E+02	1.40E+02	1.20E+02	8.77E+01	4.68E+01	1.83E+01	2.04E+00	1.36E-02	7.64E-15	0.00E+00
PM151	6.98E+01	6.87E+01	6.84E+01	6.76E+01	6.60E+01	5.99E+01	5.17E+01	3.96E+01	2.15E+01	6.65E+00	1.15E+00	1.90E-02	1.61E-06	0.00E+00	0.00E+00
PM153	2.74E+01	9.42E+00	7.24E-01	1.54E-02	6.96E-06	2.91E-19	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SM153	2.53E+01	2.53E+01	2.52E+01	2.50E+01	2.46E+01	2.32E+01	2.12E+01	1.78E+01	1.24E+01	6.10E+00	2.10E+00	1.73E-01	5.79E-04	6.98E-18	0.00E+00
TOTAL	9.55E+04	3.77E+04	2.95E+04	2.45E+04	2.04E+04	1.47E+04	1.12E+04	7.99E+03	5.37E+03	3.48E+03	2.34E+03	1.31E+03	6.39E+02	1.41E+02	2.35E+01

Table 2 Element Decay (Curies) from Target
Target irradiated 7 days at 20 kW

Isotope	0-sec	10-min	30-min	1-hour	2-hour	6-hour	12-hour	1-day	2-day	4-day	7-day	14-day	30-day	120-day	1-year
H	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.98E-03	1.97E-03	1.94E-03	1.87E-03
C	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10	5.04E-10
CO	9.95E-05	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
NI	9.03E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CU	1.52E-01	4.72E-09	3.11E-10	5.29E-12	2.20E-14	1.96E-14	1.83E-14	1.80E-14	1.22E-14	7.14E-15	3.19E-15	4.86E-16	3.36E-18	1.03E-28	0.00E+00
ZN	2.36E+00	7.10E-03	6.13E-03	6.08E-03	5.99E-03	5.64E-03	5.16E-03	4.32E-03	3.02E-03	1.48E-03	5.04E-04	4.12E-05	1.35E-07	1.40E-21	0.00E+00
GA	1.41E+01	7.87E-02	3.84E-02	2.99E-02	2.63E-02	1.75E-02	1.09E-02	6.25E-03	4.11E-03	2.09E-03	7.23E-04	5.92E-05	1.93E-07	2.01E-21	0.00E+00
GE	9.70E+01	3.56E+00	3.10E+00	2.54E+00	1.74E+00	5.63E-01	2.70E-01	1.23E-01	2.80E-02	1.47E-03	1.78E-05	5.95E-10	3.51E-20	0.00E+00	0.00E+00
AS	3.05E+02	8.74E+00	5.30E+00	4.28E+00	3.68E+00	2.00E+00	1.27E+00	1.00E+00	6.74E-01	2.90E-01	8.03E-02	4.00E-03	4.19E-06	7.35E-23	0.00E+00
SE	9.45E+02	7.80E+01	2.95E+01	1.05E+01	1.91E+00	4.17E-02	3.46E-03	2.49E-03	1.67E-03	7.21E-04	2.01E-04	1.17E-05	1.78E-06	1.77E-06	1.77E-06
BR	2.19E+03	2.60E+02	1.79E+02	1.22E+02	6.75E+01	1.70E+01	2.98E+00	1.06E-01	9.49E-03	3.96E-03	8.91E-04	3.29E-05	1.75E-08	6.70E-27	0.00E+00
KR	3.84E+03	1.37E+03	1.16E+03	1.00E+03	7.57E+02	2.81E+02	7.60E+01	7.40E+00	1.90E-01	5.63E-02	5.62E-02	5.61E-02	5.59E-02	5.51E-02	5.27E-02
RB	5.21E+03	1.33E+03	9.39E+02	5.91E+02	4.20E+02	1.57E+02	3.63E+01	1.94E+00	8.51E-03	2.77E-03	2.48E-03	1.91E-03	1.06E-03	3.73E-05	4.24E-09
SR	6.11E+03	2.43E+03	1.97E+03	1.77E+03	1.52E+03	9.24E+02	5.29E+02	2.46E+02	1.02E+02	7.13E+01	6.76E+01	6.14E+01	4.94E+01	1.47E+01	9.20E-01
Y	7.92E+03	4.12E+03	3.22E+03	2.78E+03	2.50E+03	1.82E+03	1.07E+03	4.29E+02	1.37E+02	7.73E+01	7.27E+01	6.69E+01	5.55E+01	1.94E+01	1.47E+00
ZR	4.84E+03	1.06E+03	1.04E+03	1.02E+03	9.81E+02	8.44E+02	6.77E+02	4.44E+02	2.14E+02	9.42E+01	7.37E+01	6.74E+01	5.67E+01	2.14E+01	1.50E+00
NB	6.95E+03	1.91E+03	1.90E+03	1.87E+03	1.81E+03	1.55E+03	1.22E+03	7.22E+02	2.75E+02	4.83E+01	1.67E+01	2.19E+01	3.27E+01	3.19E+01	3.21E+00
MO	3.44E+03	1.76E+03	1.15E+03	8.93E+02	8.21E+02	7.84E+02	7.37E+02	6.49E+02	5.05E+02	3.05E+02	1.43E+02	2.45E+01	4.34E-01	2.00E-03	2.00E-03
TC	3.40E+03	2.21E+03	1.46E+03	9.69E+02	7.52E+02	7.19E+02	6.91E+02	6.21E+02	4.98E+02	2.94E+02	1.38E+02	2.36E+01	4.19E-01	6.47E-06	6.47E-06
RU	2.91E+02	2.42E+02	2.26E+02	2.14E+02	1.92E+02	1.31E+02	8.87E+01	6.62E+01	6.00E+01	5.79E+01	5.46E+01	4.86E+01	3.89E+01	9.06E+00	5.40E-01
RH	3.31E+02	2.83E+02	2.66E+02	2.54E+02	2.42E+02	2.19E+02	1.96E+02	1.64E+02	1.22E+02	7.86E+01	5.60E+01	4.42E+01	3.33E+01	7.34E+00	5.30E-01
PD	2.66E+01	1.27E+01	9.83E+00	8.65E+00	7.79E+00	6.39E+00	4.94E+00	2.80E+00	9.70E-01	1.32E-01	8.49E-03	2.29E-05	6.00E-08	5.99E-08	5.99E-08
AG	3.10E+01	1.64E+01	1.41E+01	1.26E+01	1.13E+01	9.32E+00	7.23E+00	4.69E+00	2.52E+00	1.36E+00	9.34E-01	4.77E-01	1.09E-01	2.90E-05	2.10E-06
CD	2.23E+01	6.35E+00	5.16E+00	4.31E+00	3.35E+00	2.04E+00	1.54E+00	1.22E+00	8.94E-01	4.99E-01	2.02E-01	3.60E-02	1.19E-02	2.92E-03	1.07E-04
IN	7.50E+01	8.24E+00	6.93E+00	5.99E+00	4.60E+00	2.95E+00	1.99E+00	1.32E+00	9.53E-01	5.11E-01	2.01E-01	2.29E-02	1.58E-04	2.02E-07	4.49E-09
SN	6.24E+02	1.16E+02	6.17E+01	4.40E+01	2.56E+01	8.97E+00	3.01E+00	2.20E+00	1.53E+00	9.27E-01	6.21E-01	3.67E-01	1.33E-01	1.61E-02	4.39E-03
SB	1.90E+03	7.21E+02	3.92E+02	2.32E+02	1.33E+02	6.15E+01	3.29E+01	1.71E+01	1.22E+01	8.42E+00	4.93E+00	1.43E+00	1.12E-01	2.46E-02	2.07E-02
TE	4.36E+03	2.98E+03	2.27E+03	1.64E+03	1.06E+03	6.64E+02	5.89E+02	5.08E+02	4.00E+02	2.55E+02	1.34E+02	3.24E+01	3.21E+00	4.49E-01	3.60E-02
I	6.13E+03	4.19E+03	4.03E+03	3.76E+03	3.25E+03	2.29E+03	1.79E+03	1.26E+03	7.94E+02	4.46E+02	2.54E+02	9.53E+01	1.77E+01	7.13E-03	9.96E-09
XE	4.79E+03	1.83E+03	1.26E+03	1.09E+03	1.07E+03	1.13E+03	1.09E+03	9.09E+02	6.63E+02	4.90E+02	3.33E+02	1.33E+02	1.65E+01	8.06E-03	3.19E-09
CS	4.74E+03	1.62E+03	9.60E+02	5.08E+02	1.46E+02	1.62E+00	7.65E-01	7.56E-01	7.40E-01	7.11E-01	6.73E-01	6.05E-01	5.19E-01	4.51E-01	4.44E-01
BA	5.42E+03	2.58E+03	1.72E+03	1.19E+03	7.87E+02	3.85E+02	3.24E+02	3.12E+02	2.96E+02	2.86E+02	2.26E+02	1.55E+02	6.52E+01	9.19E-01	4.19E-01
LA	5.34E+03	2.79E+03	2.28E+03	1.98E+03	1.44E+03	6.87E+02	3.83E+02	2.77E+02	2.76E+02	2.77E+02	2.51E+02	1.77E+02	7.45E+01	8.99E-01	9.58E-07
CE	3.06E+03	1.50E+03	1.22E+03	1.12E+03	1.09E+03	1.00E+03	9.04E+02	7.35E+02	5.00E+02	2.70E+02	1.62E+02	1.17E+02	8.65E+01	2.21E+01	6.39E+00
PR	2.41E+03	1.63E+03	1.29E+03	1.02E+03	9.04E+02	5.77E+02	4.19E+02	3.07E+02	2.79E+02	2.72E+02	2.45E+02	1.79E+02	8.63E+01	1.24E+01	6.40E+00
ND	4.68E+02	3.73E+02	3.09E+02	2.63E+02	2.19E+02	1.50E+02	1.33E+02	1.27E+02	1.20E+02	1.05E+02	8.74E+01	5.64E+01	2.07E+01	7.34E-02	1.55E-08
PM	3.23E+02	2.73E+02	2.40E+02	2.29E+02	2.25E+02	2.12E+02	1.93E+02	1.58E+02	1.10E+02	5.43E+01	2.04E+01	3.35E+00	1.89E+00	1.79E+00	1.50E+00
SM	3.53E+01	3.31E+01	3.03E+01	2.83E+01	2.69E+01	2.47E+01	2.22E+01	1.92E+01	1.25E+01	6.11E+00	2.11E+00	1.83E-01	1.02E-02	9.62E-03	9.57E-03
EU	2.73E+00	2.60E+00	2.44E+00	2.27E+00	2.02E+00	1.61E+00	1.38E+00	1.09E+00	7.99E-01	6.25E-01	5.35E-01	3.92E-01	1.96E-01	1.72E-02	1.29E-02
GD	2.21E-01	2.01E-01	1.93E-01	1.89E-01	1.82E-01	1.57E-01	1.25E-01	9.01E-02	3.29E-02	5.49E-03	3.74E-04	7.31E-07	1.51E-08	1.17E-08	5.79E-09
TB	2.00E-02	1.90E-02	1.83E-02	1.02E-02	9.29E-03	8.99E-03	8.74E-03	8.31E-03	7.52E-03	6.15E-03	4.56E-03	2.26E-03	4.59E-04	1.37E-06	1.25E-07
DY	7.48E-04	5.42E-04	4.96E-04	4.46E-04	3.96E-04	2.01E-04	1.35E-04	1.12E-04	9.08E-05	6.04E-05	3.27E-05	7.84E-06	2.99E-07	3.15E-15	0.00E+00
HO	1.17E-04	1.18E-04	1.18E-04	1.18E-04	1.18E-04	1.20E-04	1.21E-04	1.20E-04	1.10E-04	9.26E-05	4.77E-05	1.17E-05	4.46E-07	1.99E-12	1.99E-12
TOTAL	8.55E+04	3.77E+04	2.95E+04	2.45E+04	2.04E+04	1.47E+04	1.12E+04	7.99E+03	5.37E+03	3.48E+03	2.34E+03	1.31E+03	6.39E+02	1.41E+02	2.35E+01

Requirements for Radionuclide Production

The SPR III reactor will produce research quantities of radioisotopes by fast neutron reactions. The Sandia nuclear facilities will also provide radioisotopes produced by the thermal fission of uranium-235. Production of molybdenum-99 will be the primary mission of the ACRR and HCF; however, other radioisotopes will also be produced by fission and radioactivation of appropriate targets. Because of space limitations it may be necessary to team with other consortium members, or other entities for final processing of certain radioisotopes. In addition to the criteria relating to protection of the public and the environment, other criteria must be met for the Sandia National Laboratories facilities to be a viable source of molybdenum-99.

Production Process

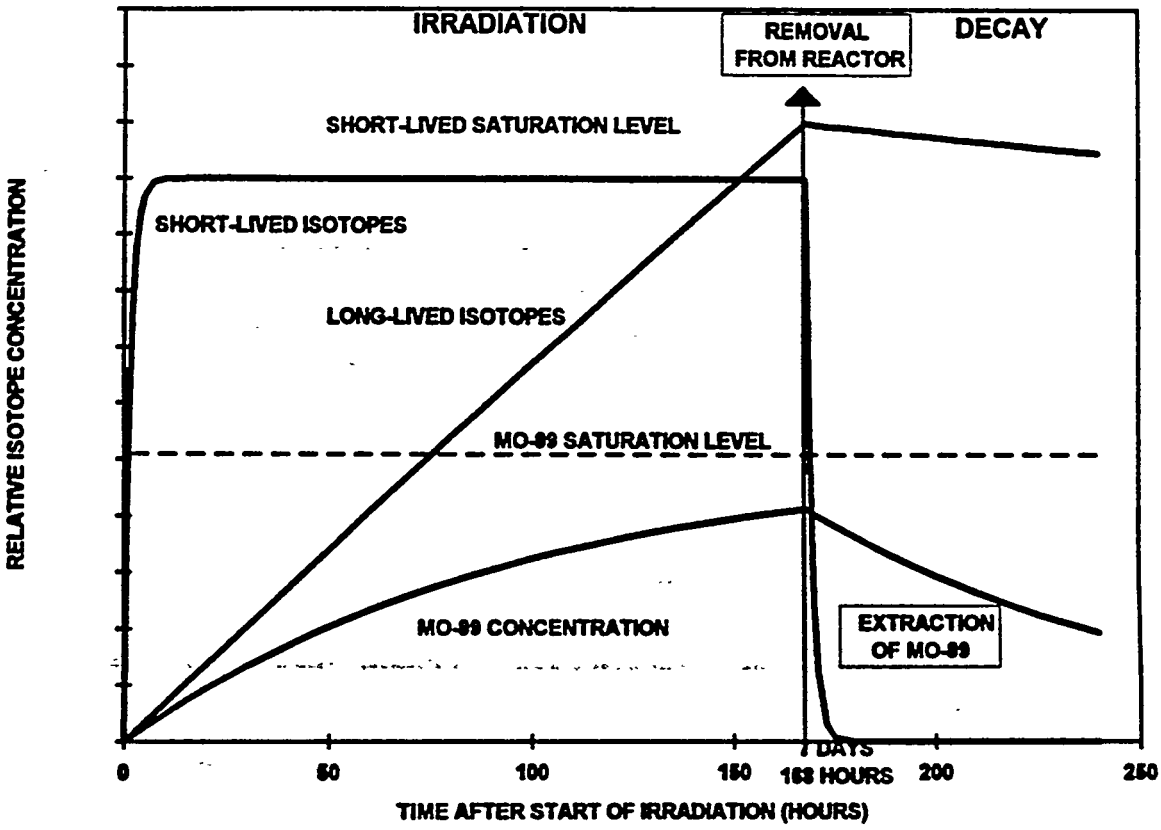
Figure 2 shows the generation of molybdenum-99 by fission in a reactor irradiation. A seven-day irradiation time is selected to optimize the molybdenum-99 generation versus the short- and long-lived fission products. A seven-day irradiation time represents ~83% of the saturated activity for molybdenum-99 and generates approximately 41 curies of molybdenum-99 per each kW of target power. Irradiating for shorter times would result in significantly less molybdenum-99 being generated per target. Irradiating for longer times would not produce significantly more molybdenum-99; however, the longer-lived fission products would increase linearly with irradiation time.

Approximately 400 kW of continuous target power generation is required to meet an assumed U.S. demand of ~16,500 Ci per week. If 7-day irradiation, 21-kW targets were to be used, 19 targets would be required to be processed weekly to meet the current U.S. demand. If 7-day irradiation, 10-kW targets were to be employed, ~40 targets would be processed weekly to meet U.S. demand.

Due to the relatively short half-life (2.75 days) of molybdenum-99 and the daily dependence of the health care system on molybdenum-99, a reactor operating in the production mode must be dedicated and reliable. It must essentially operate continuously with target additions and removals occurring at intervals of no more than a few hours. Extended reactor shutdown times for removal and/or loading of targets, inspection and maintenance, refueling, or due to component failure are costly and unacceptable from a reliability standpoint.

The reactor configuration and characteristics must be such as to accommodate (1) a relatively large number of target additions and their reactivity effect and (2) equilibrium and shutdown xenon reactivity effects. The characteristics should be such as to give as high a ratio of target power to fuel-element power as possible to minimize cost and the overall waste (target waste and spent fuel) generated.

Figure 2 Optimized Irradiation Schedule for ^{99}Mo Generation



Since reactor down time must be minimized, ready access to the targets must be available. Accessible cores such as open-tank (swimming-pool) systems may be preferable since targets can be removed or added with only short reactor power operation interruptions. Swimming-pool systems have the further advantage of underwater transfer of the hot (10,000 to 20,000 Ci) targets to transfer casks or directly to processing cells. Transportation time from the reactor to the processing facility must be minimized. Each hour lost between target irradiation and completion of processing results in a loss of 1% in the quantity of the finished product. Operation of the reactor and the processing facility should be on a common site to minimize transfer time and over-the-road shipment of highly radioactive materials.

A requirement on IPDP is that the ACRR fuel be returned in such condition that it may be used as pulsed reactor fuel. The effective neutronic core life of the ACRR has been estimated to be approximately 12 MW-y, which can be attributed to the high ^{235}U loading in the BeO fuel. For the 129 element, 19 target core configuration operating at 2 MW (core only), 24 hours per day, 7 days per week, the core could be operated for 6 years. At that time the original core configuration could be re-established and still maintain greater than the $3.00 of excess reactivity required for pulse operation. However, it would be best to replace the fuel when practical with less expensive fuel to avoid potential problems that may be encountered by pulsing fuel with significant burnup.

Required ACRR Facility Modifications

Control Console Upgrade - A new control room with an upgraded/computer-aided console has been developed for the ACRR is near completion. This upgrade will enhance the state-of-the-art control for the ACRR and, without the IPDP project, will still need to be completed.

Procurement/Installation of Heat Exchangers - The ACRR currently operates in a pulsed or steady-state mode. The current steady-state power limit is 2 MW continuous. This limit is due to the heat exchanger/cooling tower rejection limitations. The core is cooled by natural convection and calculations and experiments have shown the core to be able to run at 4 MW. Upgrading the pool cooling capacity to 4 MW and including redundant cooling is an activity that would enhance the ACRR's overall capability regardless of the IPDP project.

Removal of Central Cavity - The central cavity allows experiments to be placed in a dry, high-flux location in the core creating one of the unique features of the ACRR. Although running the core with the cavity removed and the central region flooded has never been performed, adding a removable central cavity would add significant experimental capabilities to the ACRR. It would allow irradiation experiments to be placed in the region and be cooled by the pool water.

Hardware Upgrades and Redundancy - Although yet unspecified, there may be upgrades and added redundancy features that will increase the performance of the ACRR. Regardless of the IPDP project, these types of features must be continually investigated and added in order to keep the reactor competitive and using current technology.

Ventilation and Environmental Monitoring Upgrade and Redundancy - Although the scope of this activity is as yet unspecified, the ventilation system and radiation monitoring system will be upgraded in order to make it redundant and current. Regardless of the IPDP project, these systems are continually upgraded, and with the removal of the GIF, must be modified somewhat in order to remain functioning properly.

Air Lock Addition - The air lock addition is for 24-hour operations as required by the IPDP project.

Layout of Reactor and Hot Cell Facilities

The reactor and hot cell facilities are located in Sandia National Laboratories Technical Area V in adjacent buildings as shown in Figure 3. Technical Area V is located approximately four miles south of Albuquerque, New Mexico on Department of Energy land on Kirtland Air Force Base. The layout of the ACRR Facility is shown in Figure 4. A cutaway of the reactor, tank, and cooling system is shown in Figure 5.

Reactor Safety

Core Cooling. The ACRR is cooled by natural convection. No emergency core cooling is required for this reactor as decay heat is readily removed by natural convection, conduction, and the redundant 4MW heat exchangers.

Critical Heat Flux. Experimental work performed at the University of New Mexico (Rau, D. B. and M. S. El Genk 1986), investigated the heat transfer and critical heat flux (CHF) conditions for ACRR type reactors under natural convection flow. Critical heat flux is the fuel or target element heat flux at which cooling is no longer adequate to prevent element or target failure. Correlations were developed that allow for the CHF power level in an element to be determined as a function of the mass flow rate (which is also dependent on the power under natural connective conditions), the inlet temperature conditions, and the geometry of the elements. A series of experiments was performed in the ACRR that were used as benchmarks for the calculations.

