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National Biomedical Tracer Facility (NBTF)
PROJECT DEFINITION STUDY: Phase I

Submitted by
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Submitted to
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*Manuel C. Lagunas-Solar, Principal Investigator
Crocker Nuclear Laboratory, UC Davis
February 1995*

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L. N. VANDERHOEF
Chancellor at Davis

February 14, 1995

Dr. Manuel C. Lagunas-Solar
Principal Investigator/Project Director
National Biomedical Tracer Facility Project
Crocker Nuclear Laboratory
University of California, Davis

Dear Dr. Lagunas-Solar:

UC Davis Support to the National Biomedical Tracer Facility

The University of California, Davis is pleased to declare its support for the establishment and commissioning of the National Biomedical Tracer Facility (NBTF) at UC Davis. There are several optional sites at the main campus or at equivalent sites at the UC Davis Medical Center in Sacramento. This project fits within our Long Range Development Plan and it has been discussed by the UC Davis Facilities and Enterprise Policy Committee.

We recognize that the objective of NBTF to provide and secure a broad and reliable national inventory of research radioisotopes is also critically important to our mission of teaching, research and public service. UC Davis has approximately 1,000 users of radiotracers and is completing plans for the installation of a new Environmental Services Facility to expand our capabilities for waste management. Many teaching and research faculty would benefit greatly by having access to the resources which would be provided by NBTF. The location of this facility within UC Davis would also strengthen our educational and outreach activities in the Northern California region.

The educational activities and access to the resources planned for NBTF will enhance the University's teaching, outreach and extension programs. NBTF will also be an important factor in attracting top students, researchers and faculty as well as broadening the scope of teaching and research opportunities at UC Davis.

Sincerely,

Larry N. Vanderhoef
Chancellor

February 14, 1995

Dr. Manuel C. Lagunas-Solar
Principal Investigator/Project Director
National Biomedical Tracer Facility Project
Crocker Nuclear Laboratory
University of California, Davis

National Biomedical Tracer Facility Project Definition Study

Dear Dr. Lagunas-Solar:

The Office of Research has fully supported your direction and will continue to provide its resources to develop and expand the current vision that has evolved from the Project Definition Study for the National Biomedical Tracer Facility (NBTF). We view this project as an opportunity to renew and strengthen our commitment to the nuclear sciences and applications, and to expand its impact on many basic and applied research areas, as well as to strengthen our mission and commitment to undergraduate and graduate education.

The Davis Campus has many existing academic and research organizations, such as the School of Medicine and the UC Davis Medical Center in Sacramento, the School of Veterinary Medicine, the Primate Center, and many others, which we could integrate into the mission of NBTF. As we maintain and promote many academic collaborations with the National Laboratories, with the other Northern California UC campuses (Berkeley, San Francisco, Santo Cruz) and non-UC academic institutions (Stanford University, California State University at San Jose), and with a network of clinical research and health-care institutions in the region, we anticipate that NBTF could become a unique and powerful resource for the nation and for the Northern California region.

As prospects for this project grow, we will continue to provide our support and resources.

Sincerely,

Robert N. Shelton
Vice Chancellor for Research

RNS/DGC/aek

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EXECUTIVE SUMMARY

NBTF is viewed as a national resource with clearly defined research and education missions in addition to its primary mission of radioisotope production. NBTF research will support, expand, and improve the facility's technological resources and advance the radioisotope production technologies. Basic research in the nuclear sciences will be conducted only as it relates to the objectives of NBTF. Education activities will be focused on establishing formal academic programs for basic and applied research scientists and technicians. Outreach activities will project NBTF to the scientific community and general public as a Center of Excellence, and will focus on the segment of the scientific community that uses radiotracer technologies.

In this Phase I Project Definition Study, NBTF has been designed to fulfill all the current and anticipated inventory needs for research and industrial radioisotopes. The establishment of the NBTF proposed in this report will permit the United States to lead in the accelerator-based radioisotope production technologies and their applications for decades to come.

The heart of the system, as proposed in this report, is its two cyclotrons:

- a 100–30 MeV (1–2 mA) negative ion, single particle (H^-) cyclotron (which will be the first high-intensity, high-energy cyclotron to be built as a dedicated radioisotope production machine), and
- a 40–10 MeV (1–2 mA) negative ion, single particle (H^-) cyclotron (which is based on existing commercial 30 MeV cyclotron design).