The ACRR was, of course, never brought to a condition where the CHF was attained, which would result in fuel failure. However, nucleate boiling conditions were investigated. The

Figure 3 Technical Area V Layout

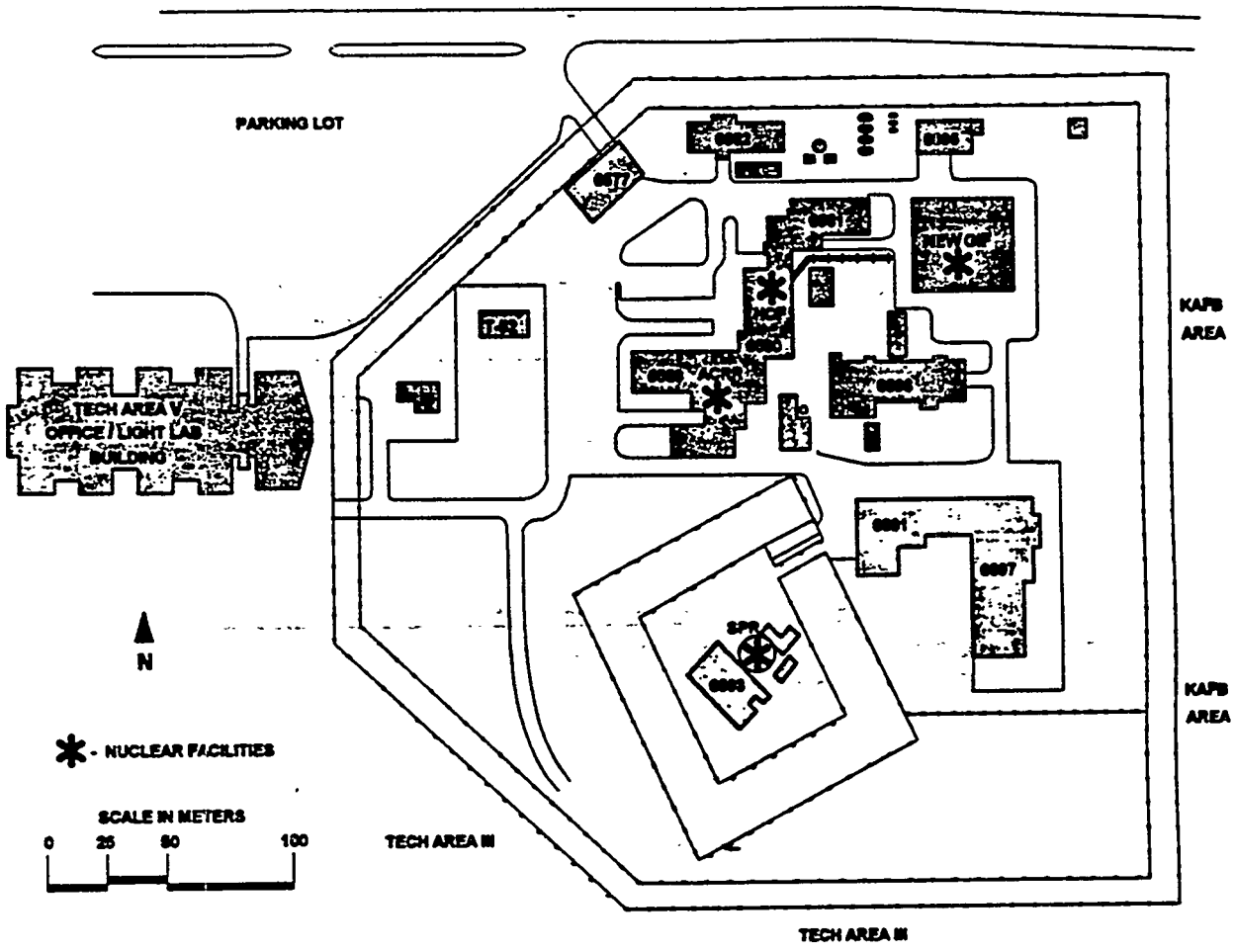


Figure 4 ACRR High Bay Layout

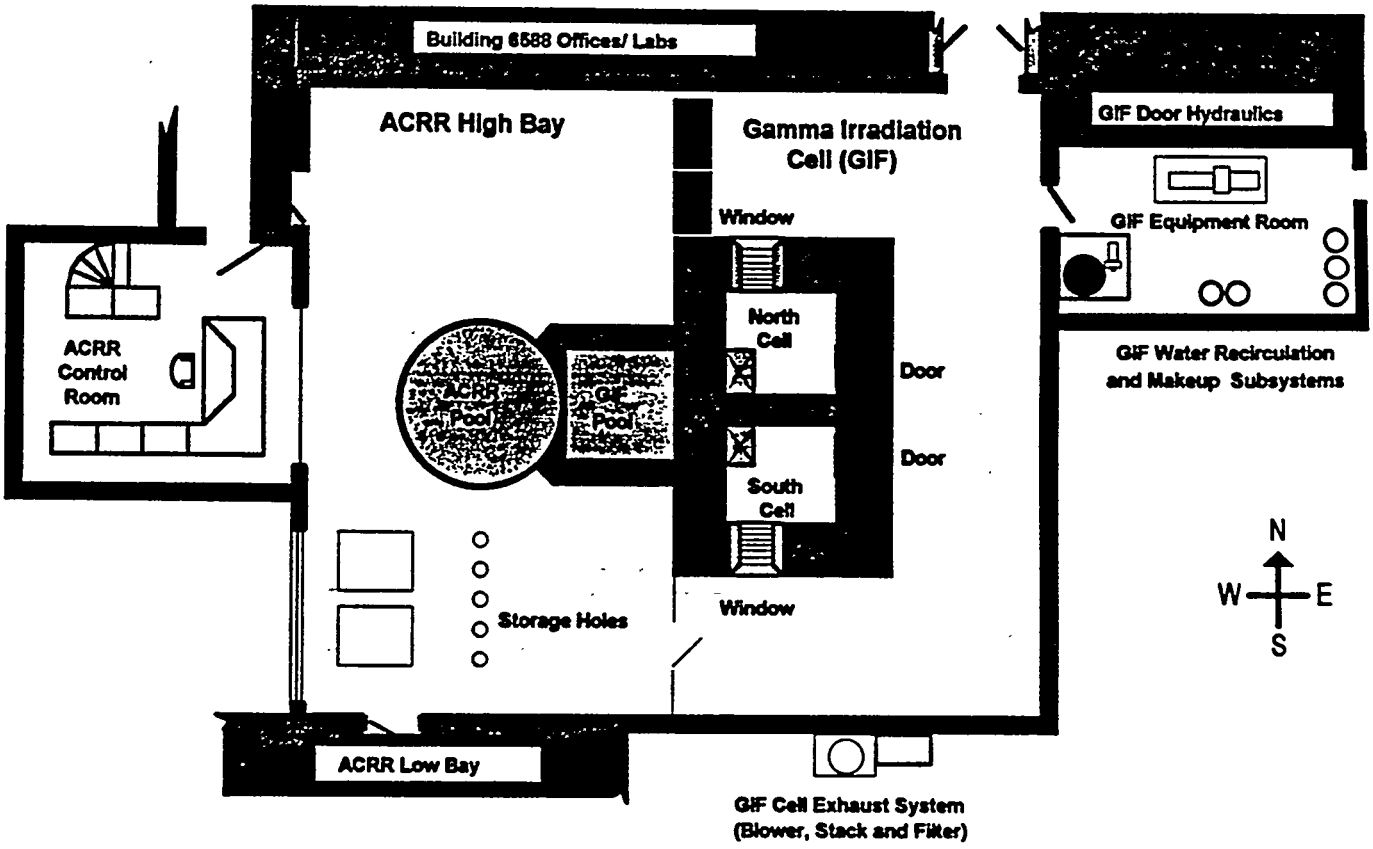
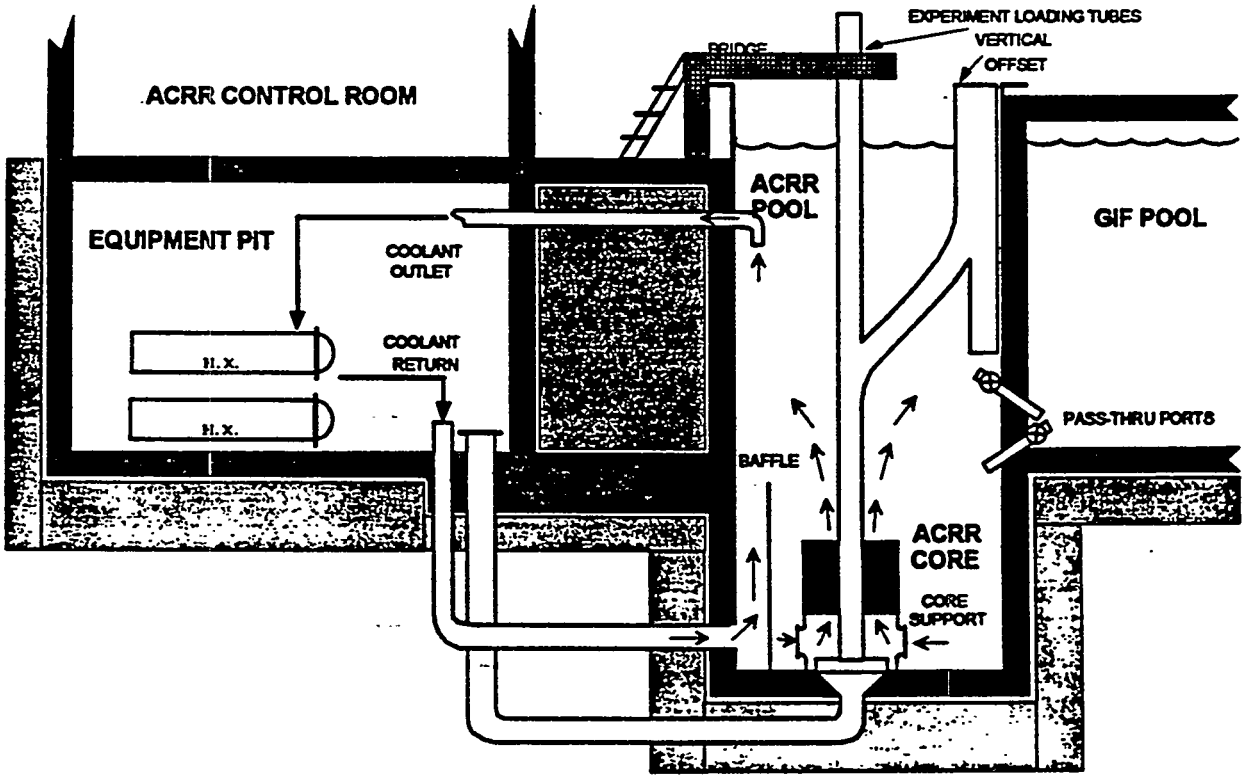


Figure 5 ACRR Reactor Tank and Cooling



experimental results provide assurance that the correlations developed can be used to conservatively predict the CHF condition.

The CHF varies linearly from 2.0 to 1.3 as the inlet temperature varies from 20 to 50 °C at a fuel element power of 27 kW. The minimum CHF ratio is the ratio of the critical heat flux to the greatest heat flux along an element or target.

Since the geometry of the targets is very similar to the fuel element, the CHF correlations were also used to determine the maximum power level attainable for the targets. The results show that for a target power of 21.1 kW, the MCHFR varies linearly from 9.5 to 6.0 as the inlet temperature varies from 20 to 50°C. This indicates that a very large margin exists in the coolability of the targets.

Initial testing will be performed on the ACRR with the targets in place to confirm that the power levels indicated can be achieved. The CHF analysis indicates that the proposed power level requirements can be easily met. However, the fuel coating in the targets must also be subjected to these power levels on an experimental basis to confirm its robustness.

Annular Core Research Reactor Characteristics and Components

The Annular Core Research Reactor is undermoderated by design to provide enhanced energy deposition in its experiment cavities. A benefit of this design for radioisotope production is that the ratio of the average power per unit mass of uranium-235 in the target is factor of five greater than in the fuel. As a consequence, the ACRR can be as effective as a thermal reactor of several times its power rating while producing much less waste in spent fuel. Key features of the ACRR facility are outlined below.

- Reactor Type
  - Open Pool Reactor
  - Epi-Thermal Flux
  - Natural Convection Core Cooling

- Fuel Type
  - 35% Enriched UO_2-BeO Segmented Disks
  - Fuel Disks Stacked in Niobium Cups
  - Niobium Cups Placed in Stainless Steel Tubes (Clad) to Form Fuel Elements

- Core Configuration
  - 236 Elements in Current Configuration
  - Triangular Pitch
  - Nickel/Water Reflected

- Power
  - Steady-State Mode -- 2-4 MW
  - Pulse Mode - 10 ms, 300 MJ
  - Specific Power in Target 1 kW/g(U-235)
  - Specific Power in Reactor Fuel 200W/g(U-235)

- Neutronic Features
  - Large Volume Thermal Flux Trap in the Central Core Region
  - Xenon Reactivity Effects Small

- Peripheral Attachments
  - Central Cavity
  - Fueled Ring External (FREC) Cavities
  - Neutron Radiography Tube

- Dimensions and Measures
  - Current Core Fuel Loading - 23 kg U-235, ~100 g U-235 per Element
  - Fuel Element Dimensions -- 3.75 cm Dia. x 52.3 cm Length
  - Core Dimensions -- ~90 cm Dia. x 52.3 cm Length

- Fuel Heating Characteristics
  - at 2 MW, Average Element Power = 8.5 kW, Peak = 11.0 kW
  - at 4.75 MW, Peak Element Power = 26 kW, Peak Fuel Temperature = 1500°C

ACRR Tank and Adjacent GIF Pool

The ACRR tank is a stainless steel cylinder about 3 m in diameter and 10 m in depth. Penetrations to the tank include a pool coolant outlet line, two pool coolant inlet lines, and two pass-through ports to the adjacent Gamma Irradiation Facility (GIF) pool (shown above in Figure 5).

The GIF pool is a rectangular stainless steel pool that has a portion open to the high bay, and a portion covered by heavily shielded dual confinement boxes. The GIF pool is 2.8 m in width, 5 m in length and 5 m in depth. The GIF is currently used for gamma-irradiation experiments with high-activity cobalt and cesium sources. However, construction on a new and separate GIF facility located in Area-V complex is scheduled to begin in July 1995. The GIF sources are scheduled to be moved to this new facility before isotope production begins. The GIF pool will be used in the isotope production program to transfer irradiated targets from the ACRR tank to the transfer cask and movement to the Hot Cell Facility. The GIF has its own separate cleanup loop to control contamination and water purity.

ACRR Cooling System

The ACRR core is cooled by natural convection. Although provisions were made during the construction of the ACRR tank to have the potential for forced cooling, (e.g., by using the bottom coolant return line), this feature has never been used, nor will it be needed for the isotope production program. The line for forced cooling is blanked off in the equipment pit. The pool is currently cooled by a 2 MW heat exchanger and a 900 GPM cooling pump. The secondary side of the heat exchanger is cooled by a cooling tower located outside and to the west of the high bay. At 2 MW the pool temperature can be kept near ambient conditions of ~20°C. The ACRR pool has its own cleanup loop for contamination control and water purity.

The cooling capacity for the ACRR will be upgraded for the molybdenum-99 program to two redundant 4 MW heat exchangers each with its own cooling pump, and redundant cooling towers rated at the same capacity.

ACRR Ventilation System

The ACRR high bay, central and FREC cavities, and GIF cells each maintains its own separate ventilation system. The high bay ventilation flow is 8,500 cfm through a HEPA filter bank. This assures that the high bay will maintain a negative pressure relative to the outside environment.

ACRR Control System

The current location of the ACRR control room is shown in Figure 4. A new computer-based control console has been designed and constructed in a room that is located approximately 30 feet west of the current control room. The new control console is undergoing modifications that would preclude pulsing if approval is obtained for isotope production. Use of this new control room is awaiting final checkout and approval by the Sandia safety committees and DOE.

The control system in the isotope production configuration will include eight fuel followed boron carbide loaded rods and three boron carbide loaded rods.

TARGET SYSTEMS

Target Design

The Cintichem target design and fabrication process will be initially employed. As shown in Figure 6, each target is constructed of 304 stainless steel tubing; ~18 in. long and 1-1/4 in. in outer diameter. Each target is fabricated by electroplating a UO_2 layer onto the inside surface of a stainless steel cylinder that welded closed at the bottom and top. The bottom and top plugs are designed for easy installation and removal from the reactor core. The top plug also includes a thin diaphragm that provides absolute closure of the tube contents until it is punctured in the fission product extraction process.

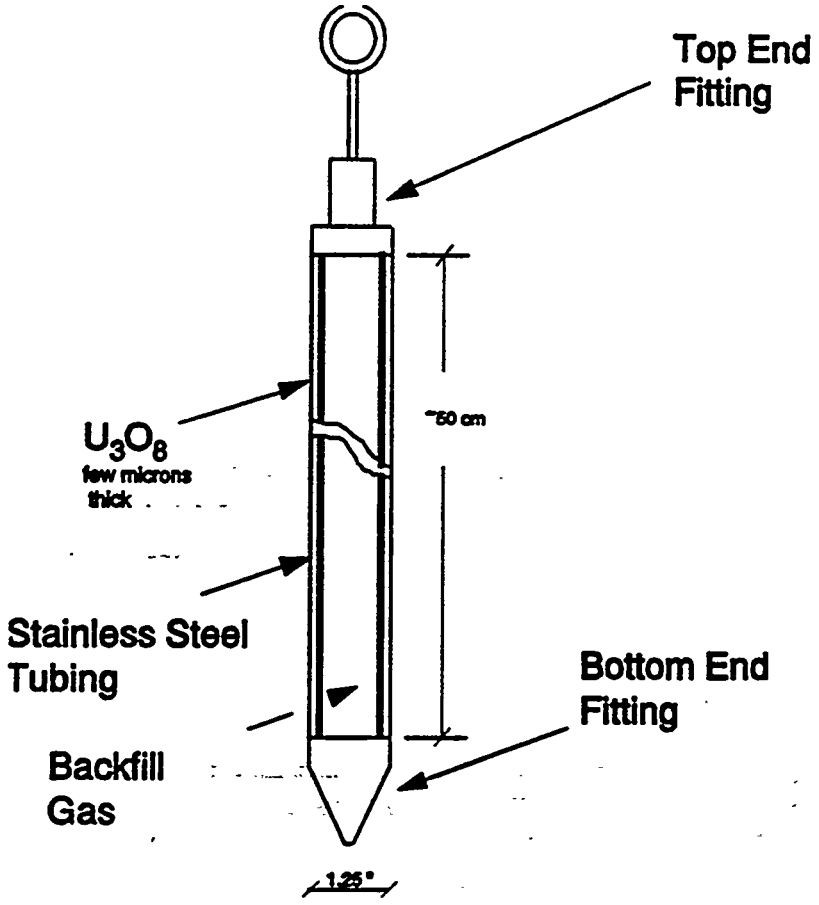
The target cylinder is evacuated and back-filled with helium gas before the top fitting is capped. Each target is loaded with 10 to 20 grams of 93 percent enriched uranium.

Although not necessarily optimum for the ACRR neutronic characteristics, the target design used in the FDA-approved Cintichem process is to be used for the production of molybdenum-99. The target can be represented, for calculation, as a hollow closed-end 0.076 cm-wall stainless-steel pipe with a thin layer of U_3O_8 (93% enriched) on the inside surface. For the purpose of these calculations, the target length is assumed to be 50 cm and the outer diameter is assumed to be 3.175 cm. The ^{235}U loading can vary but will be assumed for this study to be 20 g. Loadings as high as 25 g are achievable using the current plating process. Note that the diameter and length of the target are very similar to the ACRR fuel element design. Although this does not necessarily suggest that the targets will be optimally coupled neutronically to the core, it does facilitate the heat transfer analyses and critical heat flux calculations.

Target Analyses

Targets used in the production of molybdenum-99 must be irradiated at 400 kW total, for 7-days, 24 hours/day, to meet the U.S. demand. Not only must the reactor be capable of producing a large enough neutron flux, so that the required fission power can be produced, but target coolability must also be maintained to assure containment of the target material. This section will present both the neutronic and thermodynamic analyses performed to date for the Cintichem target/ACRR combination. The results will show that enough flexibility exists in the reactor, and that there exist enough margin in the results, to assure that the goal of meeting the U.S. demand can be achieved without upgrading the reactor significantly.

Figure 6 Target Design



Analytical Techniques for Target Configurations

Analyses were performed using the Monte Carlo code MCNP (Briemeister, J. F. 1986) with ENDF/B-V cross sections (Kinsey, R. 1979). Although there exists a number of neutronic codes that perform deterministic and Monte Carlo calculations, MCNP was chosen as the code to perform the analyses for a variety of reasons. Some of these reasons are as follows: (1) the version and cross-section sets used have been utilized for other projects in Area-V, and have produced results that allow for a high degree of confidence in the code; (2) ease of use; (3) geometries can be modeled in three dimensions; (4) the geometry package allows for rapid checking of the model; (5) the run times are relatively fast using current workstation environments; and (6) volume detectors can be easily modeled. Two unique features of the code are (1) it uses continuous energy cross sections, and (2) the scattering kernel at different moderator temperatures can be uniquely chosen for a calculation.

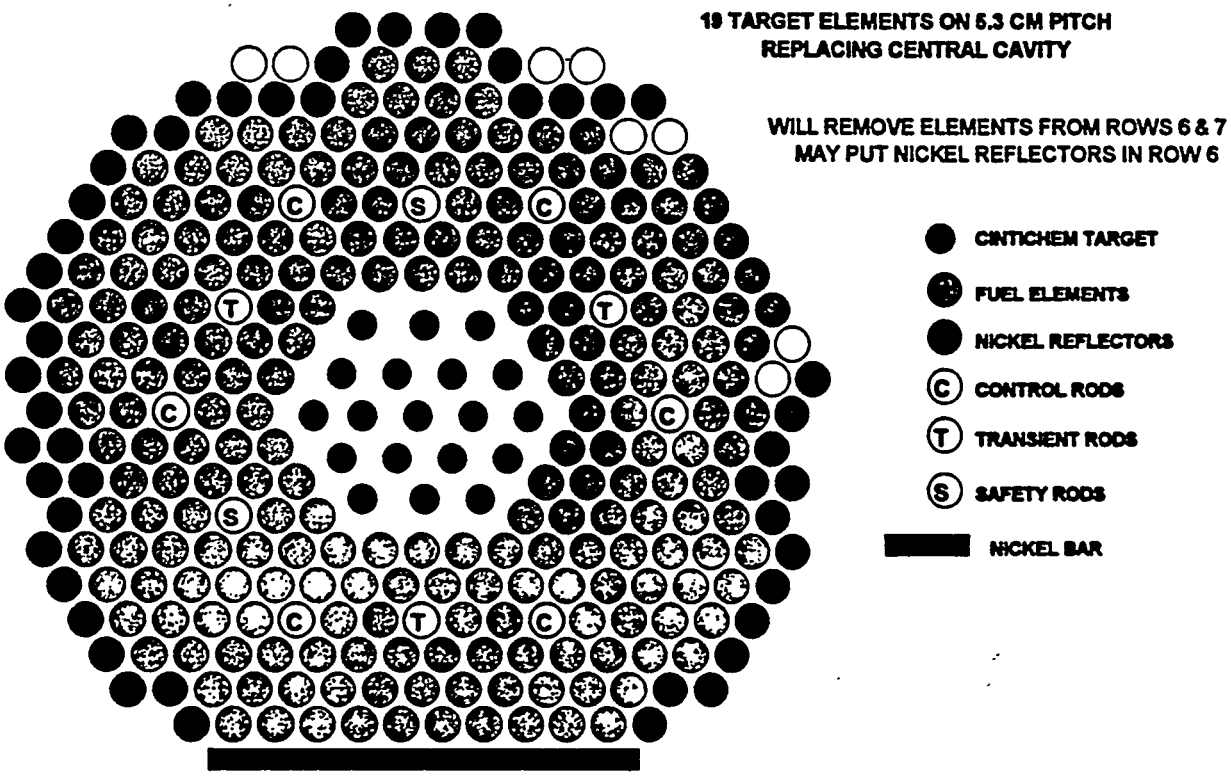
Hundreds of MCNP calculations were run to optimize the target/core configuration for efficient operating conditions and to assure that the U.S. demand for molybdenum-99 can be met using the Cintichem targets. Using the reference target design as a fixed constraint in the study, the number and location of the targets and the number and configuration of the ACRR fuel elements were varied to determine the most appropriate configurations. As the study progressed, two core/target configurations emerged as the most appropriate to pursue because of their simplicity and economic advantages. These configurations are presented below.

Target Configuration Analyses

Homogenized region as well as discrete geometric representation of the target and core geometry were employed. Independent models and persons performed the calculations to verify the results. The discrete representation of the ACRR standard core, without a FREC or the radiography tube, is shown in Figure 7. The results from this model generally gave target powers a few percent lower than those obtained using homogenized region representation since they better accounted for local flux depression due to target neutron absorption. Both cavity and grid target irradiations were examined for targets.

Flux trapping is effective in the in ACRR. The potential for increases in thermal flux and target fission density by locally increasing the moderator (water)-to-target fuel ratio through target modification is clearly evident. Three possible configurations of the core: (1) the standard ACRR core with the dry central cavity and its stainless steel liner in place; (2) the same as (1) with the cavity flooded; and (3) with the cavity liner removed (and obviously the center region flooded).

Figure 7 Standard ACRR Core Configuration With 236 Fuel Elements



Target Positioning and Performance

The results of three case studies are presented below. Case 1, targets are simply placed in the ACRR fuel element locations; Case 2, targets are placed in the central cavity with the cavity flooded; and Case 3, targets are place in the central cavity region with the cavity liner removed.

Case 1. Calculations indicate that if targets were simply placed in grid locations (i.e. ACRR fuel element locations) without any attempt to further optimize moderator or moderator-to-fuel ratios, target powers ranging from 4 to 8 kW could be achieved with 2-MW ACRR operation. The lower value corresponds to the outermost grid locations while the higher value corresponds to inner grid rows. Higher target powers could also be achieved by removing some fuel elements in the vicinity of the targets, to locally increase the moderator-to-fuel ratio and hence the local thermal-flux component. Although plausible, this configuration would require ~50 targets to be processed per week in order to meet the U.S. demand.

Case 2. Calculations indicate that for targets placed in the central cavity, with the cavity flooded with water and the cavity liner in place, target powers of 10.5 kW each can be attained for a 2-MW ACRR operation. Up to 25 targets can be placed in this configuration resulting in ~260 kW and would provide 65% of the U.S. demand. Since the cavity is normally dry, a cooling system would have to be engineered to provide adequate cooling to the targets. The amount of cooling that can be obtained by connective flow from the pool through the cavity is not known, but has been estimated to be greater than 200 kW.

Case 3. Results indicate that for the 129 element core configuration, target loadings of 19 to 37 in the central region of the core with the cavity liner removed, will meet the U.S. demand for molybdenum-99 with relatively minor modifications to the core configuration. With the 19 target configuration as the baseline, the average target power will be 21.1 kW and the core power 1.92 MW. A sufficient amount of margin and flexibility exists in the core to allow for a high degree of confidence that the U.S. demand can be met. The actual target fuel configuration to be employed depends on the production goal (fraction of U.S. demand) at any given time. However, the target/core configuration candidates chosen are robust enough to exceed 100% of current U.S. molybdenum-99 market needs.

Target Replacement

Targets will be removed from the reactor target grid manually using 30-foot long target handling tools and will be moved to the GIF pool via an underwater portal. Each target will be transferred into a shielded cask underwater then transported to the Hot Cell Facility. New targets will be inserted into the target grid using the same tools.

The molybdenum-99 targets, having been irradiated within the reactor at a power level of 20 kW for one week, will be removed only upon shutdown of the reactor. The total time between reactor shutdown for target extraction and shipment of the pharmaceutical product is anticipated to be between 6 and 12 hours which accounts for both processing time and any target decay necessary before processing is initiated.

After shutdown, a transport cask will be lowered into the GIF pool, opened, and readied for receipt of the element. It is anticipated that the operational time to place and prepare the cask within the GIF pool will be approximately 30 minutes. At that time, the fission product activity will result in 100 watts beta activity and 90 watts gamma activity, sufficiently low to prevent heat generated optical distortion within the pool. The molybdenum-99 targets will then be pulled from the reactor, transferred to the GIF pool through the fuel handling ports, and placed immediately within the transport cask. For each target removed, a new target will be inserted in the reactor.

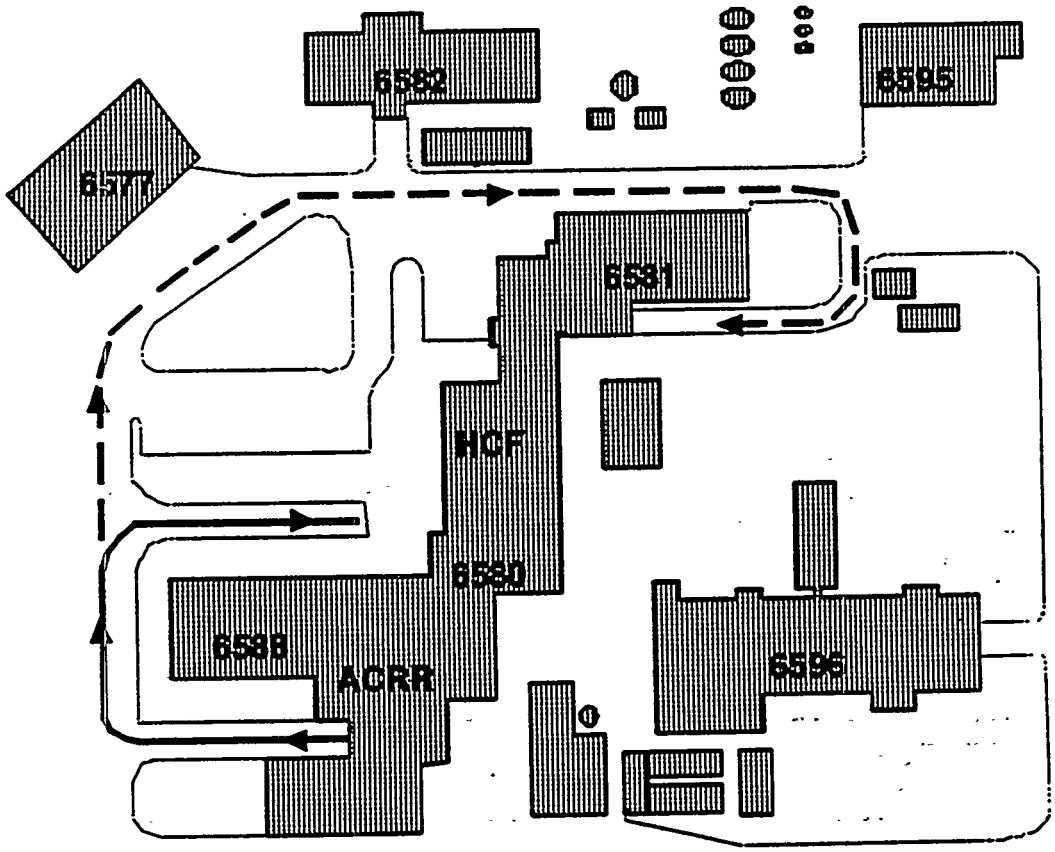
Target Transfer to Hot Cell Facility

This section describes the transfer of the target from the reactor facility to the hot cell facility, the initial cask design assumptions for such a transfer, the mobile transporter assumptions, the dose estimate to both workers and the environment, and the expected operations within the HCF. Dose rates, heat generation rates, and shielding requirements have been calculated based upon operation of the target elements at 20 kW for 7 days prior to their removal from the core. The targets are very radioactive and must be shielded from operational personnel during target movement. That shielding is provided by the pool water initially, then by the transfer cask, and finally by the shielding walls of Zone 2A within the Hot Cell Facility (HCF).

After loading the transport cask with the required number of targets (one for 25% of U.S. needs, four for 100% of U.S. needs), the cask will be closed and removed from the GIF pool. A drain hose will be attached to the cask and the system purged of the majority of GIF pool water. The system will be checked for bulk leak-tightness, and then placed within the transport cask overpack. The overpack provides both an impact mitigator and additional personnel shielding for the transportation between the reactor and hot cell locations. This additional shielding will assure that the dose on contact with the overpack is less than 1 mr/hr. Once the transfer cask is installed in the overpack, the operational crew returns to the operation of the reactor and the transfer cask awaits the arrival of the hot cell crew.

The hot cell crew will move the targets to the hot cell utilizing a mobile transporter. The transporter will exit the reactor facility through an air lock, which will permit the continued operation of the reactor, and proceed down the ramp of the Hot Cell Facility (HCF) (see Figure 8). The transporter will enter the HCF through the rollup door at the west end of the

Figure 8 Transfer Route for Irradiated Targets within TA-V



HCF, then proceed to the HCF transporter airlock. Once through the airlock, the mobile transporter will move the transport cask with overpack to the far north end of the HCF where the transfer cask will be removed from the overpack and placed within the shielded region of Zone 2A, as shown in Figure 9.

The cask is then moved below one of the dedicated processing box designed to conduct the initial molybdenum-99 extraction from the bulk fission products. The molybdenum-99 extraction process box is open to bring in one or more of the targets. Although the process box and transfer cask will be brought into contact, they will not be sealed during this transfer permitting the positive flow of air to maintain any box contamination from transferring to the cask. If parallel processing lines are operated, the transfer cask is moved below a second processing box and the remaining targets are moved from the cask to the processing box. Once emptied of the targets, the transfer cask is removed from Zone 2A, inserted into its overpack, and returned to the reactor facility to await the next day's movement of targets.

SPR III REACTOR SYSTEMS

The Sandia Pulse Reactor III (SPR III) is an unmoderated, fast burst reactor capable of pulse and steady-state operation. The reactor is designed to produce a neutron spectrum very similar to the fission spectrum. The primary experiment chamber is a large central cavity that extends through the core. Experiments may also be placed around the reactor core. SPR III is used primarily for high neutron fluence or pulsed, high dose testing of electronic devices.

Design

SPR III is a fast burst reactor, designed and constructed by Sandia National Laboratories. The SPR III core consists of 18 fuel plates mechanically fastened into two halves of nine plates each. The fuel is 93 percent 235-U alloyed with 10 weight percent molybdenum to ensure phase stabilization. See Figure 10. The nine upper plates are held stationary by the core support structure, while the nine lower plates are attached to an electromechanical drive mechanism.

Three reflector control devices are used to control the reactor, while a fourth is the burst element. The burst element is electromagnetically driven to achieve the high rates of reactivity insertion needed for pulse reproducibility. The primary shutdown mechanism in the pulse mode is the inherent negative temperature coefficient of reactivity caused by the thermal expansion of the fuel. In operation, SPR III is covered by an aluminum shroud coated with boron-10 that decouples the core from backscattered neutrons.

Figure 9 Hot Cell Facility for Processing ^{99}Mo Targets

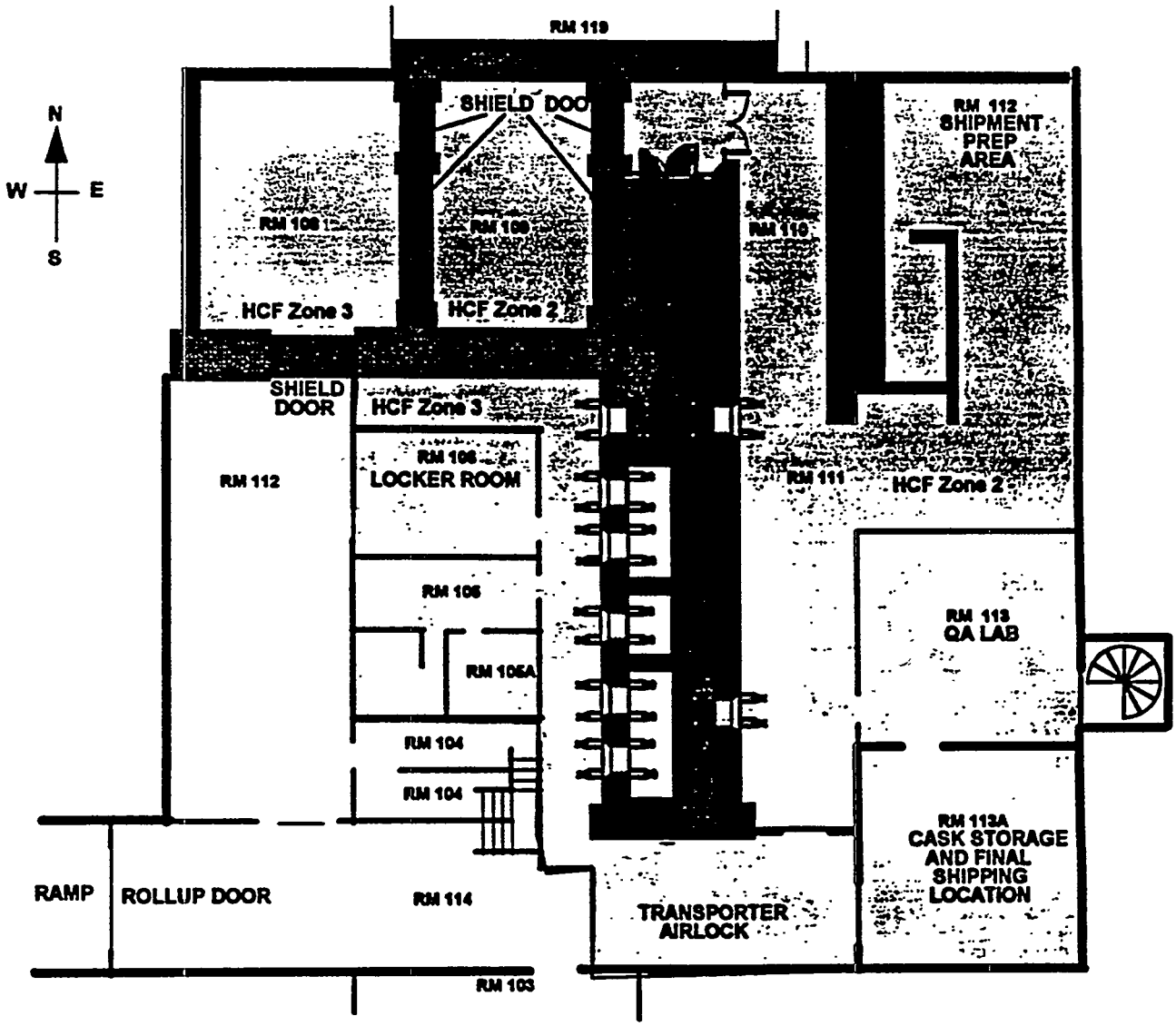
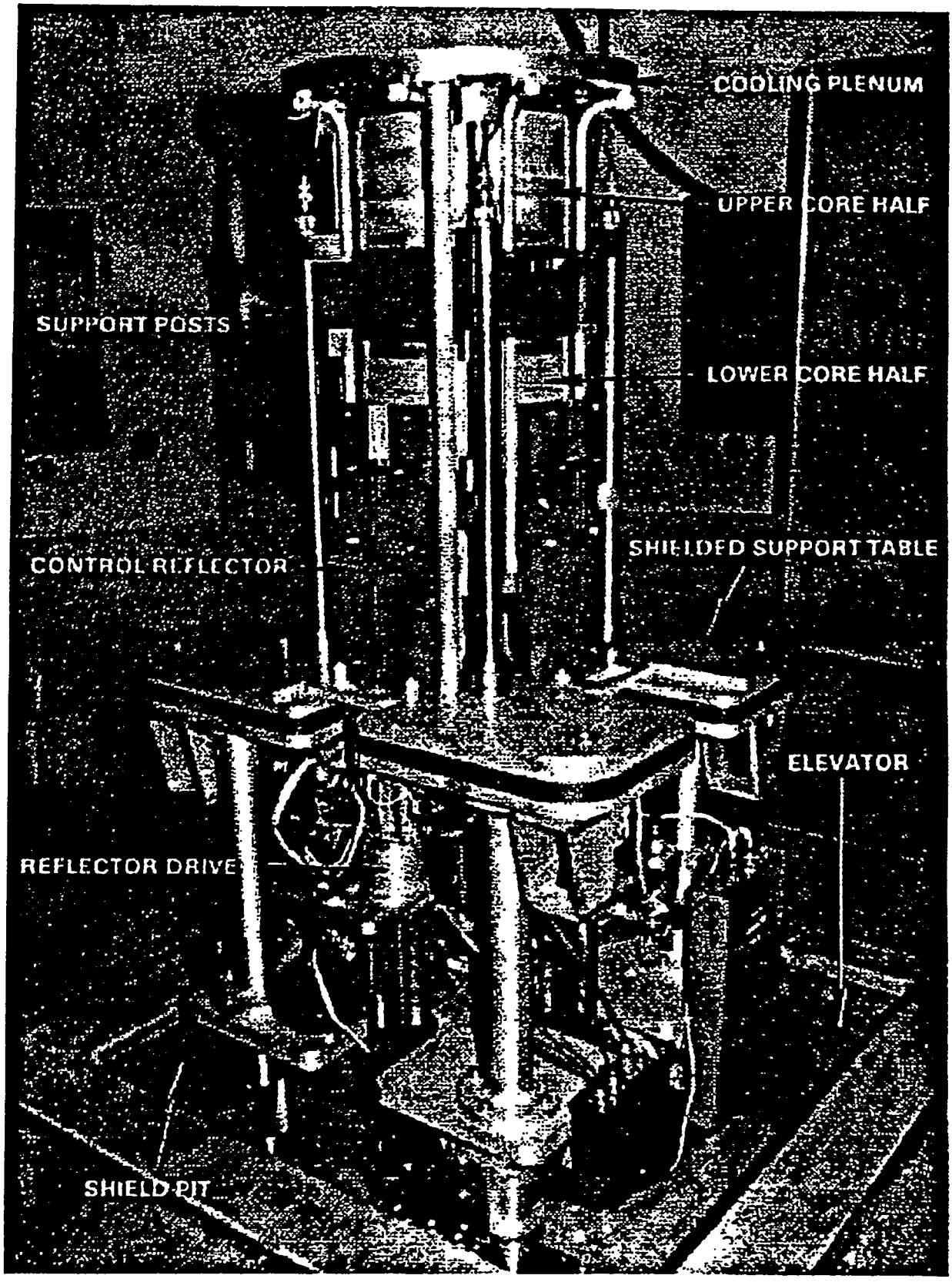


Figure 10 SPR III Reactor Without Shroud



A 17-cm diameter central cavity extending through the core is the primary experiment cavity of SPR III. (A modernized version of SPR III, SPR III M, featuring a 19-cm diameter central cavity should be available in early 1996.) Experiments may also be placed around the reactor. The reactor room has two 22.9-cm diameter beam ports, which also have 10.2-cm diameter removable plugs that allow experiments to be placed at a greater distance from the reactor. The reactor is mounted on an elevator that lowers it into a shielded pit. The reactor room can be accessed 30 minutes after an operation.

To minimize personnel radiation exposure, SPR III has the capability of remotely controlled experiment placement and retrieval. Experiments may be loaded into the experiment stand tube with a robotic arm located in an area adjacent to the reactor room. The experiment stand is set on a cart that runs on tracks into the reactor room. To load the tube into the reactor central annulus, the cart is remotely driven into position over the reactor pit and the reactor is raised, lifting the experiment stand off the cart. The cart is then withdrawn from the room to avoid its activation. Experiments are removed from SPR III by reversing this procedure.

Steady-State and Pulse Operation

SPR III can operate in the steady-state mode with steady-state operations normally limited to a power of 14 kW. In the pulse mode, pulse size can be determined very accurately by preselecting the total reactivity of the core. A "delayed tail" pulse capability is also available. Delayed tail essentially Delayed tail operation produces a square wave pulse.

SPR III Neutron Spectra

SPR III reactor spectra have been thoroughly characterized (Kelly, et al., 1993; Kelly and Vehar, 1987). The SPR III free-field neutron spectrum has fewer than 0.2% of its neutrons below 10 keV. The hard neutron spectrum allows the production of radioisotopes via the (n,p), (n,α), and (n,2n) reactions with virtually no interference from thermal capture reactions. In addition, excess burnup of enriched targets because of thermal neutron capture is virtually eliminated in this environment.

The SPR III neutron spectrum can also be tailored to provide a wide range of neutron spectra for experiments. Neutron spectra for several reactor environments are available from Sandia in the standard 640 group SAND II group structure.(Berg J., and W. M. McElroy 1967) These can be supplied to SPR III users in ASCII format on floppy disks upon request. In addition Sandia has compiled a compendium of recommended neutron activation cross sections. Rationale for the choice of the cross sections is presented in the references(Griffin, et al., 1993; Griffin, et al., 1992).

Experimental and Research Facilities

Reactor experiment and research facilities take the form of loops, rabbit tubes, and dry cavities to provide access to excess neutrons produced by the ACRR. The Radiation Metrology Laboratory provides the capability to characterize radioactive samples and develop new systems and methods in support of experimenters and researchers. Technical Area V has additional buildings and laboratories where research can be performed with moderate quantities of radioactive materials.

SANDIA RADIOCHEMICAL PROCESSING EQUIPMENT AND FACILITIES

Overview

Molybdenum is chemically extracted from the fission products of the target fuel in a Hot Cell facility. Although other isotopes of molybdenum are present in the fission products, molybdenum-99 represents more than 14% of the total molybdenum present in the fission product. After having run for 7 days at 20 kW, each target, will have 12 mg of molybdenum, of which 1.73 grams will be molybdenum-99. That 1.73 grams represents 830 curies. With extraction efficiencies and decay, 600 curies (140 six-day curies) will be delivered to the pharmaceutical companies per target.

The HCF is in the basement of building 6580 located within Sandia National Laboratories's Technical Area V on Kirtland Air Force Base. The facility has been used in the past for experimental preparations as well as post irradiation examinations. Zone 2A of the facility is approved for up to 200,000 curies of activities, and has handled in excess of 100,000 in the recent past. The facility was originally designed as a combined reactor/hot-cell, and has large hydraulically operated doors between numerous regions within the facility. Among these doors are doors between room 112 and room 108, between room 108 and room 109, and between room 109 and Zone 2A housing the bulk of the molybdenum-99 processing line. Differential air pressure is maintained between various regions within the hot cell to assure air flow always occurs from higher zone designation to lower zone designation. Zone 1 is the inside of the dedicated process boxes; Zone 2A is the region between the shielding walls, Zone 2 includes the remaining region inside the airlock located in the entrance ramp; and Zone 3 includes the airlock, west manipulator bay, changing room, and scanning electron microscope areas.

Two Hot cell configuration options are being evaluated for processing of ACRR targets and processing molybdenum-99 and other radioisotopes. The first option involves decontaminating and modifying the present Hot Cell configuration. The second option is to construct a second canyon expressly for isotope production in the Hot Cell facility thus providing backup capability, reserve capacity, and space for research and development

activities. The modifications to the Hot Cell Facility form the critical path to reach full production capability within two years. For this reason and because of cost considerations it may not be feasible to construct the second canyon.

Requirements for Molybdenum-99 Production

The HCF will require significant decontamination and refurbishment to be able to conduct this operation on a routine bases. Modifications will include the removal of the existing legacy waste from Zone 2A; removal of existing steel containment boxes from Zone 2A; rearrangement of Zone 2A closure doors to provide access to room 109; providing ventilation to room 109; providing necessary processing boxes for Zone 2A; rearrangement of several cinder brick walls to provide necessary quality assurance, airlock, and cask storage areas; and providing necessary ventilation modifications to avoid build-up of high activity areas not protected by radiological shielding.

The extraction process for molybdenum-99 is a combined chemical/distillation process in which the noble gasses and iodine are condensed from the target fill gas; the fuel and fission products are dissolved from the inside of the target; chemicals are added to maintain specific fission products in solution; the molybdenum is precipitated, filtered, and cleansed; and finally the precipitated molybdenum is re-dissolved for shipment to the necessary pharmaceutical companies. The extraction process must provide necessary radioisotopes of xenon, iodine, and molybdenum.

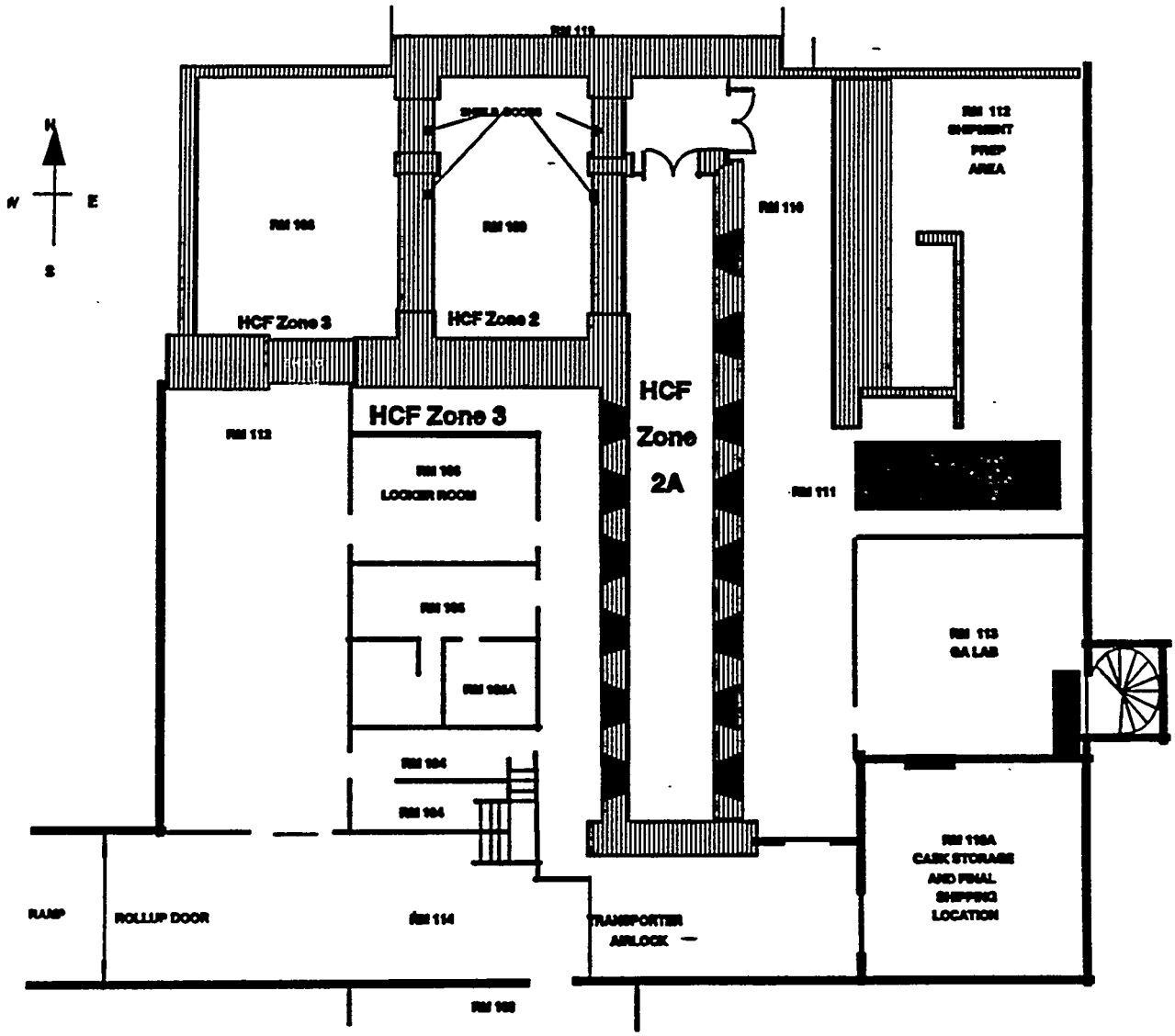
Each target will yield 600 curies of molybdenum, 1,200 curies of iodine and 900 curies of xenon one day after discharge from the reactor. One-half liter of neutralized process liquid is generated per target. This liquid is solidified, allowed to decay, and then shipped to an approved low-level waste site. Although shipments to the disposal site could be made as soon as six months after generation, sufficient storage must exist within the HCF to allow up to two years storage before waste disposal must be initiated.

Up to 20 target's process liquid will be solidified and shipped within one 55-gallon container. If shipped at the end of six months, this container's activity will be 3000 curies, and if delayed for two years this container's activity will be 160 curies. Approved DOT shipping containers must be available for either of these options.