In addition to the two cyclotrons, the proposed NBTF will include:

- a neutron source,
- eight target areas and an array of nine hot-cells,
- research, production, and radioanalytical laboratories, and
- a GMP (Good Manufacturing Practices) facility.

This configuration will make NBTF the most powerful resource in the world dedicated to radioisotope production.

NBTf has been designed to provide maximum operating flexibility. Two extracted beams (operating at two different energies, if desired) can be used simultaneously by sharing up to 1 mA (upgradable to 2 mA) in multiple target areas. Different isotopes can be produced simultaneously, with up to four targets being bombarded per cyclotron.

With this facility, we will be able to

- produce research and industrial radioisotopes
- produce research quantities of neutron-rich radioisotopes
- perform pre- and clinical studies of new radiopharmaceuticals in collaboration with the private sector
- conduct R&D on topics such as:
 - beam technology
 - targetry technology
 - nuclear reactions
 - target/product radiochemistry
 - robotics and automation for radiochemical and radiopharmaceutical syntheses

All of the needed research and industrial inventory of neutron-deficient isotopes are available with the operational proton energy range proposed for NBTF. In partnership with the private sector — which at present relies mostly on the operation of <30 MeV cyclotrons — the lower energy range capability will allow NBTF to support the development of new ready-to-transfer radioisotope production methods; development and testing of new high-power target technologies; and production of new or existing radioisotopes for pre- and clinical trials. The <20 MeV proton energy capability will support R&D on the production of short-lived positron-emitting radioisotopes. The overlap between the cyclotrons in the 40–30 MeV range will allow either cyclotron to be used to fulfill the production needs for long-lived isotopes used as industrial sources and in research.

The 100–30 MeV cyclotron will also allow establishing resources to produce research quantities of neutron-rich isotopes based on intense accelerator-produced neutron fluxes from metallic targets. The availability of an accelerator-based neutron source would then allow NBTF to explore innovations in radioisotope production technologies heretofore within the exclusive domain of reactor facilities. Therefore, we envision NBTF as a facility utilizing and integrating all the needed resources to become a driving force in every aspect of radioisotope production technologies.

Our estimated capital costs for a fully operational NBTF total just under \$50 million. This estimate includes all costs associated with designing , constructing, installing, licensing, and commissioning, as follows.

Preliminary NBTF Capital Cost Estimates (\$ Million, 1995 dollars)

Accelerators (100–30 MeV and 40–10 MeV cyclotrons)	17.0
Beamlines (8); Target Caves (8); Targetry Systems	5.7
NBTF Facility (including shielding)	11.0
Research, Production, and Other Laboratories (≈9,000 sq.ft)	11.1
Support Facilities (machine/electronic shops, computer facility, etc.)	2.0
Other Capital Costs (A&E, professional fees, reviews & approvals, etc.)	3.1
Total	49.9

Operating expenses for the proposed NBTF are estimated at \$5.23 million, and include projected costs for personnel (management and staff) and for operation of the facility. The latter includes telephones, computer maintenance, security, vehicles, site equipment rental and services, utilities, waste management, supplies, and program support.

Preliminary NBTF Annual Operating Expenses (\$ Million, 1995 dollars)

Management and Staff (45 FTE)	2.70
All Other Expenses	2.53
Total	5.23

A business plan, driven by market considerations, was developed on the basis of recent radioisotope marketing data. Existing market studies, including data from the operation of DOE's Isotope Production and Distribution Program, were utilized. Annual revenue from a fully operational NBTF was estimated to be from \$4.75 million to \$8.60 million:

Total Estimated NBTF Annual Revenue

FIRM	\$4.75M	LIKELY	\$5.95M	OPTIMISTIC	\$8.60M
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A radioisotope plan based on the overall production capabilities of the proposed NBTF was also developed during the study. Although derived from different perspectives, both plans are based on conservative estimates and easily-achievable management and operational factors. The economic goals and boundaries established in the business plan were proven to be well within the production capabilities established in the radioisotope plan. Ten "revenue" isotopes to be produced by NBTF were identified (the "Big Ten"), and we established that their production can be accomplished without any limitations on the routine availability of research isotopes. We therefore conclude that NBTF can become an economically viable facility while also achieving its support mission of maintaining a national research isotope inventory.

A five-year construction and commissioning plan is designed around well-known, operationally tested subsystems to provide a conservative, reliable base for this unique facility.

During the first three-and-a-half years the facility, the cyclotrons, and the support laboratories and equipment will be designed, specified, constructed, and placed in operation. The

commissioning of the cyclotrons will be staggered (the 40–10 MeV cyclotron being commissioned first), thus enabling some NBTF products to be available for delivery to end-users by the close of the fourth year. Full commissioning of NBTF is expected by the end of the fifth year.

Although we do not anticipate direct repayment of capital costs, the scope of NBTF should provide good return on the investment for the nation as a whole. NBTF will support and advance the technology on which a multi-million-dollar health care industry is based. The application of nuclear science has had a huge impact on diagnostic medicine; current research indicates that its future impact may be even greater on therapeutic medicine.

After analyzing several potential administrative and organizational structures, we concluded that in order for NBTF to achieve its goals and objectives, it should be established as an independent organization under DOE sponsorship, operated in a major research university environment, and generally administrated by a National Research Steering Committee composed of leading academic and private-sector scientists. In this manner, as a model for potential privatization and avoidance of micro-administration, NBTF could become an effective and functional resource serving the nation's scientific community and general public.

Finally, we concluded that plans leading to its construction and commissioning should be continued into Phase II because NBTF as proposed is technically feasible, economically viable, and capable of fulfilling critical needs in supporting and advancing the research and educational missions of the scientific community in the United States.

0.0 INTRODUCTION: OVERVIEW OF MISSION

This report describes a five-year plan for the construction and commissioning of a reliable and versatile NBTF facility for the production of high-quality, high-yield radioisotopes for research, biomedical, and industrial applications.

The report is organized in nine sections providing, in consecutive order, responses to the nine questions posed by the U.S. Department of Energy in its solicitation for the NBTF Project Definition Study.* In order to preserve direct correspondence (e.g., Sec. 3 = 3rd item), this Introduction is numbered "0." Accelerator and facility designs are covered in Section 1 (Accelerator Design) and Section 2 (Facility Design). Preliminary estimates of capital costs are detailed in Section 3 (Design and Construction Costs). Full licensing requirements, including federal, state, and local ordinances, are discussed in Section 4 (Permits). A plan for the management of hazardous materials to be generated by NBTF is presented in Section 5 (Waste Management). An evaluation of NBTF's economic viability and its potential market impact is detailed in Section 6 (Business Plan), and is complemented by the plans in Section 7 (Operating Plan) and Section 8 (Radioisotope Plan). Finally, a plan for NBTF's research, education, and outreach programs is presented in Section 9 (Research and Education Programs).

Although siting was not an issue for the Phase I study, our study has been based on the assumption that NBTF is located in Northern California, where it would interact with the rich existing network of major research universities, medical centers, and relevant industries. Many of the features and programmatic objectives were defined on the basis of the resources available in the Northern California region.

* Department of Energy, Office of Energy Research: Solicitation for a Project Definition Study for the National Biomedical Tracer Facility (NBTF); presented in the *Federal Register* of October 14, 1993 (Vol. 58, No. 197); Supplemental Information, pp. 3-4. The original list of 9 items to be covered is included as Appendix G in this Phase I Project Definition Study report.

The heart of the NBTF, as proposed in this study, is its two cyclotrons:

- a 100–30 MeV (1–2 mA) negative ion, single particle (H^-) cyclotron, and
- a 40–10 MeV (1–2 mA) negative ion, single particle (H^-) cyclotron.

In addition to the two cyclotrons, the proposed NBTF will include:

- a neutron source;
- eight target areas;
- an array of nine hot-cells;
- research, production, and radioanalytical laboratories; and
- computer, mechanical, and electronic shops for support of the various accelerator and research operations.

The design, development, engineering, construction, and full commissioning of the facility will require 5 years. Following the design-and-build phase (3.5 years for full construction and start-up of accelerators), a 1.5-year initial operations and commissioning phase is anticipated. Limited operation during the fifth year will allow NBTF to test and validate the equipment, train staff, and deliver initial products.

0.1 RADIOISOTOPE PRODUCTION TECHNOLOGIES

Previous studies and workshops established basic guidelines concerning NBTF's objectives [Moody & Petersen, 1989; Holmes, 1991; Kliewer & Green, 1992; see App. F]. Consistent mission statements evolved from these reports, indicating that NBTF's main objective should be to advance accelerator-based radioisotope production technologies. It was also implied, by identifying a series of needed radioisotopes for research, that NBTF should be implemented as a dedicated national resource focused on the production and distribution of accelerator-made neutron-deficient radioisotopes.