Layout of Hot Cell Facilities

There are two options under consideration for the layout of the Hot Cell Facility. The leading option is shown in Figure 11.

Figure 11 Sandia Hot Cell Facility (HCF) Floorplan



Safety

The Hot Cell Facility must provide adequate space, equipment, shielding, and proper ventilation to perform the work of radioisotope separation safely. Shielding and manipulator stations are shown in the facility layout.

The ventilation and filtration system for the Hot Cell Facility is shown schematically in Figure 12.

Steel Containment Box Lines

A series of redundant steel containment boxes will be assembled in a modular fashion to enhance reliability of production. An option reconfiguration of the HCF will leave the existing steel containment box line in place and add another line. This will assure that additional space is available for production of other radioisotopes and process development activities.

Glove Box Laboratory

Shielded glove boxes and blisters with less shielding than the Hot Cell steel containment box line will be available in the facility for molybdenum-99 production and other activities.

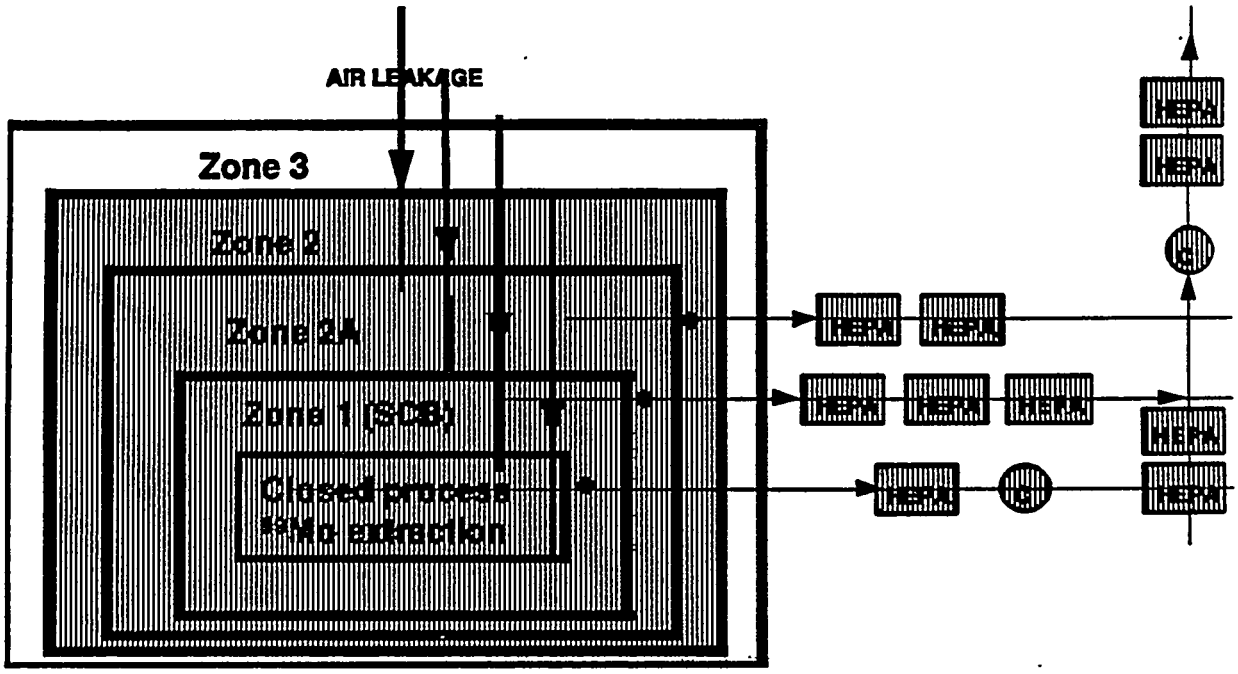
Waste Storage Facility

Two heavily shielded storage rooms are available in Rooms 108 and 109 of the Hot Cell Facility. An automated waste handling system will be used to move waste into, out of, and within the storage areas.

Quality Laboratory

Product quality control will most likely be performed within room 113 of the HCF. This room is within Zone 2 of the HCF, and its use will prevent having to take high activity molybdenum from the HCF. The quality control process involves the extraction of one-to-two micro-liter sample from the 10 cc vial of product. This sample will contain approximately 100 millicuries of molybdenum-99 that will be further diluted to prevent excessive dead-time within the gamma-spectroscopy equipment. By examining the gamma signatures of the sample, the isotopic content of the original vial can be determined, permitting a material survey sheet to be generated that will accompany the shipment to the respective pharmaceutical company.

Figure 12 Hot Cell Facility Ventilation and Filtration System



Materials Survey Sheet

Specification	Mo-99
Half life	66 hrs
Inventory generated in fission target	835 curies
Processing method	dissolution & precipitation
Approximate time to complete processing	1 day
Production capability per target	585 curies (shipment curies)
Product Data Sheet (at shipping time)	
Chemical form	Na_2MoO_4 in dilute NaOH
Concentration	>200 mCi/mL 1200 typical
Specific Activity	> 10^4 Ci/gm

Alternatively diluted samples will be moved to another location within Building 6580 or to Building 6594 for counting.

OTHER POTENTIAL SANDIA CONTRIBUTIONS TO THE NBTF PROGRAM

Advanced Manufacturing

Sandia has expertise in the development of improved manufacturing processes and automation.

Biomedical Engineering

The Sandia a Biomedical Engineering Program that has an active nuclear medicine thrust area. This vehicle can facilitate the establishment of cooperative research projects with NBTF.

Microelectronics

Sandia's expertise in radiation hardened electronics can be accessed to develop durable systems and detectors for accelerator operations and automation of processes.

Automation and Robotics

Sandia National Laboratories has grown to be the leading robotics research and development

effort in the U.S. This growth has been fueled by Sandia's innovative approaches which: (1) focus research and development on problems of critical national concern, such as hazardous waste cleanup and manufacturing; (2) reduce the cost and time of advanced technology development; (3) reduce the time and cost for the insertion of advanced technology into practical systems; (4) vastly increase the accessibility of advanced technologies to operating personnel; (5) improve the speed and quality of operations; (6) improve the safety of potentially hazardous operation; and (7) stress teaming with the university and industrial sectors and with other Federal entities

The Sandia Intelligent Systems and Robotics Center (ISRC) at Sandia National Laboratories is home to the Department of Energy Office of Defense Programs Center of Excellence for Automation and Robotics. Its mission is to integrate intelligence with emerging technology and commercial equipment. Its activities include research, development, and applications. Production, processing, and applications of radioisotopes can benefit from Sandia's expertise in automation and robotics.

The Intelligent Systems and Robotics Center performs research, development, and application of intelligent systems and robotics technology. The ISRC has a staff of more than 130 and has developed one of the largest automation and robotics development laboratories in the country. Areas of expertise include model and sensor based controls, force control, vision systems, real-time sensors, graphical programming, laser mapping, and system integration. Sandia technology is being used in a wide range of applications for a broad customer base that spans waste tank clean-out to eye surgery.

The Manufacturing Systems Department of the ISRC integrates intelligence with emerging technology developed at Sandia, other government laboratories and agencies, universities, and private industry into one-of-a-kind systems to address a wide range of problems within the weapons complex. Systems employ commercial technology as a starting point whenever possible and are developed in close cooperation with the end user. Current activities in the department include plutonium packaging and storage, pit handling and processing, explosive component manufacture, and component cleaning.

A three-stage process is employed to develop application systems. In the first phase a proof on principle and operational development is performed. System requirements are developed and documented with close cooperation between the ISRC and the end user. The user has responsibility for requirements definition, operational procedure development, and interfacing with the site infrastructure (ES&H, security and safeguards, facilities, operations, etc.) Safety and operational reviews are initiated and any special nuclear material handling requirements are identified. The automated process is identified and developed to meet specifications. The end user plays a key review and approval role in the development process. Equipment is procured, hardware and software systems are integrated and developed, and the system operation is demonstrated. Extensive hardware and software

testing is performed.

In the second phase the prototype system is transferred to the user site and the user assumes responsibility for system operation and maintenance. Any unfinished safety and operational reviews are completed. The system is modified and upgraded as necessary to meet any additional user specifications.

In the third phase the hot-site qualified system is installed at its operational location and approval for operation is obtained. Additional development support is provided by Sandia as needed.

An example of an application useful to NBTF is the Automated Glovebox System. The automated Glovebox Bagout (AGB) has provided the basis for the development of other automated plutonium handling projects. The focus of activities is in two directions: automated systems which process material out of glovebox lines and automated systems which perform in-glovebox operations.

In partnership with Los Alamos National Laboratory, the development of an Automated Glovebox Can-Out (AGC) is underway. This system will process plutonium metal and oxide out of a glovebox line for long-term storage. An automated system to process larger items out of plutonium lines into drums has been proposed. It is possible to integrate AGB, AGC, and drum-out operations into a single area to support waste acceptance and packaging for ultimate disposal.

A close collaboration with the plutonium processing personnel in TA-55 at Los Alamos National Laboratory is being used to develop these systems. Production personnel, including the technicians that perform the operations, have been intimately involved in the specification of requirements and procedures, development and review of system concepts and designs, and identification of needs for future applications. The ultimate goal is to implement automated systems the remove operators from hazardous conditions while maintaining and/or increasing the capability and productivity of the facility.

Materials Development and Target Designs

Sandia's expertise in materials and accelerator target design can support NBTF activities.

Test Facilities

Sandia's testing facilities such as the Electron Beam High-Energy Heat Deposition Facility, that is used to test fusion reactor plasma-facing components, can be used to support target characterization and other NBTF and production facility needs.

Support Facilities

Sandia is completing an 83,000 sq-ft Technology Support Center (Building 6585) adjacent to Technical Area V, containing office, light laboratory, and conference space, that will be ready for occupancy in the Summer of 1995. The building will provide office space for visiting scientists, a 165 seat auditorium, a 40 person and two 25 person conference rooms. In addition the Sandia Technology Transfer Center, Building 825, offers a 500 seat auditorium for larger gatherings.

References

Berg, J., and W. M. McElroy 1967, A Computer-Automated Iterative Method for Neutron Flux and Spectra Determination by Foil Activation, Atomic International, Tech. Rep. No. AFWL-TR-67-41, September 1967

Briemeister, J. F. 1986, MCNP - A General Purpose Monte Carlo Code for Neutron and Photon Transport, LA-7396-M, Rev. 2, Los Alamos National Laboratory, 1986.

Griffin, P. J, J. G. Kelly, and T. F. Luera 1990, Effect of ENDF/B-VI Cross Sections on Neutron Dosimetry, Seventh ASTM-EURATOM Symposium on Reactor Dosimetry, Strasbourg, France, Aug. 1990.

Griffin, P. J, J. G. Kelly, T. F. Luera, and J. VanDenburg 1993, SNL RML Recommended Dosimetry Cross Section Compendium, SAND92-0094, Nov. 1993.

Kelly, J. G., P. J. Griffin, D. C. Raupach, T. H. Daubenspect, J. S. Bennion, and D. L. Newell 1993, Interlaboratory Verification of Neutron Spectra Used for the Testing of Electronic Parts, *IEEE Trans. Nucl. Sci., Vol. NS-40, No. 6,* Dec. 1993.

Kelly, J. G. 1987, Neutron Spectrum Adjustment with SANDII Using Arbitrary Trial Functions, Proceedings of the Sixth ASTM-EURATOM Conference, Jackson Hole, WY (1987).

Kinsey, R. 1979, Editor, ENDF-102, Data Formats and Procedures for the Evaluated Nuclear Data File, ENDF, BNL-NCS-50496 (ENDF-102) 2nd Edition (ENDF/B-V), October 1979.

Rau, D. B. and M. S. El Genk 1994, Critical Heat Flux Predictions for Sandia ACRR, SAND 90-7089, Sandia National Laboratories, August 1994.

APPENDIX VII

UNIVERSITY OF NEW MEXICO FACILITIES AND PROGRAMS SUPPORTING THE NATIONAL BIOMEDICAL TRACER FACILITY

Background

The participation by the University of New Mexico (UNM) in this NBTF proposal is a joint and dedicated effort by investigators from the Colleges of Pharmacy and Engineering, augmented with expertise from other academic and research disciplines. This dedication is underscored by the leadership of UNM in the Nuclear Medicine Consortium of New Mexico (NMCNM) which is committed to enhance the future of nuclear medicine nationwide.

UNM has long recognized the importance of nuclear medicine and the need to re-establish the leadership of the U.S. scientific community in nuclear medicine and its supporting disciplines. To this end, UNM has established a strong education and research cross-disciplinary alliance. The alliance serves as the center for education and research to support specialized education in all aspects of radiopharmaceutical and nuclear medicine sciences and technology required by the nuclear medicine profession. In addition, the alliance has created a national focus for the much needed training and education of a new generation of students in nuclear medicine and radiopharmaceutical sciences. The alliance fosters education, research, and technology transfer in:

- Production, separation, and purification of radionuclides for scientific and nuclear medicine communities;
- Development of techniques for radiotracer synthesis and application;
- Radiation protection and safety;
- Waste management and reduction and environmental remediation; and
- Medical imaging.

The value of education and training in these fields and the crucial needs in these areas are well established. According to the National Academy of Sciences, the nation faces a severe shortage of adequately trained people to meet the national needs for several sectors of medicine, science, and technology, inclusive of those listed above.

This alliance of the Colleges of Pharmacy and Engineering at UNM draws on the expertise in production of radioisotopes based on accelerator and reactor technologies, production of radiopharmaceuticals, good manufacturing practice, medicinal chemistry and

radiopharmaceutical chemistry, health and radiological physics, radiation dosimetry, waste management and environmentally related sciences, and medical imaging. Experts in these fields are drawn from full-time and adjunct faculty from Colleges of Pharmacy, Engineering, Arts and Sciences, the School of Medicine, and Sandia and Los Alamos National Laboratories.

Functional Structure of the UNM Research Alliance

The UNM cross-disciplinary alliance can best be described in terms of its strengths in education, research, and technology transfer. These functional areas are described below.

Education

Both the Colleges of Pharmacy and Engineering have dedicated undergraduate and graduate programs in radiopharmacy, medicinal chemistry, toxicology, radiological physics and radiation dosimetry, shielding analysis, and radioactive waste management. These colleges have formed a cross-disciplinary system in which the faculty have joint appointments and students can learn from a variety of courses across these diverse fields in support of their degree programs.

> ***One educational goal of this alliance is to train engineers, pharmacists, and scientists and deliver well-informed graduates to American industry. This is extremely crucial for the technological leadership of the United States, which has been challenged and, in some areas, surpassed by foreign competition.***

The alliance has also developed a program to train nuclear medicine professionals in other countries through short and advanced training programs. These courses are tailored to help local hospitals prepare patient dosages and interpret the results obtained from nuclear medicine practice. In addition, an exchange program is being established to facilitate sharing of expertise and facilities by the faculty and students from U.S. and other countries.

In addition to its internationally recognized faculty members, UNM has managed to enhance the quality of its programs through the addition of several volunteer faculty from national laboratories, other academic institutions, the National Institute of Health, and private industry. This extension has allowed students to have access to the very best and current knowledge in both education and research.

UNM also recognizes that students need practical training. To this end, active research programs have been fostered and developed with Sandia and Los Alamos National

Laboratories, Syncor International Corporation, and the Inhalation Toxicology Institute. UNM also believes that being an integral part of the NBTF Association will only enhance this objective. The participation of UNM in the NBTF Association at all levels of administrative, education, and research will undoubtedly create a strong international program in nuclear medicine for the Southwest region of the United States.

College of Pharmacy. The College of Pharmacy has one of the most highly regarded educational programs for nuclear pharmacy and the radiopharmaceutical sciences in the country. The program has been educating professionals since 1972, and is one of the oldest programs in the country. The faculty not only provide didactic instruction but also practical training through a full-function dispensing radiopharmacy.

Radiopharmaceutical and Medicinal Chemistry. Nuclear medicine is currently facing a shortage of organic and inorganic chemists and nuclear pharmacists who also have advanced training in the radiopharmaceutical sciences. There is well-established recognition that radiopharmaceutical chemists with pharmaceutical practice are in short supply. Such personnel are needed to develop new pharmaceuticals and to supervise the routine production and quality control of radiopharmaceuticals. The College of Pharmacy has also long recognized the need to train radiopharmacists and radiopharmaceutical chemists, and the importance of this training to the welfare of nuclear medicine. Due to a desire to enhance participation in the NTRI NBTF project, the college plans to consider recruitment of at least one additional full-time faculty member with experience and training in radiopharmaceutical development and the specialized analytical and quality control procedures for them. To date, the college has filled this gap with support from adjunct professors from the national laboratories.

Toxicology. The College of Pharmacy and the UNM Health Science Center have a proven track record in both educating and conducting scientific research projects in toxicology and human health effects. The Toxicology Program is housed in the College of Pharmacy and has active research and education collaborations with the UNM Medical School, Cancer and Treatment Center, the University Hospital, and others.

College of Engineering. The waste management, risk assessment, and health physics concentrations of the College of Engineering are among the best recognized and well-funded programs in the nation. Through its Waste management Education and Research Consortium, the College of Engineering is committed to perform fundamental research in hazardous and radioactive waste and to educate professionals in environmental maintenance and enhancement as well as waste management, reduction, and remediation.

In alliance with the College of Pharmacy, the education and training activities of the College of Engineering have been expanded to train students in nuclear pharmacy with specializations in organic and inorganic synthesis, analytical chemistry and biochemistry with a focus in

radiochemical techniques and instrumentation. The alliance also trains students in the nuclear and radiopharmaceutical chemistry fields with specializations in such areas as design of new radionuclide generators, optimization of radionuclide production, development of new applications in areas such as environmental restoration and minimization of waste, and radiological physics and radiation dosimetry.

Radiological Physics and Radiation Dosimetry. The College of Engineering established a radiation protection engineering program in 1990 to respond to the identified need for trained practitioners. This program brings together the faculty and students from the Medical School, the College of Pharmacy, Biology Department, and several disciplines in Engineering with concentration on radiological physics and radiation dosimetry. In addition to classroom education, the students must sign up for practicum experience with Kirtland Air Force Base, Sandia National Laboratories, and the UNM Hospital. During its short life, this program has proven to be an invaluable asset to the national laboratories and has helped alleviate local shortages of trained personnel.

Waste and Environmental Management. Through its Waste management Education and Research Consortium (WERC), the College of Engineering offers Professional Certificate programs in conjunction with B.S., B.A., M.S., and Ph.D. degrees in biology, chemistry, geology, pharmacy, public administration, law, and engineering. Concentration areas in risk assessment and biomedical engineering are also highly recognized and support the commitment of UNM to a strong program in support of nuclear medicine education and research.

Instructional Teleconference Education. Another strong component of the College of Engineering is its instructional teleconference programs that reach more than 2,000 professionals and students each year. More than 80 sites around the United States receive both academic courses and specialized topics.

Research

The availability of radionuclides for various research programs is of immense importance. New radionuclides are needed for many biomedical applications, both in diagnosis and therapy. To this end, UNM is fully committed to nuclear medicine research. In the past, the United States was the focal point for training in the nuclear sciences, and aspiring students came to this country to learn the science and technology of nuclear medicine. Our preeminence, however, has eroded to such an extent that vacant positions for nuclear medicine scientists, physicians, and technologists are increasing. The United States faces a critical shortage of undergraduate and graduate students to fulfill existing needs. The United States graduate students and faculty members in nuclear medicine often travel abroad to seek advanced study and training in nuclear medicine because research radioisotopes are more

available in other countries.

A collaboration among the researchers at UNM, investigators at the national laboratories and the medical centers has created a unique opportunity to fertilize cross cultural communication in the field of medical imaging. This project has also enjoyed technical support or collaboration from investigators from Arizona State University and the University of Texas Southwestern Medical Center in Dallas. Another active area of research at UNM is waste management, safety assessment, and public communication. An as an outgrowth of WERC, UNM has established the Center for Radioactive Waste Management (CeRaM). This center is dedicated to the study of radioactive and mixed waste issues—both in classroom and laboratory. The research activities of CeRaM include environmental fate and transport of radionuclides associated with different types of radioactive wastes, environmental restoration and remediation, and health physics and radiation monitoring.

Other specific research programs are:

- Developing new radiopharmaceuticals for clinical use;
- Developing methods for improved targeting of radiopharmaceuticals;
- Investigating factors that affect radiopharmaceutical stability;
- Assessing reliability and enhancing the continued operation of production facilities;
- Exploiting the production of other radioisotopes;
- Optimizing target design;
- Developing and optimizing flowsheets;
- Separating radioisotopes;
- Investigating radioisotope imaging/data fusion and image analysis;
- Designing new collimators and detectors for image analysis;
- Spinning-off radioisotope technology to industry; and
- Investigating process automation.

Technology Transfer

The two colleges have also recognized the need for a mechanism to transfer the developed technology to the commercial market. Therefore, these two entities have formed a technology commercialization venture to foster rapid transfer, development, and commercialization of research products. Through a university foundation, this venture is also designed to return a significant portion of its profit to UNM in support of both education

and research in nuclear medicine.

APPENDIX VIII

UNIVERSITY OF OKLAHOMA COLLEGE OF PHARMACY SAMPLE NUCLEAR PHARMACY CURRICULUM

The following is an example of one of the existing degree programs currently available at the universities and medical centers of the consortium that prepared this proposal. The program detailed below is located in Oklahoma City, approximately 150 miles north of the proposed NBTF site on Interstate Highway 35, which provides a direct link between Denton and Oklahoma City. Students in the nuclear pharmacy program at OU will have the opportunity to work directly with NBTF scientists and medical professionals at the NBTF and its affiliates.

The University of New Mexico also offers a graduate program in nuclear pharmacy. The New Mexico program is described in Appendix VII.

GRADUATE PROGRAMS IN NUCLEAR PHARMACY

I. WHAT IS NUCLEAR PHARMACY?

Nuclear Pharmacy is a patient-oriented service that embodies the scientific knowledge and professional judgement required to improve and promote health through the safe and efficacious use of radiopharmaceuticals for diagnosis and therapy. Nuclear Pharmacy is the first board-certified specialty practice in pharmacy. The University of Oklahoma, College of Pharmacy, offers a comprehensive graduate program in this specialty area.

II. OPPORTUNITIES

Graduates trained in Nuclear Pharmacy, Nuclear Pharmacy Administration, or Radiopharmaceutical Chemistry have a choice of career opportunities. Master of Science graduates who are registered pharmacists will be able to manage a Nuclear Pharmacy located in any hospital, medical center, or regionalized pharmacy. Graduates are also attracted to supervisory positions in industry and government. Doctor of Philosophy graduates in Nuclear Pharmacy or Radiopharmaceutical Chemistry use their skills as educators in academic institutions, researchers, or administrators in the radiopharmaceutical industry.

III. EMPHASIS OF THE AREA

A. Faculty in the Nuclear Pharmacy area are varied in background and interest. The main focus are such areas as Radiopharmaceutical Chemistry, Clinical Nuclear Pharmacy, and Nuclear Pharmacy Management.

B. The focus of the on-going research in the OU HSC Nuclear Pharmacy area is in the area of development of new radiopharmaceuticals radiolabeled with Tc-99m and I-123 for use as diagnostic agents for imaging the heart and the brain, and the development of radiolabeled monoclonal antibodies for diagnosis and therapy.

IV. EDUCATIONAL PREPARATION

A. In addition to the General Admission Requirement to the Graduate College of the University of Oklahoma, the following are prerequisites:

1. A bachelor's degree in Pharmacy for students who wish to receive a M.S. or Ph.D. in Clinical Nuclear Pharmacy or Nuclear Pharmacy Administration.

2. A bachelor's degree or equivalent in the physical or biological sciences for students who wish to receive a M.S. or Ph.D. in Radiopharmaceutical Chemistry/Nuclear Medicinal Chemistry.

B. Plan of Study:

The requirements of the Graduate College for the M.S. and Ph.D. program are in force for this specialty.