However, as a result of our Phase I Project Definition Study, we envision an NBTF capable of providing both proton and neutron beam capabilities and dedicated to exploring all the relevant aspects of both of these radioisotope production technologies. This is technically feasible and is advisable on many grounds. Technological resources are available for investigating alternatives to reactor-based radioisotope production technologies as well for advancing accelerator-based radioisotope production technologies. Both are key missions that should be undertaken by NBTF. Although this is a clear departure from its previously conceived mission, we feel that this dual research mission is essential to a well-planned NBTF.

0.1.1 Accelerator-Based Radioisotope Production Technology

Accelerator-based radioisotope production began as a commercial activity in the United States in the late 1960s, when Medi-Physics Inc., then located in Emeryville, California, began producing and distributing Fluorine-18 and Iodine-123. Accelerator-produced radioisotopes have a low neutron-to-proton ratio and are thus known as neutron-deficient isotopes. These isotopes are generally characterized by short half lives (minutes to a few days); decay modes such as electron capture (releasing a cascade of Auger electrons), isomeric transition, and positron decay; and relatively low energy gamma-ray emissions. These physical properties make the accelerator-based isotopes well suited for use as tracers or as sources in diagnostic medical procedures as well as in a variety of other scientific and industrial applications. The production of accelerator-based, neutron-deficient isotopes is critical as it supports multi-billion-dollar industries such as medicine and diagnostic imaging instrumentation.

Today, nearly 30 commercially operated cyclotrons are in use at about 10 locations worldwide for the production of medical and industrial isotopes. However, none of these commercial facilities has capabilities approaching those proposed for NBTF. Many are operating at maximum capacity, and none has the surplus capacity or the budget required to undertake research. Technology transfer of NBTF-developed technologies to the commercial sector could

help these companies keep up with the growing demand for a routine supply of accelerator-produced radioisotopes for the commercial market.

0.1.2 Reactor-Based Radioisotope Production Technology

Reactors are also used in commercial radioisotope production, as they provide an excellent and reliable source of neutrons in high fluxes. Nuclear reactions (n ,capture; n ,fission) have been applied commercially with great success to produce neutron-rich isotopes. These isotopes are generally characterized by longer half lives (days or longer) and particle (β) decay processes, making them appropriate as high-dose emitters, primarily in cancer therapy applications.

The proliferation and easy access to neutrons in the early 1960s prompted a focus on developing reactors as sources of radioisotopes — using government subsidized reactor research facilities — and resulted in the large inventory of medical, industrial, and research radioisotopes now in use. Among nuclear medicine's most heavily used diagnostic and therapeutic radioisotopes, Technetium-99m (from the decay of Molybdenum-99) and Iodine-131 are reactor products. Their production today is based on a handful of aging, government-subsidized reactor facilities operating in foreign countries.

Many reactor-produced isotopes are now becoming scarce, as the remaining reactor facilities are concentrating their activities on a few highly-profitable isotopes. The supply and routine availability of many reactor-produced research isotopes has already been affected. The availability of reactor-produced research isotopes in the future is expected to be even further reduced as many reactors are decommissioned because of their age, financial health, or public concerns about health and the environment.

Today, while the use of accelerators for radioisotope production continues to expand, the future use of reactors for radioisotope production is uncertain. None has operated in the United States since 1991. In January 1991, potentially serious problems developed at the Chalk

River Laboratories operated by Atomic Energy of Canada (AECL) for the National Research Council of Canada. It is estimated that AECL produces nearly 90% of the worldwide production needs for Molybdenum-99.* Partly in response to the threat to medical care in the United States posed by the Chalk River scare, the U.S. Department of Energy's Isotope Production and Distribution Program developed a plan for a national strategy (*U.S. Department of Energy National Isotope Strategy*, August 1994).

Although a commercial reactor dedicated solely to radioisotope production is expected by the end of the century in Canada, this project (MAPLE X) has remained stalled in the planning stage since the early 1990s, and has encountered public opposition as well as lengthy financial and legal reviews. Current difficulties are due to its increased projected capital costs and to many questions regarding future financial liability for its ultimate decommissioning and waste management costs.

Even assuming that MAPLE X is eventually built, total reactor capacity worldwide is diminishing as most decommissioned reactors are not being replaced. Further, MAPLE X is being tailored to the production of Molybdenum-99 and a few other commercially attractive radioisotopes. Therefore, MAPLE X is not to be considered as a forthcoming solution to the expected restrictions in the traditionally rich spectrum of reactor isotopes which have been generally available since the 1970s. The full spectrum of the current inventory of reactor radioisotopes is then also in jeopardy and is expected to be reduced in the future.