The Core course requirements for the M.S. and Ph.D. degrees are:

Course	Description	Hours
	COMMON TO ALL STUDENTS	
PHSC 5324	Radionuclide Methodology	4 hours
PHSC 5334	Nuclear Pharmacy	4 hours
RADI 5222	Intro. of Radiobiology	2 hours
BSE 5163	Biostatistics Methods I	3 hours
PHSC 6970	Seminar in Pharmaceutical Sciences	2 hours

FOR ALL STUDENTS IN RADIOPHARMACEUTICAL CHEMISTRY, ADD:

PHSC 6313	Design and Development of Radiophar.	3 hours
PHSC 5123	Research Techniques	3 hours
RADI 6623	Principles of Nuclear Medicine	4 hours

FOR STUDENTS IN NUCLEAR PHARMACY MANAGEMENT, ADD:

ACCT G5013	Quantitative Financial Controls	3 hours
MGMT G5083	Human Resources Management	3 hours
PHAD -----	Nuclear Pharmacy Administration	3 hours
PHAD 5703	Pharmacy Administration Res. Methods	3 hours

FOR STUDENTS IN CLINICAL NUCLEAR PHARMACY, ADD:

RADI 6623	Principles of Nuclear Medicine	3 hours
PHSC 5643	Pharmacokinetics	3 hours
PHSC 6313	Design & Development of Radiopharm.	3 hours
PHSC 5990	Special Studies in Nuclear Pharmacy	4 hours

ELECTIVE COURSES

PHSC 5113	Advanced Medicinal Chemistry I	3 hours
PHSC 5423	Pharmacodynamics	3 hours
PHSC 5643	Pharmacokinetics	3 hours
PHSC 6113	Advanced Medicinal Chemistry II	3 hours
PHSC 5990	Special Studies in Nuclear Pharmacy	1-10 hours
PHSC 6960	Readings in Pharmaceutical Sciences	1-3 hours
PHSC 5012	Clinical Pharmacotherapeutics	2 hours
PHSC 5113	Qualitative Spectroscopic Methods	3 hours
PHSC 5133	Biologically Active Peptides	3 hours
PHSC 5413	Pharmacodynamics of Current Therapeutic Agents	3 hours
PHSC 5624	Quantitative Spectroscopic Methods	4 hours
PHSC 5634	Chromatographic Methods	4 hours
PHSC 6133	Macromolecular Separation and Characterization Techniques	3 hours
PHSC 6711	Pharmacy Education Methods	1 hour
CHEM 5323	Advanced Organic Chemistry	3 hours
CHEM 6443	Advanced Organic Chemistry	3 hours
BIOC 5753	Principles of Biochemistry	3 hours
BSE 5173	Biostatistics Methods II	3 hours

PCOL 6013	Neuropharmacology	3 hours
PCOL 6004	Cardiovascular/Renal Pharmacology	4 hours
PCOL 6032	Principles of Animal Surgery	2 hours

ALL M.S. STUDENTS ARE REQUIRED TO ENROLL CONTINUOUSLY IN:

PHSC 5980	Research Master's Thesis (at least)	4 hours

ALL Ph.D. STUDENTS ARE REQUIRED TO ENROLL CONTINUOUSLY IN:

PHSC 6980	Research for Doctor's Dissertation Up to a maximum of	45 Credit Hours

V. FACILITIES

In addition to a modern, computerized Regional Nuclear Pharmacy, housed in the New College of Pharmacy Building (serving the needs of over 16 area hospitals), modern low-and high-level radioactive labeling laboratories and fully equipped research laboratories are available for programmatic support. The Nuclear Medicine facilities of the Oklahoma Medical Center and the Veterans Administration Hospital are also available for research.

MASTER'S AND DOCTORAL DEGREE PROGRAMS IN NUCLEAR PHARMACY

1. M.S. AND Ph.D. PLAN OF STUDY

A. Specific Courses:

i. Core Course requirements of all students M.S. and Ph.D.:

PHSC 5324 - Radionuclide Methodology
Principles of radioactive tracer methodology used in health research. Basic radiation physics, radionuclide calculations, interactions of radiation with matter, methods of radiation detection and determination, experimental design, radiological safety and application of radionuclides to research. Laboratory included. - Fall Semester.

PHSC 5334 - Nuclear Pharmacy
Introduction to the field of nuclear pharmacy. Topics include radiopharmaceutical

quality control, stability and labeling techniques. Laboratory included. - Spring Semester.

RADI 5222 - Introduction to Radiation Biology and Radiation Chemistry
(Course taught by Department of Radiological Sciences)
Effects of ionizing radiation on chemical and biological systems. Covers effects on water and biological macromolecules, acute and chronic effects on germ cells, embryo and adult tissues. These data are then used to develop a scientific basis for radiation therapy and the rationale for current radiation protection practices. - Spring Semester, every other year.

BSE 5163 - Biostatistics Methods I
(Course taught by Department of Biostatistics and Epidemiology)
A deep probe into theory as well as application of common statistical tests. Intended primarily for students who plan to major or have a strong minor in the field of statistics. Varies, Spring, Fall & Summer Semesters.

PHSC 6970 - Seminar in Pharmaceutical Sciences
A general seminar for all divisions of graduate study in pharmaceutical sciences. Every Semester.

ii. For M.S. students in Radiopharmaceutical Chemistry, add:

PHSC 6313 - Design and Development of Radiopharmaceuticals
Prerequisite: PHSC 5324 and PHSC 5334. The essential properties of desired radionuclides and the chemical and biological factors involved in the design of new radiopharmaceuticals. The design concepts: Empirical, semi-empirical and mechanistic. - Spring Semester.

PHSC 5123 - Qualitative Spectroscopic Methods
The theory and applications of the qualitative analysis of organic molecules using four energy probes: Infrared, ultraviolet, nuclear magnetic resonance and mass spectrometry. Fall Semester.

RADI 6623- Principles of Nuclear Medicine
(Course taught by Department of Radiological Sciences)
The physical and physiological principles underlying the procedures of nuclear medicine. Instrumentation, radiopharmaceuticals, dosimetry, quality assurance, and evaluation of the function procedures. Every other year, Spring Semester.

iii. For M.S. students in Clinical Nuclear Pharmacy, add:

RADI 6623 - Principles of Nuclear Medicine

PHSC 5643 - Pharmacokinetics
Fundamental principles, mathematical models, and clinical applications of pharmacokinetics.

PHSC 6313 - Design and Development of Radiopharmaceuticals

PHSC 5990 - Special Studies in Nuclear Pharmacy (4 cr).
A three month clinical rotation at the Nuclear Medicine Departments of Oklahoma Medical Center (OMH and Children's) and Veteran's Medical Center.

iv. For M.S. students in Nuclear Pharmacy Management, add:

ACCT 5013 - Quantitative Financial Controls
(Course taught on the Norman Campus, Accounting Department, College of Business Administration) - Spring Semester

MGMT G5083 - Human Resources Management
(Course taught on the Norman Campus, Management Department, Environmental Analysis and Policy) - Spring Semester

PHSC 5990 - Special Studies in Nuclear Pharmacy (3 cr.)
A three month rotation in the Nuclear Pharmacy Service Unit.

PHAD 5703 - Pharmacy Administration Res. Methods
(New Course to be formulated).

v. For Ph.D. students add from list of Elective Courses:

(See attached list and example of M.S. and Ph.D. plan of study in Radiopharmaceutical Chemistry and M.S. Plan of study in Nuclear Pharmacy Management).

The core course requirements for the M.S. and Ph.D. degrees are:

Course	Description	Hours
	Common to all students:	
PHSC 5324	Radionuclide Methodology	4 hours
PHSC 5334	Nuclear Pharmacy	4 hours

RADI 5222	Introduction to Radiobiology	2 hours
BSE 5163	Biostatistics Methods I	3 hours
PHSC 6970	Seminar in Pharmaceutical Sciences	2 hours

For students in Radiopharmaceutical Chemistry, add:

PHSC 6313	Design and Development of Radiophar.	3 hours
PHSC 5123	Qualitative Spectro. Methods	3 hours
RADI 6623	Principles of Nuclear Medicine	4 hours

For students in Nuclear Pharmacy Management, add:

ACCT G5013	Quantitative Financial Controls	3 hours
MGMT G5083	Human Resources Management	3 hours
PHSC 5990	Special Studies in Nuclear Pharmacy	3 hours
PHAD 5703	Pharmacy Administration Res. Methods	3 hours

Elective Courses:

PHSC 5113	Advanced Medicinal Chemistry I	3 hours
PHSC 5423	Pharmacodynamics	3 hours
PHSC 5643	Pharmacokinetics	3 hours
PHSC 6113	Advanced Medicinal Chemistry II	3 hours
PHSC 5990	Special Studies in Nuclear Pharmacy	1-10 hours
PHSC 6960	Readings in Pharmaceutical Sciences	1-3 hours
PHSC 5012	Clinical Pharmacotherapeutics	2 hours
PHSC 5113	Qualitative Spectroscopic Methods	3 hours
PHSC 5133	Biologically Actives Peptides	3 hours
PHSC 5413	Pharmacodynamics of Current Therapeutic Agents	3 hours
PHSC 5624	Quantitative Spectroscopic Methods	4 hours
PHSC 5634	Macromolecular Separation and Characterization Techniques	3 hours
PHSC 6711	Pharmacy Education Methods	1 hour
CHEM 5323	Advanced Organic Chemistry	3 hours
CHEM 6443	Advanced Organic Chemistry	3 hours
BIOC 5218	General Biochemistry	8 hours
BSE 5173	Biostatistics Methods II	3 hours
PCOL 6013	Neuropharmacology	3 hours
PCOL 6004	Cardiovascular/Renal Pharmacology	4 hours
PATH 6032	Principles of Animal Surgery	2 hours

All M.S. students are required to enroll continuously in:

PHSC 5980	Research Master's Thesis (at least)	4 hours

All Ph.D. students are required to enroll continuously in:

PHSC 6980	Research for Doctor's Dissertation - Up to a maximum of	45 credit hours

APPENDIX IX

BUSINESS PLAN

I. Overview

The National Biomedical Tracer Facility (NBTF) and the commercial production facility (AITI) will be the key foundational facilities in the NBTF core facilities. These core facilities, to be located in North Central Texas, will be affiliated with other centers of excellence through an *Association* (the *NBTF Association*), whose membership will include universities, medical centers, national laboratories, and private industry. This business plan is based on the fundamental assumptions listed in the following section.

A. Summary of Fundamental Elements of the Planned Approach

- The U.S. Department of Energy (DOE), in coordination with the U.S. Office of Management and Budget (MBO), provides a $25 million interest-free loan to be amortized over 30 years for construction of the NBTF. Approximately $15.4 million will be used to purchase an 80 MeV, 1.0 mA cyclotron, including associated beam lines, installation, and commissioning. The cyclotron will be purchased from an established commercial vendor under a firm, fixed price contract with guarantees of performance. A portion of these funds (approximately $5 million) will be devoted to improvement of existing facilities, shielding, and the construction of a research and education facility, with teaching laboratories.

- The consortium that prepared this proposal will form an association, to be called the *NBTF Association*, which will help to coordinate the production of research radioisotopes (and isotope-related research) by the NBTF and other Association facilities in order to supply the needs of the nuclear medicine research community.

- The North Texas Research Institute (NTRI) will operate the cyclotron for the NBTF and provide the facilities to house the cyclotron, which will have adequate electrical power, water, and sewage services. NTRI will lease beam lines and targets for commercial radioisotope production to AITI and to others on a priority basis that does not impede production of research isotopes.

- AITI will invest up to $15 million to purchase a 70 MeV, 1 mA linac for commercial radioisotope production. This will include an H^+ ion source, RFQ and tanks #1,2,3,4, klystrons, modulators, electronics, and power supplies, plus assembly, installation, and commissioning.

- AITI will lease beam time on the cyclotron from NTRI at a standard commercial rate during linac downtime and maintenance periods. AITI will construct the radioisotope processing facility under a ground lease from UNT and provide processing, marketing, and distribution of radioisotopes for the NBTF through a business contract.

- AITI (and other radiopharmaceutical companies) will provide proprietary contracts to the NBTF for research and development of new radioisotopes, target development, radiochemical processing, and other developments.

- AITI will enter into exclusive licensing arrangements with the NBTF for new developments and will pay standard royalties.

Success of the business plans associated with construction and operation of the commercial facility and the NBTF will depend on a coordinated effort among industry, academia, state, and federal agencies. The proposed DOE $25 million interest-free loan will be matched by a private investment of approximately $28 million from AITI and affiliated industry and investors. The combined source and application of funds is shown in Table 1. Under sources, the State of Texas Investment is from the Texas Department of Commerce Product Development Fund. The University of North Texas' contribution is the donation/reduced-rate lease of the Nike Site to the R&D facility and the commercial facility. The lease/purchase mortgage is for the commercial facility's buildings. The estimated construction cost/replacement value to the NBTF project of the Nike Site vaults and associated land is estimated to exceed $5 million.

Table 1

COMBINED SOURCE & APPLICATION OF CONSTRUCTION FUNDS

SOURCE OF FUNDS	(x1000)
Advanced Isotope Technologies, Inc. (Private Investment)	$10,540
State of Texas Investment (Texas DOC Product Development Fund)	$3,000
U.S. Department of Energy (Loan to NTRI)	$25,000
University of North Texas (Facilities Donated/Reduced Rate-Lease)	$2,800
Industrial Revenue Bond (Supporting AITI Construction/Operation)	$15,000
Lease/Purchase Mortgage (For AITI facilities)	$5,000
TOTAL	**$61,340**

APPLICATION OF FUNDS	
Linac (By AITI)	$10,800
Cyclotron Purchase (By NTRI)	$13,563
Beam Lines (Combined Commercial & R&D Facilities)	$4,000
Laboratory Equipment and Furnishings (By NTRI)	$6,400
Production Equipment (Commercial Facility)	$5,886
Construction Cost (Combined Facilities)	$12,400
Working Capital	$8,291
TOTAL	**$61,340**

B. Background and Critical Success Factors

1. Introduction

The North Texas Research Institute (NTRI), a not-for-profit affiliate of the University of North Texas, and AITI (formerly NTR&D), have been involved for several years in a project whose goal is to build and operate a facility much like the NBTF. The previous efforts of NTRI/AITI and the work performed for DOE under a previous contract have led to the conclusions embodied in this business plan.

Our efforts have convinced us that an entity such as the NBTF must address a broad set of issues associated with radioisotope and stable isotope technology. Therefore, we think that it is critical to develop the NBTF in the context of interdependent non-commercial *and* commercial *core facilities*. Further, the presence of an isotope-using facility among the core facilities, such as the proposed Advanced Medical Imaging Center, will be of substantial benefit.

The purpose of the core facilities will be to: (1) produce research quantities of radionuclides for the nuclear medicine research community (through the NBTF); (2) produce radionuclides for the radiopharmaceutical industry (through AITI); (3) conduct research into radioisotope production and related technologies (primarily through the NBTF); (4) provide opportunities for education and training in radioisotope production, radiochemistry, accelerator operation, and associated disciplines (through the NBTF and members of the NBTF Association); and (5) conduct research into technologies that will benefit from and enhance the market for new radiopharmaceuticals (through the NBTF and the Association).

The North Texas Research Institute, Inc. (NTRI) is a not-for-profit Texas corporation organized in accordance with Section 501(c)(3) of the Internal Revenue Service code. As a separate corporate affiliate of the University of North Texas (UNT), whose sole purpose is to benefit the university, NTRI provides a mechanism through which UNT's outstanding resources may be brought to bear on the regional and national needs in business and industry.

Advanced Isotope Technologies, Inc. (AITI), originally incorporated as NTR&D, is a for-profit Texas corporation, chartered in August 1991. AITI's primary purpose is to commercialize technology and intellectual property developed by UNT and other selected institutions. AITI is currently bringing two new technologies to the marketplace. The first is its *Pulsed Sealed Neutron Tube*™, which creates a neutron flux sufficient to convert stable isotopes into isotopically pure radionuclide products in quantity. The second is an *Intense Laser Source* which is expected to advance the art of stable isotope separation.

We propose to manage the NBTF as a division of NTRI. The commercial production facility will be managed by AITI. The two entities will enter into mutually supporting contractual agreements. Future members of the core facilities in North Central Texas could be either not-for-profit or for-profit entities. The previously mentioned Advanced Medical Imaging Center will be managed by the University of Texas Southwestern Medical Center at Dallas (UTSMC) in a not-for-profit context.

The NBTF will provide two basic groups of products and four categories of services.

The groups of products are:

1. Research radionuclides for the nuclear medicine and industrial communities, and

2. Specialized commercial radionuclide products.

The categories of services are:

1. Contract research and development for AITI and other companies,

2. Service irradiations and back-up production for AITI and other companies,

3. Technology transfer of NBTF developed technology, and

4. Education and training.

The availability of research radionuclides and improved radioisotope production technology is critical to the future of nuclear medicine. New imaging techniques, capitalizing on the greatly improved resolution of higher energy gamma photons, hold the promise of revolutionizing the field and providing much more cost effective diagnostic procedures. The development of such technologies is very strongly correlated to the ability to use new and specialized radioisotopes. The establishment of the NBTF within the proposed interdependent core facilities creates the critical atmosphere needed for the NBTF to be a truly viable entity.

The main objective of the NBTF and the NBTF Association is to establish the National Biomedical Tracer Facility (NBTF) as a world-class research and development facility with linkages among institutions to advance diagnostic and therapeutic health care through cooperation among universities, nuclear medicine professionals, and the radiopharmaceutical industry.

Several factors are critical to the success of the NBTF. The context in which the NBTF is located is crucial to its financial stability. Co-location with a commercial production facility and an experimental imaging facility allows the NBTF to reduce capital and operating expenditures through the availability of shared resources. For example, waste handling and ES&H functions will be operationally shared through business contracts for these services. Also, exchange of specialized personnel support under contract will reduce the labor costs that will be experienced by a stand-alone facility. The commercial production facility will also be a revenue source for the NBTF.

The proximity of good transportation services is also key to the success of the venture. Location near a major hub airport with *easy access to both coasts* from its central national location is very important for the distribution of short lived isotopes.

2. Business Environment

Billings by U.S. health care providers for over 11,000,000 nuclear medicine procedures totaled over $8 billion in 1993. Eighty-five percent of these procedures were done in a hospital setting. To generate this activity, the providers purchased approximately $500 million of radiopharmaceuticals, including the cold kits developed by the radiopharmaceutical manufactures to be combined with radioisotopes to create an injected patient dose. Over 75% of this revenue went to the big three radiopharmaceutical companies — Du Pont-Merck, Mallinckrodt, and the Medi+Physics division of Amersham International.

To generate the above revenue, the radiopharmaceutical manufactures make or buy approximately $70 million of bulk radiochemicals for their use in the production of radiopharmaceuticals. Approximately 60% of this bulk radiochemical product is manufactured in the drug companies' own cyclotron facilities, while another 30% is purchased from one supplier, Nordion of Canada. The remaining 10% is acquired from various sources, the chief one being DOE's Isotope Production and Distribution Program (IPDP). The most important single product in the marketplace is the molybdenum-99 generator, whose daughter product, technetium-99m, is used in over 75% of all nuclear medicine procedures. Nordion is the leading producer and marketer of Mo-99.

Nuclear medicine procedures are estimated to be growing at approximately 5% annually; however, cardiovascular studies are growing at 10%, and oncology studies have tripled between 1992 and 1994. Tumor diagnosis and therapy is projected to be the most exciting growth area in the next few years. The advent of high resolution imaging equipment that can use higher energy gamma photons will stimulate the use of a greater range of new radionuclides.

The radionuclide industry, in many ways, is a mature industry, but in other ways, many changes are bringing new challenges to management. Events in recent years have led to concern over the reliability of the supply of even the most widely used radioisotope in nuclear medicine. Commercial production of radionuclides has concentrated on a few products which are highly profitable. These and other factors have combined to put the supply of other radioisotopes, and particularly research radioisotopes, in jeopardy.

Several new technologies are critically dependent on a reliable supply of research isotopes. Changing political and regulatory forces have threatened the research radioisotope supply. DOE has attempted for a number of years to maintain an adequate supply, but the national laboratories have historically had other programmatic priorities which have interrupted or limited isotope production. The growth of the market and the development of new procedures and technologies is intimately tied to the supply of research isotopes.

The principal elements of a regulatory nature which will affect the construction and continued development of the NBTF are state and federal environmental, safety, and health requirements. These will be addressed by both NTRI and AITI simultaneously in a joint effort during the first two years of the project, thus achieving some economy of scale in accomplishing the required ES&H studies, certification, and licensing. Some applications planned for the NBTF will require special permits for the transportation and storage of moderate quantities of radioactive materials. The team assembled by NTRI for this proposal has specific personnel skilled in the transportation, storage, and control of such substances. Hence, the development of procedures necessary to meet state and federal requirements is considered low-risk.

The primary sources of competition to the NBTF are the national laboratories and sources outside the United States. Federal policy will strongly impact the interaction between the NBTF and the national laboratories.

It is anticipated that the NBTF and its associated members will be in continued competition for education and research grants. The Association of local and regional universities, medical centers, laboratories, and industries will enhance their competitive position for these grants.

The principal potential barriers to achieving the goals of the NBTF are:

1. Timely decisions and funding necessary to maintain program momentum,

2. A coordinated DOE policy toward radioisotope production with strong support for the NBTF, and

3. Obtaining commitments from key customers to use facility products, once complete, to a level projected in the marketing plan.

3. Risks and Opportunities

The first major strength of the proposal is the presence of a highly qualified team, capable of addressing all aspects of radionuclide and stable isotope production. As summarized in Section 2.1 of the main body of this report, and detailed in Appendices I and II, the team behind this proposal is extremely well qualified and represents an outstanding resource on which to draw.

The second major strength is the context in which we propose to develop the NBTF. Co-locating the NBTF with a commercial production facility and an imaging research facility is a significant advantage. Further, the Dallas-Fort Worth regional location is perfectly positioned for national and North American continental distribution.

The greatest barriers to success of the proposed NBTF are the uncertainty of DOE policy and the international market. By its actions, DOE could choose to support or undermine the NBTF through the national laboratories. This proposal is based on the assumption that DOE supports the mission of the NBTF and the goals contained in the recent Institute of Medicine report, *Isotopes for Medicine and the Life Sciences* (Adelstein and Manning, 1994) and interests expressed by related organizations.

C. Description of Products and/or Services

The products and/or services of the proposed NBTF are described in detail in Section 4.0 of this report and further discussed in Sections 7.0 (research) and 8.0 (education).

II. Management and Operational Plan

A. Proposed Management Structure

The management and operational plan is discussed in Section 6.0 of this report. The NBTF will be structured and operated as a key component of the NBTF core facilities, located in North Central Texas. The other key component of the proposed core facilities is a privately-funded, state-of-the-art commercial production facility under development by Advanced Isotope Technologies, Inc. (AITI). The center will be further enhanced by the addition of an Advanced Medical Imaging Center, also independently funded and managed by the University of Texas Southwestern Medical Center (UTSMC) at Dallas.

The *NBTF Association* will be formed to tie together the core facilities located in Texas with affiliated centers of excellence elsewhere in North America. This Association, open to both the public and the private sector, will address all isotope-related issues raised in the

recently-released study by the Institute of Medicine of the National Academy of Sciences, *Isotopes for Medicine and the Life Sciences* (Adelstein and Manning, 1994). The Association will be both a forum for the discussion of such issues and an instrument for solving problems through the proposed NBTF core facilities in North Texas and the collaborative efforts of its individual members. The IOM report suggested the formulation of a *national isotope policy*. The NBTF Association will be a step toward this goal. The charter membership of the NBTF Association will be the members of this proposal consortium, but the Association will be open to all other responsible entities who wish to join.

As shown in Figure 1, the NBTF Association will unite the NBTF core facilities located in North Central Texas with multiple centers of excellence elsewhere. Figure 2 highlights the facilities proposed for the NBTF core facilities. These include the NBTF, the commercial production facility, and the proposed Advanced Medical Imaging Center. The center could also encompass other for-profit or not-for-profit facilities, such as a regional radiopharmacy or a training center operated by a community college or state technical college.
The NBTF will be a division of NTRI, the not-for-profit corporate affiliate and technology transfer arm of the University of North Texas. The director of the NBTF will be appointed by the executive director of NTRI and ratified by the NBTF Association and NTRI's boards of directors. NTRI is suggested as the NBTF manager because it is an existing, corporate entity set up to facilitate R&D and bridge the gap between the not-for-profit sector and technology-based industries.

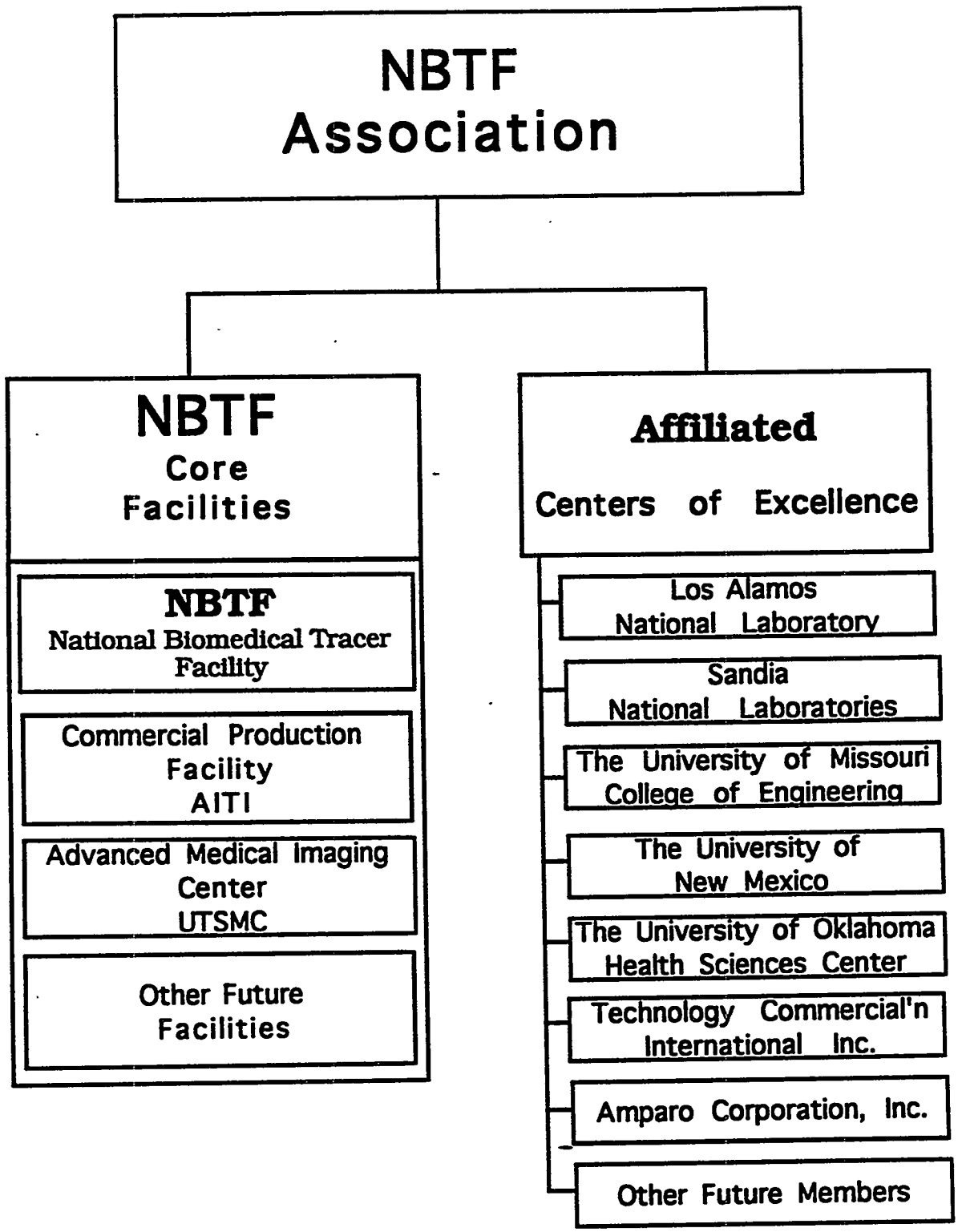


Fig. 1 NBTF Association

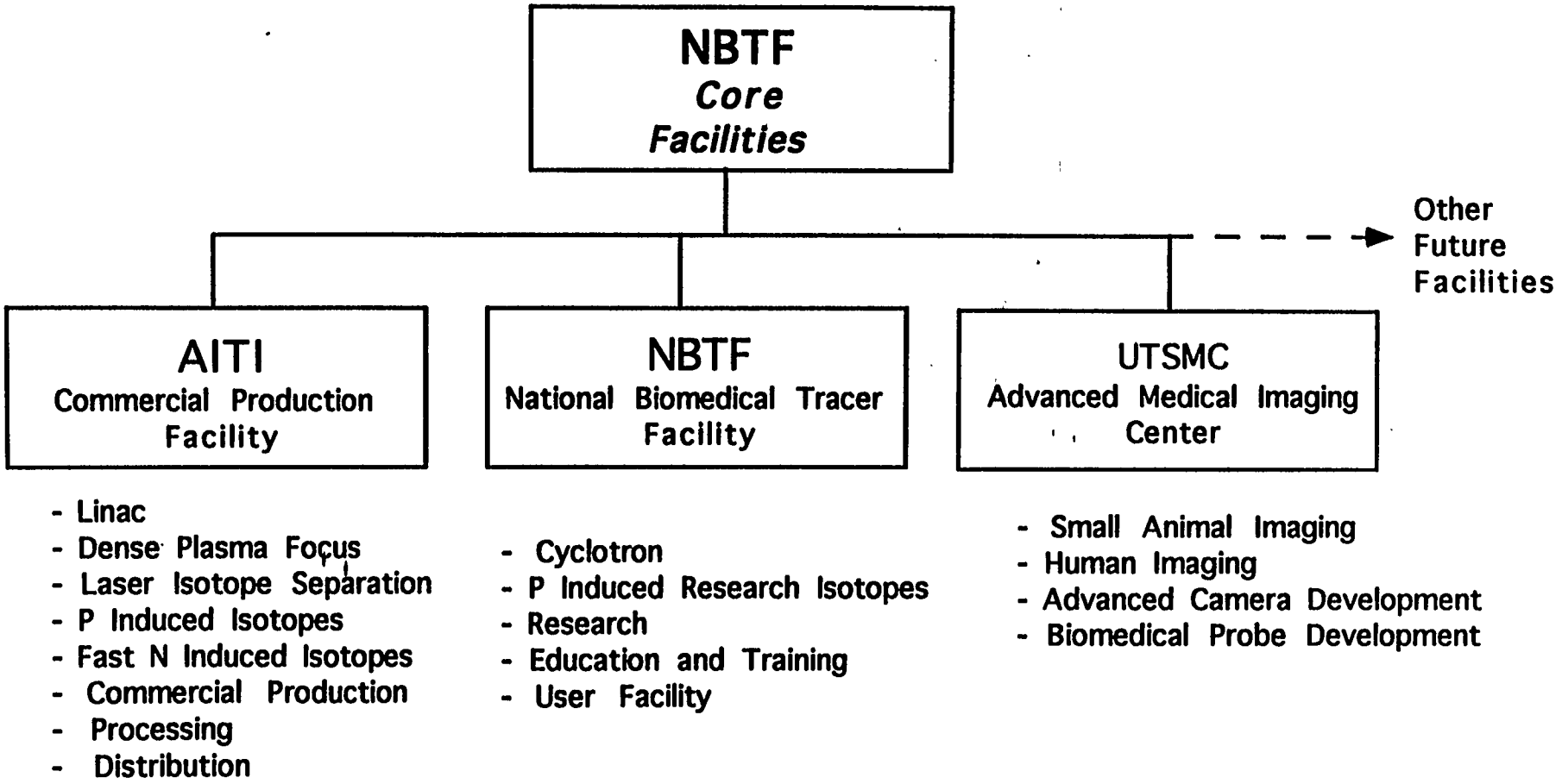


Fig. 2 NBTF Core Facilities

B. Operational Management of the NBTF and its Affiliates

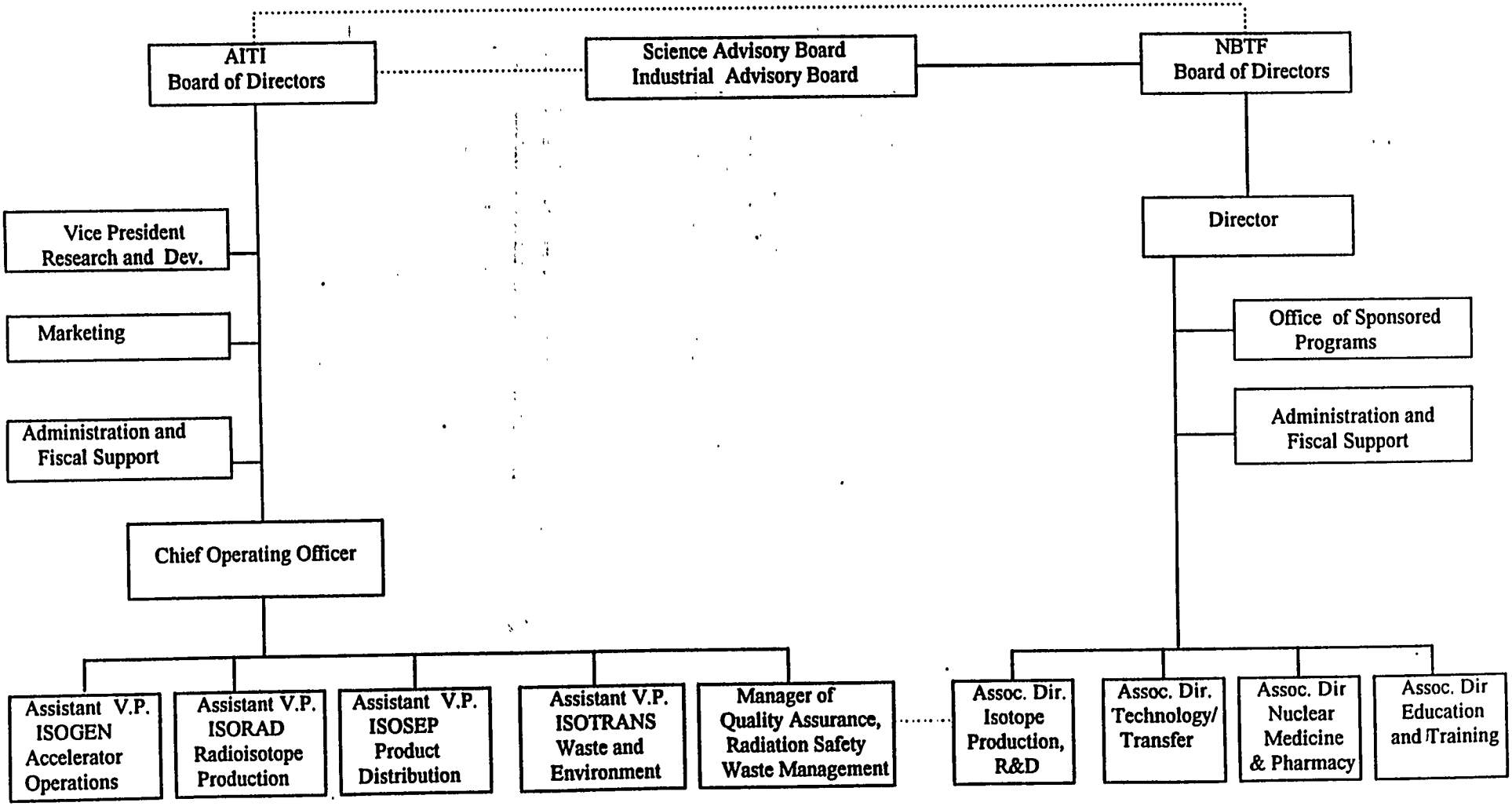
The NBTF and the proposed commercial production facility will share some operational functions through mutually-supporting contractual arrangements. For example, the cyclotron will provide a high intensity beam to back up the linac, an arrangement that will provide an additional revenue stream to help sustain the operations of the cyclotron-based research and educational unit. As recommended in the recent IOM report, *Isotopes for Medicine and the Life Sciences* (Adelstein and Manning, 1994), high activity research isotopes produced by the cyclotron will be processed by the commercial operator. Other functions, such as radiological safety, waste management/handling, QA/QC, product shipping, etc., also will be shared under specific contractual arrangements between the for-profit commercial company and the NBTF. The administration and fiscal support of each facility will be entirely separate, since the sources of revenue will be generated through different channels.

The operational management of the NBTF and its affiliates is discussed in more detail in section 6.0 of this report. The NBTF key personnel are detailed in Appendix I of the report. Figure 3 sketches the relationship between the NBTF and the commercial facility. This structure is subject to modification with further study.

C. Facilities and Equipment

The Facilities and Equipment are detailed in section 3.0 of the main body of the report.

FUNCTIONAL RELATIONSHIPS BETWEEN NBTF AND AITI
(Substantive Interactions are through Standard Business Contracts)



III. Financial Plan

The NBTF is expected to operate at a break even point within four to five years after the installation and commissioning of the cyclotron and associated facilities. The source of funds for NBTF construction are a $25 million government guaranteed interest free loan, and in kind facilities donated by UNT. The sections below describe and analyze the operating revenues and the operating expenses.

A. NBTF Operating Revenues

The estimated annual revenue by category is shown in Table 2. These estimates are based on the market size and expected market penetration.

- Income from the sale of research isotopes will grow to be approximately $3.5 million, which is about 40% of the research isotope market, including imaging, therapeutic, industrial, and biomedical/special life sciences radionuclides. The estimate of market penetration is based on a previous market survey commissioned by NTRI, market surveys done in connection with the DOE-funded study of salvaging SSC assets, and a market survey of research isotopes done by NTRI as a part of the NBTF project definition study. The estimate also rests on the assumption that isotope production will decrease at LAMPF. If DOE chooses to limit commercial production of research isotopes at BLIP, the market penetration will be much greater. The market penetration in year one of operation is estimated to be 5% and grows to 40% in year five of operation.

- The radiopharmaceutical companies will be a source of R&D contract revenue, service irradiation revenue, revenue from production contracts for specialized products, and revenue from technology transfer royalties. Discussions with major radiopharmaceutical representatives have resulted in the revenue estimates shown in Table 2. A variety of outside users and user groups, including but not limited to the radiopharmaceutical companies, will use and support the four beam lines in the amount of $800,000 per year; e.g., for example four major users or user groups at $200,000 per year. (A rate structure will be established that will permit individual researchers and those seeking preliminary data to participate without excessive fees, as appropriate.)

- Commercial radioisotope production as a backup to the linac production facility is estimated to grow to $970,000 annually in year seven, based on projected downtime and maintenance of the linac. AITI will also purchase R&D support from the NBTF. The estimated revenue (by year) is included in Table 2.

- Continuing support by DOE, NIH, NSF, and other federal agencies for operation is expected to grow to $2,750,000 per year. These funds will be obtained through the standard competitive research grant and contract systems.

- Discussions with state officials indicate that support for education and training is an additional source of revenue as shown in Table 2. Also shown in the table is a modest amount of revenue from continuing education and distance learning fees.

B. NBTF Operating Expenses

An NBTF full-time-equivalent staffing summary is shown in Table 3. The full time equivalents are separated by labor class and year. The manning summary and the NTRI salary for each labor class are used to calculate the total annual expenses for salaries and wages.

The operating expenses are summarized in Table 4.

NTRI fringe benefits are 23% of the salaries and wages as set by the NTRI standard rates, not including any personnel insurance premium contributions.

The NTRI permanent and expendable equipment are estimated on the bases of the schedule of activities, number of personnel, and past experience.

The NTRI supplies and materials include equipment lease, equipment maintenance, housekeeping, utilities, facilities lease, office supplies, professional symposia, dues and subscriptions, meetings and conferences, and stable isotopes. The three largest of these subcategories (utilities, stable isotopes, and equipment maintenance) are estimated based on the expected products and operating schedules for the proposed equipment.

The NTRI publications, reproduction, communication, and computer expenses are based on long experience and the estimated staffing levels.

The NTRI subcontracts include waste removal, legal services, insurance, licenses, and marketing & distribution. The NTRI indirect costs are the standard NTRI off-campus rates. Other operating expenses include amortization of the $25 million 30-year interest free loan.

Revenue Category	Year 1 Est'd. Rev.	Year 2 Est'd. Rev.	Year 3 Est'd. Rev.	Year 4 Est'd. Rev.	Year 5 Est'd. Rev.	Year 6 Est'd. Rev.	Year 7 Est'd. Rev.
Nuclear Medicine Community							
Imaging Radionuclides	$0	$0	$100,000	$250,000	$650,000	$1,000,000	$1,500,000
Therapy Radionuclides	$0	$0	$48,000	$96,000	$180,000	$360,000	$720,000
Industrial Radionuclides	$0	$0	$225,000	$450,000	$600,000	$750,000	$900,000
Biomedical/Specialty Life Sciences Radi	$0	$0	$50,000	$100,000	$200,000	$300,000	$375,000
Radiopharmaceutical Companies							
R&D Contracts	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Service Irradiations	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Low Demand Comercial Products	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Tech. Transfer and Royalties	$0	$0	$0	$0	$100,000	$175,000	$250,000
Production Rights Advance	$750,000	$750,000					
AITI							
R&D Support	$0	$0	$300,000	$300,000	$300,000	$300,000	$300,000
Backup Production	$0	$0	$278,000	$556,000	$695,000	$834,000	$973,000
Department of Energy							
Education and Training	$0	$0	$250,000	$500,000	$750,000	$900,000	$1,000,000
R&D Grants and Contracts	$500,000	$500,000	$500,000	$750,000	$900,000	$1,100,000	$1,250,000
Other Federal Agencies							
R&D Grants and Contracts	$0	$0	$500,000	$500,000	$500,000	$500,000	$500,000
States of TX,OK,NM							
Support for Education and Training	$0	$0	$150,000	$150,000	$150,000	$150,000	$150,000
Professional Training							
Cont. Educ. & Distance Learning	$0	$0	$25,000	$50,000	$75,000	$100,000	$125,000
Totals	$1,250,000	$1,250,000	$2,726,000	$4,302,000	$6,000,000	$7,669,000	$9,543,000

Table 2 NBTF Estimated Annual Revenue by Category

Labor Class	Yr 1 FTE	Yr 2 FTE	Yr 3 FTE	Yr 4 FTE	Yr 5 FTE	Yr 6 FTE	Yr 7 FTE
Director	1	1	1	1	1	1	1
Research Scientists							
Radiochemist	2	2	2	2	2	2	2
Pharmaceutical Chemist	0	1	1	2	2	2	2
Physicist	1	1	1	2	2	2	2
ES&H Scientist	0.25	0.25	1	1	1	1	1
Research Associates							
Post Doctoral Associates	0	0	2	4	6	8	8
Research Assistants	0	0	1	2	3	4	4
Operations							
Accelerator Operators	0	0.5	1.5	2	2.55	3	3
Health Physics Techs.	0	1	1	1	1	1	1
Process/Chemical Techs.	0	1	2	2	2	2	2
Target Dev.&Prep. Techs.	0	0.5	2	2	2	2	2
QA/QC Staff	0	0.5	1	2	2	2	2
Mechanical Techs.	0	1	1	2	3	3	3
Education & Training Staff	0	0	1	1	1	1	1
Administration	1	1	2	2	2	2	2
Total FTEs	**5.25**	**10.75**	**20.5**	**28**	**32.55**	**36**	**36**

Table 3 NBTF Labor Full Time Equivalents

Table 4 NBTF Annual Operating Expenses By NTRI Expense Class

Expense Category	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
A. NTRI Salaries and Wages							
Staff Salaries and Wages	$260,000	$527,500	$894,500	$1,269,000	$1,435,750	$1,558,000	$1,558,000
Management Salaries	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000
Technical/Admin. Salaries	$26,000	$26,000	$52,000	$52,000	$52,000	$52,000	$52,000
B. NTRI Fringe Benefits @ 23%	$88,780	$150,305	$240,695	$326,830	$365,183	$393,300	$393,300
C. NTRI Permanent Equipment	$0	$0	$35,000	$20,000	$15,000	$15,000	$15,000
D. NTRI Expendable Equipment	$1,000	$2,000	$3,500	$4,500	$5,000	$5,000	$5,000
E. NTRI Supplies Mat'ls and Serv's							
Equipment Lease	$7,000	$14,000	$5,000	$0	$0	$0	$0
Equipment Maintenance	$0	$0	$50,000	$300,000	$450,000	$450,000	$450,000
Housekeeping	$0	$0	$22,000	$45,000	$46,000	$46,000	$46,000
Utilities	$5,000	$100,000	$200,000	$300,000	$375,000	$450,000	$450,000
Facilities Lease	$6,000	$12,000	$12,000	$0	$0	$0	$0
Office Supplies	$5,000	$5,000	$10,000	$15,000	$20,000	$20,000	$20,000
Professional Symposiums	$1,500	$3,500	$5,500	$6,300	$7,000	$7,000	$7,000
Dues and Subscriptions	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Meetings and Conferences	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Stable Isotopes	$0	$20,000	$100,000	$150,000	$225,000	$300,000	$300,000
F. NTRI Travel							
General Travel	$20,000	$15,000	$10,000	$10,000	$7,000	$7,000	$7,000
G. NTRI Publications	$0	$0	$5,000	$10,000	$10,000	$10,000	$10,000
H. NTRI Reproduction	$2,000	$4,000	$6,000	$8,000	$10,000	$10,000	$10,000
I. NTRI Communication	$6,000	$12,000	$12,000	$8,000	$9,000	$9,000	$9,000
J. NTRI Computer	$1,000	$2,000	$3,400	$4,500	$5,000	$5,000	$5,000
K. NTRI Consultants	$80,000	$125,000	$85,000	$30,000	$20,000	$20,000	$20,000
L. NTRI Subcontracts							
Waste Removal	$0	$0	$5,000	$10,000	$15,000	$15,000	$15,000
Legal Services	$30,000	$20,000	$12,000	$10,000	$10,000	$10,000	$10,000
Liability Insurance	$0	$0	$7,000	$7,000	$7,000	$7,000	$7,000
Licenses	$0	$0	$11,000	$11,000	$11,000	$11,000	$11,000
Marketing & Distribution	$0	$0	$30,000	$80,000	$80,000	$80,000	$80,000
M. NTRI Ind't Costs MTDC def @26%	$144,633	$264,499	$467,895	$697,094	$831,982	$910,078	$910,078
Subtotal Annual Expenses	$785,913	$1,406,804	$2,392,490	$3,483,224	$4,121,915	$4,500,378	$4,500,378
Other Operating Costs							
Amortization	$0	$0	$0	$833,000	$833,000	$833,000	$833,000
Total Annual Costs	$785,913	$1,406,804	$2,392,490	$4,316,224	$4,954,915	$5,333,378	$5,333,378

C. Analysis of Annual Revenues and Expenses

Table 5 shows an analysis of annual revenues and expenses. The expenses begin in year one, and the isotope revenue does not start until year three when the cyclotron is commissioned. Similarly, the amortization of the 30-year loan does not begin until the fourth year after the NBTF is fully operational.

The operating expenses are separated into the standard NTRI expense categories and those that fall outside of the normal NTRI expense categories. No indirect costs are applied to the non-normal categories.

The excess (deficiency) of operating expenses is debited by a depreciation amount of $1.25 million per year. This amount is a straight line result of depreciating $25 million worth of equipment and facilities over 20 years.

The bottom line excess (deficiency) of revenues over expenses shows a deficit through year five or the third year of cyclotron operation. The deficit averages ~$1 million per year and peaks in year four at approximately ~$1.2 million. Self sufficiency is achieved in year six or the fourth year of cyclotron operation. A project construction master schedule is shown in Appendix A. A detail of the cyclotron fabrication and commissioning schedule also is shown in Appendix A. The cyclotron construction schedule is the critical path for the project. The current cyclotron includes full assembly and testing at the manufacturer's plant before shipping. Substantial time savings may be achieved if the cyclotron is assembled and tested at the North Texas site.

D. Analysis of Cash Flows

Table 6 shows an analysis of cash flows. The excess (deficiency) of operating revenues over operating expenses is adjusted to determine the total cash provided by (used in) operating activities.

The cash flow from investing and financing activities is summarized and added to that of the operating activities to achieve the net increase (decrease) in cash. The annual net increase (decrease) is then used to determine the beginning and end of period cash balances. Project construction costs, summarized in Table 6, are accounted for in this category.

In the sixth year, or the fourth year of cyclotron operation, the operating revenues becomes positive as full operational status is approached. At this point, the cash flow begins to accumulate capital for the replacement of equipment, as it reaches the end of its useful life. Thus self-sufficiency, dependent on achieving the estimated market penetration, is achieved in year six or the fourth year of cyclotron operation.

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Operating Revenues							
Total Revenues from all Constituencies	$1,250,000	$1,250,000	$2,726,000	$4,302,000	$6,000,000	$7,669,000	$9,543,000
Operating Expenses							
A. Salaries and Wages	$386,000	$653,500	$1,046,500	$1,421,000	$1,587,750	$1,710,000	$1,710,000
B. Fringe Benefits @ 23%	$88,780	$150,305	$240,695	$326,830	$365,183	$393,300	$393,300
C. Permanent Equipment	$0	$0	$35,000	$20,000	$15,000	$15,000	$15,000
D. Expendable Equipment	$1,000	$2,000	$3,500	$4,500	$5,000	$5,000	$5,000
E. Supplies Mat'ls and Serv's	$26,500	$158,500	$412,500	$825,300	$1,133,000	$1,283,000	$1,283,000
F. Travel	$20,000	$15,000	$10,000	$10,000	$7,000	$7,000	$7,000
G. Publications	$0	$0	$5,000	$10,000	$10,000	$10,000	$10,000
H. Reproduction	$2,000	$4,000	$6,000	$8,000	$10,000	$10,000	$10,000
I. Communication	$6,000	$12,000	$12,000	$8,000	$9,000	$9,000	$9,000
J. Computer	$1,000	$2,000	$3,400	$4,500	$5,000	$5,000	$5,000
K. Consultants	$80,000	$125,000	$85,000	$30,000	$20,000	$20,000	$20,000
L. Subcontracts	$30,000	$20,000	$65,000	$118,000	$123,000	$123,000	$123,000
M. Indirect Costs MTDC def @ 26%	$144,633	$264,499	$467,895	$697,094	$831,982	$910,078	$910,078
Total Annual Operating Expenses	$785,913	$1,406,804	$2,392,490	$3,483,224	$4,121,915	$4,500,378	$4,500,378
Excess (Deficiency) of Operating Revenues Over Operating Expenses *Before Other Expenses*	*$464,087*	*($156,804)*	*$333,510*	*$818,776*	*$1,878,085*	*$3,168,622*	*$5,042,622*
Other Expenses							
Amortization	$0	$0	$0	$833,000	$833,000	$833,000	$833,000
Excess (Deficiency) of Operating Revenues over Operating Expenses	$464,087	($156,804)	$333,510	($14,224)	$1,045,085	$2,335,622	$4,209,622
Depreciation			$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000
Excess (Deficiency) of Revenues over Expenses	$464,087	($156,804)	($916,490)	($1,264,224)	($204,915)	$1,085,622	$2,959,622

Table 5 Analysis of Annual Revenues and Expenses In CY1995 Dollars

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Cash Flows from Operating Activities							
Excess (Deficiency) of Operating Revenues over Operating Expenses	$464,087	($156,804)	($916,490)	($1,264,224)	($204,915)	$1,085,622	$2,959,622
Add Adjustments to Reconcile Excess (Deficiency) of Operating Revenues to Net Cash Provided by (Used in) Operating Activities							
Depreciation			$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000
Total Adjustments	$0	$0	$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000
Total Cash Provided by (Used in) Operating Activities	$464,087	($156,804)	$333,510	($14,224)	$1,045,085	$2,335,622	$4,209,622
Cash Flow from Investing Activities							
Construction and Development Costs	($4,000,000)	($8,700,000)	($10,800,000)				
ES&H Expenditures	($800,000)	($800,000)					
Total Cash Provided by (Used in) Investment Activities	($4,800,000)	($9,500,000)	($10,800,000)	$0	$0	$0	$0
Cash Flow from Financing Activities							
DOE Interest Free Loan	$25,000,000						
Total Cash Provided by (Used in) Financing Activities	$25,000,000	$0	$0	$0	$0	$0	$0
Net Increase (Decrease) in Cash	$20,664,087	($9,656,804)	($10,466,490)	($14,224)	$1,045,085	$2,335,622	$4,209,622
Cash, Beginning of Period		$20,664,087	$11,007,283	$540,793	$526,569	$1,571,654	$3,907,276
Cash, End of Period	$20,664,087	$11,007,283	$540,793	$526,569	$1,571,654	$3,907,276	$8,116,898

Table 6 Analysis of Cash Flows in CY1995 Dollars

E. Payback of Loan

Table 7, page IX-23, shows an analysis of the payback of the $25 million government-guaranteed, interest-free loan and the associated cost to the government.

	Amount of loan			Annual NBTF Federal Costs — A —	Amount of loan			Annual NBTF Federal Costs — B —	Difference A - B
	$25,100,000	$25,100,000		$26,355,000	$25,100,000	$25,100,000		$24,489,000	$1,866,000
Year		Repayment of principal	Principal remaining	▼▼▼ 6%		Repayment of principal	Principal remaining	▼▼▼ 6%	
1	$25,100,000	$0	$25,100,000	$1,506,000	$4,800,000	$0	$4,800,000	$288,000	$1,218,000
2		$0	$25,100,000	$1,506,000	$9,500,000	$0	$14,300,000	$858,000	$648,000
3		$0	$25,100,000	$1,506,000	$10,800,000	$0	$25,100,000	$1,506,000	$0
4		$836,667	$24,263,333	$1,455,800		$836,667	$24,263,333	$1,455,800	$0
5		$836,667	$23,426,667	$1,405,600		$836,667	$23,426,667	$1,405,600	$0
6		$836,667	$22,590,000	$1,355,400		$836,667	$22,590,000	$1,355,400	$0
7		$836,667	$21,753,333	$1,305,200		$836,667	$21,753,333	$1,305,200	$0
8		$836,667	$20,916,667	$1,255,000		$836,667	$20,916,667	$1,255,000	$0
9		$836,667	$20,080,000	$1,204,800		$836,667	$20,080,000	$1,204,800	$0
10		$836,667	$19,243,333	$1,154,600		$836,667	$19,243,333	$1,154,600	$0
11		$836,667	$18,406,667	$1,104,400		$836,667	$18,406,667	$1,104,400	$0
12		$836,667	$17,570,000	$1,054,200		$836,667	$17,570,000	$1,054,200	$0
13		$836,667	$16,733,333	$1,004,000		$836,667	$16,733,333	$1,004,000	$0
14		$836,667	$15,896,667	$953,800		$836,667	$15,896,667	$953,800	$0
15		$836,667	$15,060,000	$903,600		$836,667	$15,060,000	$903,600	$0
16		$836,667	$14,223,333	$853,400		$836,667	$14,223,333	$853,400	$0
17		$836,667	$13,386,667	$803,200		$836,667	$13,386,667	$803,200	$0
18		$836,667	$12,550,000	$753,000		$836,667	$12,550,000	$753,000	$0
19		$836,667	$11,713,333	$702,800		$836,667	$11,713,333	$702,800	$0
20		$836,667	$10,876,667	$652,600		$836,667	$10,876,667	$652,600	$0
21		$836,667	$10,040,000	$602,400		$836,667	$10,040,000	$602,400	$0
22		$836,667	$9,203,333	$552,200		$836,667	$9,203,333	$552,200	$0
23		$836,667	$8,366,667	$502,000		$836,667	$8,366,667	$502,000	$0
24		$836,667	$7,530,000	$451,800		$836,667	$7,530,000	$451,800	$0
25		$836,667	$6,693,333	$401,600		$836,667	$6,693,333	$401,600	$0
26		$836,667	$5,856,667	$351,400		$836,667	$5,856,667	$351,400	$0
27		$836,667	$5,020,000	$301,200		$836,667	$5,020,000	$301,200	$0
28		$836,667	$4,183,333	$251,000		$836,667	$4,183,333	$251,000	$0
29		$836,667	$3,346,667	$200,800		$836,667	$3,346,667	$200,800	$0
30		$836,667	$2,510,000	$150,600		$836,667	$2,510,000	$150,600	$0
31		$836,667	$1,673,333	$100,400		$836,667	$1,673,333	$100,400	$0
32		$836,667	$836,667	$50,200		$836,667	$836,667	$50,200	$0
33		$836,667	($0)	($0)		$836,667	($0)	($0)	$0

BUSINESS PLAN APPENDICES

A. Schedule of Major Project Construction Events

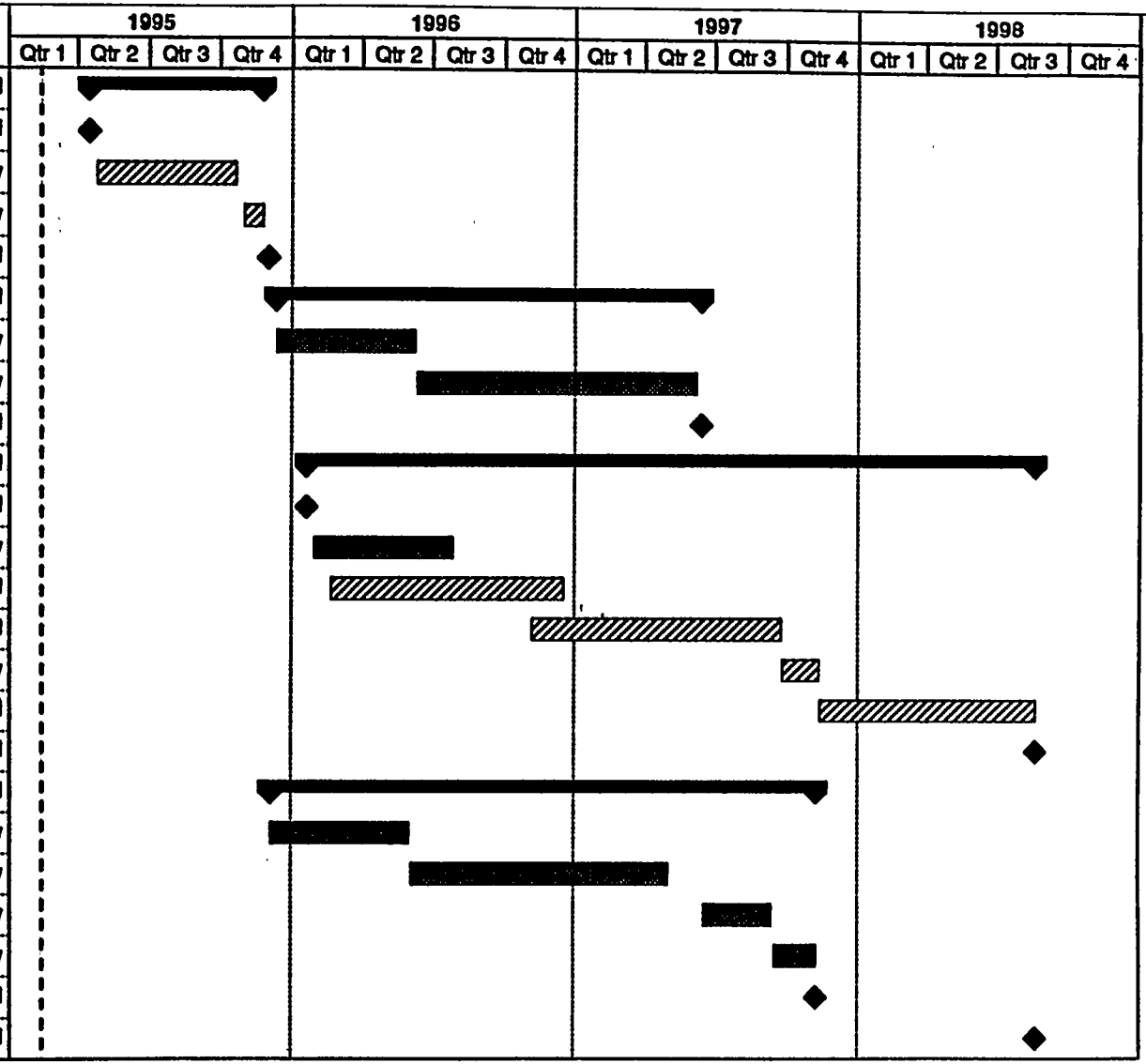
B. Facility Operations Manpower Forecasts

C. Facilities Annual Operating Expenses

D. Revenue Forecast

E. Construction Cost Estimate Summary

ID	Name	Duration
1	Site Specific Project Definition Study	160d
2	Authorization to Proceed on Site Spec.	0d
3	Site Specific Project Definition Study	26w
4	Study Review	4w
5	Project Authorization	0d
6	Conventional Facilities	395d
7	Conventional Facilities Design	26w
8	Conventional Facilities Construction	52w
9	Beneficial Occupancy	0d
10	Cyclotron	672d
11	Cyclotron Project Start	0d
12	Cyclotron Study and Development	26w
13	Cyclotron Procurements	216d
14	Cyclotron Assembly	231d
15	Transport	7w
16	On site Installation & Commissioning	200d
17	Cyclotron Complete	0d
18	Isotope Technical Systems	505d
19	Technical Systems Design	26w
20	Technical Systems Fabrication	48w
21	Technical Systems Installation	13w
22	Technical Systems Commissioning	8w
23	Technical Systems Accepted	0d
24	NBTF Operational	0d

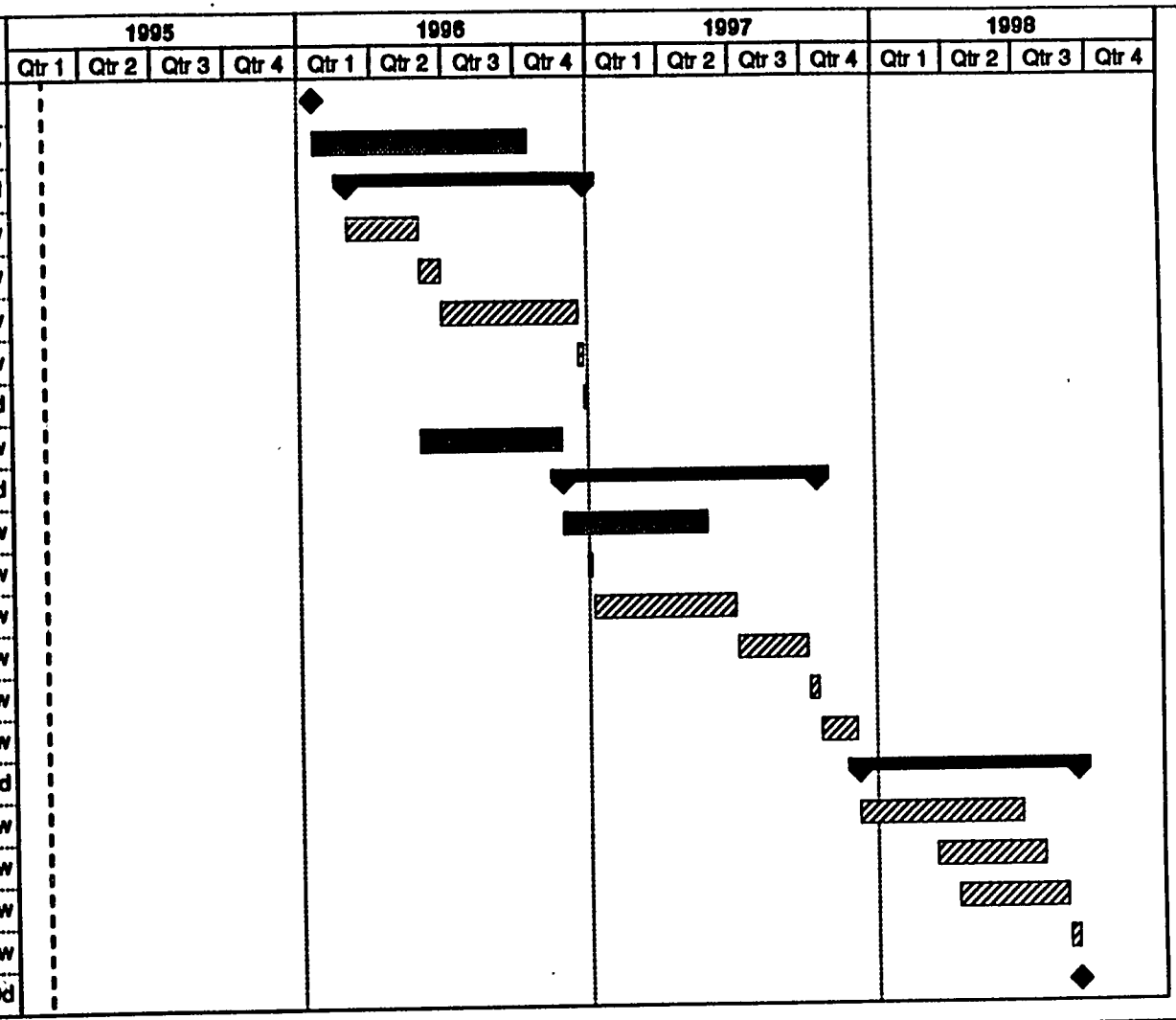


Project: NTRI NBTF
Date: 2/12/95

Critical
Noncritical
Progress
Milestone ◆
Summary
Rolled Up ◇

Appendix A-1 NBTF Project Master Schedule

ID	Name	Duration
1	Cyclotron Project Start	0d
2	Cyclotron Study and Development	39w
3	Procurements	216d
4	Steel Procurement	13w
5	Steel Oxycutting Procurement	4w
6	Yoke Machining	25w
7	Yoke Painting	1w
8	Yoke Delivery to IBA	1d
9	Other Part Procurements	26w
10	Cyclotron Assembly at IBA	231d
11	Other Parts Assembly	26w
12	Yoke Assembly	1w
13	Mapping & Subsystem Startup and Test	26w
14	Overall Systems Test	13w
15	Packing	2w
16	Transport	7w
17	On Site Installation	200d
18	Cyclotron Assembly and Startup	30w
19	Four Beam Lines Assembly and Startup	20w
20	Four Ad'tnl Beam Lines ASSY & Startup	20w
21	Acceptance Tests	2w
22	Cyclotron Complete	0d



Project: NTRI NBTF
Date: 2/12/95

Critical
Noncritical
Progress
Milestone
Summary
Rolled Up

Appendix A-2 NBTF Cyclotron Schedule

Appendix B

Labor Data Input

Labor Class	Yr 1 h	YR 1 %	Yr 2 h	Yr %	Yr 3 h	Yr 3 %	Yr 4 h	Yr 4 %	Yr 5 h	Yr 5 %	Yr 6 h	Yr 6 %	Yr7 h	Yr 7 %
Director	1	100%	1	100%	1	100%	1	100%	1	100%	1	100%	1	100%
Research Scientists														
Radiochemist	2	100%	2	100%	2	100%	2	100%	2	100%	2	100%	2	100%
Pharmaceutical Chemist			1	100%	1	100%	2	100%	2	100%	2	100%	2	100%
Physicist	1	100%	1	100%	1	100%	2	100%	2	100%	2	100%	2	100%
ES&H Scientist	1	25%	1	25%	1	100%	1	100%	1	100%	1	100%	1	100%
Research Associates														
Post Doctoral Associates					2	100%	4	100%	6	100%	8	100%	8	100%
Research Assistants					2	50%	4	50%	6	50%	8	50%	8	50%
Operations														
Accelerator Operators			1	50%	2	75%	2	100%	3	85%	3	100%	3	100%
Health Physics Techs.			1	100%	1	100%	1	100%	1	100%	1	100%	1	100%
Process/Chemical Techs.			1	100%	2	100%	2	100%	2	100%	2	100%	2	100%
Target Dev.&Prep. Techs.			1	50%	2	100%	2	100%	2	100%	2	100%	2	100%
QA/QC Staff			1	50%	1	100%	2	100%	2	100%	2	100%	2	100%
Mechanical Techs.			1	100%	1	100%	2	100%	3	100%	3	100%	3	100%
Education & Training Staff					1	100%	1	100%	1	100%	1	100%	1	100%
Administration	1	100%	1	100%	2	100%	2	100%	2	100%	2	100%	2	100%
Total Personnel	6		13		22		30		36		40		40	

Appendix B

Labor - Unloaded Direct Salary Input

Labor Class	Salary
Director	$100,000
Research Scientists	
Radiochemist	$80,000
Pharmaceutical Chemist	$80,000
Physicist	$80,000
ES&H Scientist	$80,000
Research Associates	
Post Doctoral Associates	$35,000
Research Assistants	$32,000
Operations	
Accelerator Operators	$45,000
Health Physics Techs.	$40,000
Process/Chemical Techs.	$40,000
Target Dev.&Prep. Techs.	$40,000
QA/QC Staff	$50,000
Mechanical Techs.	$40,000
Education & Training Staff	$35,000
Administration	$26,000

Appendix B

Unloaded Direct Labor Costs

Labor Class	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Director	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000
Research Scientists							
Radiochemist	$160,000	$160,000	$160,000	$160,000	$160,000	$160,000	$160,000
Pharmaceutical Chemist	$0	$80,000	$80,000	$160,000	$160,000	$160,000	$160,000
Physicist	$80,000	$80,000	$80,000	$160,000	$160,000	$160,000	$160,000
ES&H Scientist	$20,000	$20,000	$80,000	$80,000	$80,000	$80,000	$80,000
Research Associates							
Post Doctoral Associates	$0	$0	$70,000	$140,000	$210,000	$280,000	$280,000
Research Assistants	$0	$0	$32,000	$64,000	$96,000	$128,000	$128,000
Operations							
Accelerator Operators	$0	$22,500	$67,500	$90,000	$114,750	$135,000	$135,000
Health Physics Techs.	$0	$40,000	$40,000	$40,000	$40,000	$40,000	$40,000
Process/Chemical Techs.	$0	$40,000	$80,000	$80,000	$80,000	$80,000	$80,000
Target Dev.&Prep. Techs.	$0	$20,000	$80,000	$80,000	$80,000	$80,000	$80,000
QA/QC Staff	$0	$25,000	$50,000	$100,000	$100,000	$100,000	$100,000
Mechanical Techs.	$0	$40,000	$40,000	$80,000	$120,000	$120,000	$120,000
Education & Training Staff	$0	$0	$35,000	$35,000	$35,000	$35,000	$35,000
Administration	$26,000	$26,000	$52,000	$52,000	$52,000	$52,000	$52,000
Total Direct Labor Costs	$386,000	$653,500	$1,046,500	$1,421,000	$1,587,750	$1,710,000	$1,710,000

Appendix B

Manning Summary (Heads)

Labor Class	Yr 1 Heads	Yr 2 Heads	Yr 3 Heads	Yr 4 Heads	Yr 5 Heads	Yr 6 Heads	Yr 7 Heads
Director	1	1	1	1	1	1	1
Research Scientists							
Radiochemist	2	2	2	2	2	2	2
Pharmaceutical Chemist	0	1	1	2	2	2	2
Physicist	1	1	1	2	2	2	2
ES&H Scientist	1	1	1	1	1	1	1
Research Associates							
Post Doctoral Associates	0	0	2	4	6	8	8
Research Assistants	0	0	2	4	6	8	8
Operations							
Accelerator Operators	0	1	2	2	3	3	3
Health Physics Techs.	0	1	1	1	1	1	1
Process/Chemical Techs.	0	1	2	2	2	2	2
Target Dev.&Prep. Techs.	0	1	2	2	2	2	2
QA/QC Staff	0	1	1	2	2	2	2
Mechanical Techs.	0	1	1	2	3	3	3
Education & Training Staff	0	0	1	1	1	1	1
Administration	1	1	2	2	2	2	2
Total Personnel	**6**	**13**	**22**	**30**	**36**	**40**	**40**

Appendix C

NBTF ANNUAL OPERATING EXPENSES BY NTRI EXPENSE CLASS

Expense Category	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
A. NTRI Salaries and Wages							
Staff Salaries and Wages	$260,000	$527,500	$894,500	$1,269,000	$1,435,750	$1,558,000	$1,558,000
Management Salaries	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000
Technical/Admin. Salaries	$26,000	$26,000	$52,000	$52,000	$52,000	$52,000	$52,000
B. NTRI Fringe Benefits @ 23%	$88,780	$150,305	$240,695	$326,830	$365,183	$393,300	$393,300
C. NTRI Permanent Equipment	$0	$0	$35,000	$20,000	$15,000	$15,000	$15,000
D. NTRI Expendable Equipment	$1,000	$2,000	$3,500	$4,500	$5,000	$5,000	$5,000
E. NTRI Supplies Mat'ls and Serv's							
Equipment Lease	$7,000	$14,000	$5,000	$0	$0	$0	$0
Equipment Maintenance	$0	$0	$50,000	$300,000	$450,000	$450,000	$450,000
Housekeeping	$0	$0	$22,000	$45,000	$46,000	$46,000	$46,000
Utilities	$5,000	$100,000	$200,000	$300,000	$375,000	$450,000	$450,000
Facilities Lease	$6,000	$12,000	$12,000	$0	$0	$0	$0
Office Supplies	$5,000	$5,000	$10,000	$15,000	$20,000	$20,000	$20,000
Professional Symposiums	$1,500	$3,500	$5,500	$6,300	$7,000	$7,000	$7,000
Dues and Subscriptions	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Meetings and Conferences	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Stable Isotopes	$0	$20,000	$100,000	$150,000	$225,000	$300,000	$300,000
F. NTRI Travel							
General Travel	$20,000	$15,000	$10,000	$10,000	$7,000	$7,000	$7,000
G. NTRI Publications	$0	$0	$5,000	$10,000	$10,000	$10,000	$10,000
H. NTRI Reproduction	$2,000	$4,000	$6,000	$8,000	$10,000	$10,000	$10,000
I. NTRI Communication	$6,000	$12,000	$12,000	$8,000	$9,000	$9,000	$9,000
J. NTRI Computer	$1,000	$2,000	$3,400	$4,500	$5,000	$5,000	$5,000
K. NTRI Consultants	$80,000	$125,000	$85,000	$30,000	$20,000	$20,000	$20,000
L. NTRI Subcontracts							
Waste Removal	$0	$0	$5,000	$10,000	$15,000	$15,000	$15,000
Legal Services	$30,000	$20,000	$12,000	$10,000	$10,000	$10,000	$10,000
Liability Insurance	$0	$0	$7,000	$7,000	$7,000	$7,000	$7,000
Licenses	$0	$0	$11,000	$11,000	$11,000	$11,000	$11,000
Marketing & Distribution	$0	$0	$30,000	$80,000	$80,000	$80,000	$80,000
M. NTRI Ind't Costs MTDC def @26%	$144,633	$264,499	$467,895	$697,094	$831,982	$910,078	$910,078
Subtotal Annual Expenses	$785,913	$1,406,804	$2,392,490	$3,483,224	$4,121,915	$4,500,378	$4,500,378
Other Operating Costs							
Amortization	$0	$0	$0	$833,000	$833,000	$833,000	$833,000
Total Annual Costs	$785,913	$1,406,804	$2,392,490	$4,316,224	$4,954,915	$5,333,378	$5,333,378

Appendix C

Summary of NBTF ANNUAL OPERATING EXPENSES BY NTRI EXPENSE CLASS

Expense Category	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
A. NTRI Salaries and Wages	$386,000	$653,500	$1,046,500	$1,421,000	$1,587,750	$1,710,000	$1,710,000
B. NTRI Fringe Benefits @ 23%	$88,780	$150,305	$240,695	$326,830	$365,183	$393,300	$393,300
C. NTRI Permanent Equipment	$0	$0	$35,000	$20,000	$15,000	$15,000	$15,000
D. NTRI Expendable Equipment	$1,000	$2,000	$3,500	$4,500	$5,000	$5,000	$5,000
E. NTRI Supplies Mat'ls and Serv's	$26,500	$158,500	$412,500	$825,300	$1,133,000	$1,283,000	$1,283,000
F. NTRI Travel	$20,000	$15,000	$10,000	$10,000	$7,000	$7,000	$7,000
G. NTRI Publications	$0	$0	$5,000	$10,000	$10,000	$10,000	$10,000
H. NTRI Reproduction	$2,000	$4,000	$6,000	$8,000	$10,000	$10,000	$10,000
I. NTRI Communication	$6,000	$12,000	$12,000	$8,000	$9,000	$9,000	$9,000
J. NTRI Computer	$1,000	$2,000	$3,400	$4,500	$5,000	$5,000	$5,000
K. NTRI Consultants	$80,000	$125,000	$85,000	$30,000	$20,000	$20,000	$20,000
L. NTRI Subcontracts	$30,000	$20,000	$65,000	$118,000	$123,000	$123,000	$123,000
M. NTRI Ind't Costs MTDC def @26%	$144,633	$264,499	$467,895	$697,094	$831,982	$910,078	$910,078
Subtotal Annual Operating Expenses	$785,913	$1,406,804	$2,392,490	$3,483,224	$4,121,915	$4,500,378	$4,500,378
Other Annual Costs Amortization	$0	$0	$0	$833,000	$833,000	$833,000	$833,000
Total Annual Costs	$785,913	$1,406,804	$2,392,490	$4,316,224	$4,954,915	$5,333,378	$5,333,378

Appendix B

Labor Full Time Equivalents

Labor Class	Yr 1 FTE	Yr 2 FTE	Yr 3 FTE	Yr 4 FTE	Yr 5 FTE	Yr 6 FTE	Yr 7 FTE
Director	1	1	1	1	1	1	1
Research Scientists							
Radiochemist	2	2	2	2	2	2	2
Pharmaceutical Chemist	0	1	1	2	2	2	2
Physicist	1	1	1	2	2	2	2
ES&H Scientist	0.25	0.25	1	1	1	1	1
Research Associates							
Post Doctoral Associates	0	0	2	4	6	8	8
Research Assistants	0	0	1	2	3	4	4
Operations							
Accelerator Operators	0	0.5	1.5	2	2.55	3	3
Health Physics Techs.	0	1	1	1	1	1	1
Process/Chemical Techs.	0	1	2	2	2	2	2
Target Dev.&Prep. Techs.	0	0.5	2	2	2	2	2
QA/QC Staff	0	0.5	1	2	2	2	2
Mechanical Techs.	0	1	1	2	3	3	3
Education & Training Staff	0	0	1	1	1	1	1
Administration	1	1	2	2	2	2	2
Total FTEs	**5.25**	**10.75**	**20.5**	**28**	**32.55**	**36**	**36**

Appendix C

NBTF ANNUAL OPERATING EXPENSES BY FUNCTIONAL CATEGORY

Expense Category	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year7
Personnel Related							
A. NTRI Salaries and Wages							
Staff Salaries and Wages	$260,000	$527,500	$894,500	$1,269,000	$1,435,750	$1,558,000	$1,558,000
B. NTRI Fringe Benefits @ 23%	$88,780	$150,305	$240,695	$326,830	$365,183	$393,300	$393,300
Facility Related							
C. NTRI Permanent Equipment			$35,000	$20,000	$15,000	$15,000	$15,000
D. NTRI Expendable Equipment	$1,000	$2,000	$3,500	$4,500	$5,000	$5,000	$5,000
Equipment Lease	$7,000	$14,000	$5,000				
Equipment Maintenance			$50,000	$300,000	$450,000	$450,000	$450,000
Housekeeping			$22,000	$45,000	$46,000	$46,000	$46,000
Utilities	$5,000	$100,000	$200,000	$300,000	$375,000	$450,000	$450,000
Facilities Lease	$6,000	$12,000	$12,000				
Operations Related							
E. NTRI Supplies Mat'ls and Serv's							
Office Supplies	$5,000	$5,000	$10,000	$15,000	$20,000	$20,000	$20,000
Professional Symposiums	$1,500	$3,500	$5,500	$6,300	$7,000	$7,000	$7,000
Dues and Subscriptions	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Meetings and Conferences	$1,000	$2,000	$4,000	$4,500	$5,000	$5,000	$5,000
Stable Isotopes		$20,000	$100,000	$150,000	$225,000	$300,000	$300,000
F. NTRI Travel							
General Travel	$20,000	$15,000	$10,000	$10,000	$7,000	$7,000	$7,000
G. NTRI Publications			$5,000	$10,000	$10,000	$10,000	$10,000
H. NTRI Reproduction	$2,000	$4,000	$6,000	$8,000	$10,000	$10,000	$10,000
I. NTRI Communication	$6,000	$12,000	$12,000	$8,000	$9,000	$9,000	$9,000
J. NTRI Computer	$1,000	$2,000	$3,400	$4,500	$5,000	$5,000	$5,000
K. NTRI Consultants	$80,000	$125,000	$85,000	$30,000	$20,000	$20,000	$20,000
L. NTRI Subcontracts							
Waste Management/Handling			$5,000	$10,000	$15,000	$15,000	$15,000
Marketing Related							
Marketing & Distribution			$30,000	$80,000	$80,000	$80,000	$80,000
Management Related							
Management Salaries	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000	$100,000
Technical/Admin. Salaries	$26,000	$26,000	$52,000	$52,000	$52,000	$52,000	$52,000
Legal Services	$30,000	$20,000	$12,000	$10,000	$10,000	$10,000	$10,000
Liability Insurance			$7,000	$7,000	$7,000	$7,000	$7,000
Licenses			$11,000	$11,000	$11,000	$11,000	$11,000
M. NTRI Ind't Costs MTDC def @26%	$144,633	$264,499	$467,895	$697,094	$831,982	$910,078	$910,078
Subtotal Annual Expenses	$785,913	$1,406,804	$2,392,490	$3,483,224	$4,121,915	$4,500,378	$4,500,378
Other Operating Costs							
Amortization	$0	$0	$0	$833,000	$833,000	$833,000	$833,000
Total Annual Expenses	$785,913	$1,406,804	$2,392,490	$4,316,224	$4,954,915	$5,333,378	$5,333,378

APPENDIX X

LIST OF ACRONYMS, INITIALISMS, AND ABBREVIATIONS

AAIP	Alliance of American Isotope Production
AC, ac	Alternating Current
AccSys	Accelerator Systems Technology, Inc. (Pleasanton, CA)
ACNP	American College of Nuclear Physicians
ACRR	Annular Core Research Reactor (at Sandia National Laboratories, Albuquerque, NM)
A&E	Architecture and Engineering
AEA	Atomic Energy Act
AEC	Atomic Energy Commission (superseded; functions now included in the U.S. Department of Energy)
AECL	Atomic Energy of Canada, Ltd.
AGB	Automated Glovebox Bagout
AGC	Automated Glovebox Canout
AITI	Advanced Isotope Technologies Incorporated (Denton, TX; a for-profit company dedicated to commercial isotope applications and development; originally incorporated as North Texas Research and Development Corporation — NTR&D)
ALARA	As Low as Reasonably Achievable
AMS	Accelerator Mass Spectrometry
ANL	Argonne National Laboratory (Chicago, IL)
ANS	Advanced Neutron Source (proposed nuclear reactor, Oak Ridge National Laboratory, TN)
ANL	Argonne National Laboratory
atm	Atmosphere (pressure)
AVLIS	Atomic Vapor Laser Isotope Separation
BLIP	Brookhaven Linac Isotope Production facility (Long Island, NY)
BNL	Brookhaven National Laboratory (Long Island, NY)
BRC	Below Regulatory Concern
CAA	Clean Air Act
CAT	Computerized Axial Tomography (also CT)
CCDTL	Coupled Cavity Drift Tube Linac
CCL	Cavity Coupled Linac
CEBAF	Continuous Electron Beam Facility (Newport News, VA)
CeRaM	Center for Radioactive Waste Management (at the University of New Mexico)
CEU	Continuing Education Unit (academic credit)
cfm	Cubic Feet per Minute
CFR	Code of Federal Regulations
CHF	Critical Heat Flux

Ci	Curie (measure of radioactivity)
μCi	Microcurie (measure of radioactivity)
CME	Continuing Medical Education (units for academic credit)
CRADA	Cooperative Research and Development Agreement
CRISLA	Chemical Reaction by Isotope Selective Laser Activation
CT	Computerized Tomography (also CAT)
CWA	Clean Water Act
D^+	Deuteron (positively charged deuterium ion)
DC, dc	Direct Current
DFW	Either Dallas-Fort Worth International Airport or the Dallas-Fort Worth-Denton Metropolitan Area (also DFW Metroplex or Metroplex)
DOE	Department of Energy
DOD	Department of Defense
DPF	Dense Plasma Focus
DTL	Drift Tube Linac
EA	Environmental Assessment
Ebco	Ebco Technologies, Inc. (Vancouver, BC)
EIA	Environmental Impact Assessment
ENDF	Evaluated Nuclear Data File
EPA	Environmental Protection Agency
ERDA	Energy Research and Development Agency (functions now incorporated in the U.S. Department of Energy)
ES&H	Environment, Safety, and Health
FDA	U.S. Food and Drug Administration
eV	Electron Volt
FFTF	Fast-Flux Test Facility (Richland, WA)
FONSI	Finding of No Significant Impact
FREC	Fueled Ring External
GAO	U.S. General Accounting Office
GIF	Gamma Irradiation Facility (Sandia National Laboratories, Albuquerque, NM)
GLA	General Licensing Agreement
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
H^-	Negatively charged hydrogen ion
H^+	Positively charged hydrogen ion (proton)
HARC	Houston Area Research Consortium (Houston, TX)
HCF	Hot Cell Facility (at Sandia National Laboratories, Albuquerque, NM)
HEPA	High-Efficiency Particulate Air (filter)
HPLC	High Performance Liquid Chromatography
HVAC	Heating, Ventilation, Air Conditioning
HVPS	High Voltage Power Supply
Hz	Hertz (cycles per second)

IBA	Ion Beam Applications s.a. (cyclotron manufacturer, Louvain-la-Neuve, Belgium)
IBMAL	Ion Beam Modification and Analysis Laboratory (at UNT, Denton, TX)
IDM	International Digital Modeling Corporation, Inc. (Austin, TX)
INEL	Idaho National Engineering Laboratory
IND	Investigative New Drug (application)
IOM	Institute of Medicine (of the National Academy of Sciences)
IP	Isotope Production
IPDP	Isotope Production and Distribution Program (of the U.S. Department of Energy)
IPF	Isotope Production Facility (at LANL/LAMPF, NM)
IR, ir	Infrared
IRE	Institut National des Radioélélements (Belgium)
ISRC	Intelligent Systems and Robotics Center (Sandia National Laboratories, Albuquerque, NM)
I/UCRC	Industry/University Cooperative Research Center (UNT, Denton, TX)
MJ	Mega Joule
KAFB	Kirtland Air Force Base (Albuquerque, NM)
keV	Kilo Electron Volts
KW, kW	Kilowatt
KWH, kWh	Kilowatt Hour
k$	$1,000
LAMPF	Los Alamos Meson Physics Facility (NM)
LANL	Los Alamos National Laboratory (NM)
LNL	Lawrence Berkeley Laboratory (CA)
LCW	Low Conductivity Water
Linac	Linear Particle Accelerator
LLNL	Lawrence Livermore National Laboratory
LLRW	Low Level Radioactive Waste (same as LLW)
LLW	Low Level Waste (same as LLRW)
LLLW	Low Level Liquid Waste
LLRW	Low Level Radioactive Waste
μA	Microampere
mA	Milliampere
mb	Millibarns (nuclear reaction cross section measurement)
MCHFR	Minimum Critical Heat Flux Ratio
mCi	Millicurie (measure of radioactivity)
MCNP	Monte Carlo Neutronic Program
MeV	Million Electron Volts
MJ	Mega Joule
MLIS	Multiple-Photon Laser Isotope Separation
mr	Millirad (radiation exposure measure)
MRI	Magnetic Resonance Imaging (formerly NMR)
MSDS	Material Safety Data Sheets

ms, msec	Millisecond
MU	University of Missouri — Columbia
MURR	University of Missouri Research Reactor Center, Columbia
MW	Mixed Waste or Megawatt
MW-y	Megawatt-year
NAE	National Academy of Engineering
NAS	National Academy of Sciences
NBTF	National Biomedical Tracer Facility (proposed)
NEPA	National Environmental Policy Act
NESHAP	National Emission Standards for Hazardous Air Pollutants
NIP	National Isotope Program (proposed)
NIH	National Institutes of Health
NIST	National Institute of Science and Technology (formerly U.S. Bureau of Standards)
NMCNM	Nuclear Medicine Consortium of New Mexico
NMR	Nuclear Magnetic Resonance (now MRI)
Nox	Nitrogen Oxides (NO_2, NO_3, etc.)
NPR	New Production Reactor (ID)
NRC	Nuclear Regulatory Commission or National Research Council
NSF	National Science Foundation
NTR&D	North Texas Research and Development Corporation (Denton, TX; a forerunner of AITI, now a subsidiary)
NTRI	North Texas Research Institute (Denton, TX; a not-for-profit corporate affiliate of UNT)
OER	U.S. DOE Office of Energy Research
OHENP	U.S. DOE Office of High-Energy and Nuclear Physics
OHER	U.S. DOE Office of Health and Environmental Research
ORAU	Oak Ridge Associated Universities (TN)
ORNL	Oak Ridge National Laboratory (TN)
OMB	U.S. Office of Management and Budget
OSHA	Occupational Health and Safety Administration
OU	University of Oklahoma (Norman and Oklahoma City, OK)
OUHSC	University of Oklahoma Health Science Center (Oklahoma City, OK)
PET	Positron-Emission Tomography
PMQ	Permanent Magnet Quadrupole
ppm	Parts per Million
pps	Pulses per Second
PSI	Paul Sherrer Institut (Villigen, Switzerland)
PTF	Proton Therapy Facility (proposed, based on SSC assets)
QA	Quality Assurance
QC	Quality Control
RAM	Radioactive Materials *or* Reliability, Availability, Maintainability

RCC	Radiochemical Company (a division of AECL)
R&D	Research and Development
RF, rf	Radio Frequency
RFP	Request for Proposal
RFQ	Radio-Frequency Quadrupole
RPF	Radioisotope Production Facility (proposed, based on SSC assets)
RML	Radiation Metrology Laboratory (at Sandia National Laboratories, Albuquerque, NM)
RMTC	Regional Medical Technology Center (proposed, based on SSC assets)
SAIC	Science Applications International Corporation
SAND II	Neutron Spectrum Adjustment Code
SBIR	Small Business Innovative Research (grant)
SDI	Strategic Defense Initiative
SLAC	Stanford Linear Accelerator Center (CA)
SFI	Santa Fe Institute (NM)
SPR III	Sandia Pulse Reactor III
Sv	Sievert (radiation exposure measure)
SNL	Sandia National Laboratory
SNM	Society of Nuclear Medicine
Sox	Sulfur Oxides
SPECT	Single-Photon-Emission Computed Tomography
SREB	Southern Regional Education Board
SSC	Superconducting Super Collider
SSCL	SSC Laboratory
SURA	Southern University Research Association
SwRI	Southwest Research Institute (San Antonio, TX)
SWU	Separative Work Unit
$/$\mu$A-hr	Cost per Microampere-Hour
TEAMS	Trace Element AMS
TCI	Technology Commercialization International, Inc. (Albuquerque, NM)
TNRLC	Texas National Research Laboratory Commission
TRCR	Texas Radioactive Control Regulations
TRIUMF	Tri-University Meson Facility (Vancouver, BC)
TSTC	Texas State Technical College (system)
TTI	Technology Transfer International, Inc. (Albuquerque, NM)
μA	Microampere
μCi	Microcurie
UM	University of Missouri System
UNM	University of New Mexico (Albuquerque, NM)
UNT	University of North Texas (Denton, TX)
URA	Universities Research Association (Fermilab and former SSC management group)
USIC	United States Industry Coalition

μs, μsec	Microsecond
UTSMC	University of Texas Southwestern Medical Center at Dallas
UV, uv	Ultraviolet
VAC	Vacuum Arc Centrifuge (isotope separation method)
VOC's	Volatile Organic Compounds
WPCA	Water Pollution Control Act
WERC	Waste Management Education and Research Consortium (NM)
WM	Waste Management
Wmin	Waste Minimization

Appendix D

MARKET POTENTIAL BY REVENUE CATEGORY and ESTIMATED MARKET PENETRATION

Revenue Category	Market Potential	Year 1 % of Mkt	Year 2 % of Mkt	Year 3 % of Mkt	Year 4 % of Mkt	Year 5 % of Mkt	Year 6 % of Mkt	Year 7 % of Mkt
Nuclear Medicine Community								
Imaging Radionuclides	$5,000,000			2%	5%	13%	20%	30%
Therapy Radionuclides	$1,200,000			4%	8%	15%	30%	60%
Industrial Radionuclides	$1,500,000			15%	30%	40%	50%	60%
Biomedical/Specialty Life Sciences Radionuclides	$500,000			10%	20%	40%	60%	75%
Radiopharmaceutical Companies								
R&D Contracts	$1,000,000			10%	20%	30%	40%	50%
Service Irradiations	$1,000,000			10%	20%	30%	40%	50%
Low Demand Comercial Products	$1,000,000			10%	20%	30%	40%	50%
Tech. Transfer and Royalties	$500,000			0%	0%	20%	35%	50%
Production Rights Advance	$1,500,000	50%	50%					
AITI								
R&D Support	$600,000			50%	50%	50%	50%	50%
Backup Production	$1,390,000			20%	40%	50%	60%	70%
Department of Energy								
Education and Training	$5,000,000			5%	10%	15%	18%	20%
R&D Grants and Contracts	$5,000,000	10%	10%	10%	15%	18%	22%	25%
Other Federal Agencies								
R&D Grants and Contracts	$5,000,000			10%	10%	10%	10%	10%
States of TX,OK,NM								
Education and Training	$300,000			50%	50%	50%	50%	50%
Professional Training								
Cont. Educ. & Distance Learning	$500,000			5%	10%	15%	20%	25%
Totals	$30,990,000							

Appendix D

ESTIMATED ANNUAL REVENUE BY CATEGORY

Revenue Category	Year 1 Est'd. Rev.	Year 2 Est'd. Rev.	Year 3 Est'd. Rev.	Year 4 Est'd. Rev.	Year 5 Est'd. Rev.	Year 6 Est'd. Rev.	Year 7 Est'd. Rev.
Nuclear Medicine Community							
Imaging Radionuclides	$0	$0	$100,000	$250,000	$650,000	$1,000,000	$1,500,000
Therapy Radionuclides	$0	$0	$48,000	$96,000	$180,000	$360,000	$720,000
Industrial Radionuclides	$0	$0	$225,000	$450,000	$600,000	$750,000	$900,000
Biomedical/Specialty Life Sciences Radi	$0	$0	$50,000	$100,000	$200,000	$300,000	$375,000
Radiopharmaceutical Companies							
R&D Contracts	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Service Irradiations	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Low Demand Comercial Products	$0	$0	$100,000	$200,000	$300,000	$400,000	$500,000
Tech. Transfer and Royalties	$0	$0	$0	$0	$100,000	$175,000	$250,000
Production Rights Advance	$750,000	$750,000					
AITI							
R&D Support	$0	$0	$300,000	$300,000	$300,000	$300,000	$300,000
Backup Production	$0	$0	$278,000	$556,000	$695,000	$834,000	$973,000
Department of Energy							
Education and Training	$0	$0	$250,000	$500,000	$750,000	$900,000	$1,000,000
R&D Grants and Contracts	$500,000	$500,000	$500,000	$750,000	$900,000	$1,100,000	$1,250,000
Other Federal Agencies							
R&D Grants and Contracts	$0	$0	$500,000	$500,000	$500,000	$500,000	$500,000
States of TX,OK,NM							
Support for Education and Training	$0	$0	$150,000	$150,000	$150,000	$150,000	$150,000
Professional Training							
Cont. Educ. & Distance Learning	$0	$0	$25,000	$50,000	$75,000	$100,000	$125,000
Totals	$1,250,000	$1,250,000	$2,726,000	$4,302,000	$6,000,000	$7,669,000	$9,543,000

Appendix D

ESTIMATED ANNUAL REVENUE BY SOURCE TYPE

Revenue by Source Typ	Year 1 Est'd. Revenue	Year 2 Est'd. Revenue	Year 3 Est'd. Revenue	Year 4 Est'd. Revenue	Year 5 Est'd. Revenue	Year 6 Est'd. Revenue	Year 7 Est'd. Revenue
Nongovernment	$750,000	$750,000	$1,301,000	$2,352,000	$3,625,000	$4,919,000	$6,518,000
Federal Government	$500,000	$500,000	$1,250,000	$1,750,000	$2,150,000	$2,500,000	$2,750,000
State Governments	$0	$0	$150,000	$150,000	$150,000	$150,000	$150,000
Professional Trainees	$0	$0	$25,000	$50,000	$75,000	$100,000	$125,000
Total	**$1,250,000**	**$1,250,000**	**$2,726,000**	**$4,302,000**	**$6,000,000**	**$7,669,000**	**$9,543,000**

Appendix E

NBTF Project Construction Cost Estimate

		W.O. Contingency	Contingency Incl.
Project Total		$23,583,000	$24,913,000
Equipment Total		$18,093,000	$18,639,000
Cyclotron	$13,563,000		
Beamlines	$1,800,000		
Target Stations	$300,000		
Target Transfer Systems	$150,000		
Education,Training, &Res. Hot Lab Equipment	$500,000		
*****Processing Equipment Supplied by AITI	$0		
Laboratory Equipment	$575,000		
Laboratory Furniture	$225,000		
General Facility Furnishings	$100,000		
Auditorium Furnishings	$100,000		
Control & Safety Systems	$250,000		
Shop Equipment	$100,000		
Exhaust Systems	$100,000		
Target Station Caves	$200,000		
Chilled Water System	$80,000		
Deionized System	$50,000		
Facilities Total		$3,920,000	$4,704,000
Architect	$180,000		
A-E	$300,000		
Construction Total		$3,440,000	
Below Grade Facilities Total		$480,000	
Accelerator Vault (Modification of Existing Facilit	$50,000		
Tunnels	$65,000		
Waste Tank Containment Vault	$50,000		
Above Grade Facilities Total		$2,960,000	
Control Building	$160,000		
Res, Education & Training Building	$2,500,000		
*****Processing Facility supplied by AITI	$0		
Waste Holding & Reduction Facility	$200,000		
Site Preparation	$100,000		
ES&H Total		$1,570,000	$1,570,000
ES&H Systems Total		$570,000	
Storage Tanks	$150,000		
Stack	$100,000		
Stack Monitoring	$80,000		
Water Monitoring	$80,000		
Air Monitoring	$80,000		
Personnel Monitoring	$40,000		
Waste Monitoring	$40,000		
ES&H Compliance Programs		$1,000,000	