Our concept in designing the NBTF proposed in this study is based on available technical resources that allow using proton accelerators as a means to generate high-intensity neutron fluxes ($>10^{13}$ n/cm²sec at <0.625 eV) which are nearly equivalent to neutron fluxes available

* This product is distributed by Nordion International Inc., a commercial subsidiary of AECL, in Kanata (Ottawa). Although Nordion is currently purchasing excellent quality, low-priced radioisotopes from a Russian source, marketplace uncertainty precludes reliance on this source.

from reactors. By adding a neutron research facility to the conventional features of a proton accelerator facility, the development of alternatives to reactor neutron fluxes can be explored.

0.2 UNDERLYING TECHNOLOGICAL, ECONOMIC, AND LOGISTIC FACTORS

The following factors greatly influenced the conclusions and recommendations summarized in this report:

(a) Accelerator Design and Capabilities NBTF is designed to provide superior technologies in accelerated proton energies (100–30 MeV and 40–10 MeV), beam intensity (1 mA, upgradable to 2 mA for each accelerator), and the ability for each accelerator to irradiate two targets simultaneously (by sharing up to 1 mA, upgradable to 2 mA).

This accelerator capability will enable NBTF to rapidly process, separate, control, and distribute radioisotope products throughout the United States.

(b) Neutron Beam Capability A proton-to-neutron conversion target and research area will allow investigation of alternatives to reactor technologies. By developing high-intensity conversion targets, we expect to be able to produce research amounts of current and new neutron-rich (β -emitting) radioisotopes.

We anticipate integrating the numerous efforts now being conducted at various national laboratories for the development of accelerators as sources of intense neutron beams for a variety of defense and non-defense purposes.

(c) Revenue Projections The NBTF revenue projections in this study are based on existing needs for certain well-established radioisotopes (firm estimates), on increased use for other research radioisotopes (likely estimates), and on an expectation of improving the nation's inventory and research use of many other radioisotopes (optimistic estimates).

NBTF's economic viability will be largely dependent on its capabilities to produce large quantities of the "revenue" isotopes — safely, routinely, reliably, and at low cost. NBTF is designed to be capable of accomplishing its research and education missions while at the same time operating an effective

production program for the revenue isotopes. To remain competitive in the face of rapidly changing market forces, NBTF should also have an administrative structure capable of rapid adjustment.

(d) Research vs. Services Balance A critical aspect of these revenue projections is the linkage between the production capabilities of NBTF and the balance between the demands for research and industrial radioisotopes. Research demands usually can be satisfied with relatively low intensity, short bombardments, but operational flexibility (including a diversity of targets and radiochemical facilities) is required. This results in a low volume production of a broad spectrum of radioisotopes with a relatively low level of revenue. On the other hand, industrial radioisotopes (i.e., Cadmium-109, Cobalt-57, Germanium-68, Palladium-103, and other long-lived isotopes) require high volume, long and high-intensity bombardments, dedicated facilities, and the allocation of larger fractions of the operational schedules.

To balance these two opposing requirements, NBTF has been designed as a two-cyclotron facility covering the entire 100–10 MeV proton energy range, with each cyclotron capable of high efficiency operation (1 mA beam each) and sufficiently versatile to allow the execution of various simultaneous tasks (four target caves per cyclotron). In addition, to cover future market demands, NBTF (including its shielding) has been designed to accommodate future upgrade to 2 mA per cyclotron.

(e) Research Focus The R&D activities will focus on relevant aspects of the nuclear sciences and its applications, including nuclear physics (nuclear reaction mechanisms, cross sections), radiochemistry (new separation techniques), and radiopharmaceutical chemistry (rapid radiolabeling reactions). Other applied areas, such as material sciences (high-power targetry) and particle physics (beam diagnosis and transport), are also expected to provide opportunities to advance new technologies for radioisotope production.

(f) Technology Transfer Many of the technological advances made at NBTF are expected to be transferred to commercial radioisotope production communities around the world. Examples include improved targetry technology and target/product radiochemistry. In addition, and in coordination with the

radiopharmaceutical and biotechnology industries, NBTF could support pre- and clinical trials and feasibility studies for a variety of products requiring the use and application of radiotracer techniques. These activities would take place — under strict confidentiality agreements — at the Good Manufacturing Practices (GMP) facility planned at the UC Davis Medical Center in Sacramento.

0.3 ADMINISTRATIVE OPTIONS FOR NBTF

Uncertainties exist on the options available for establishing NBTF and for structuring its administration in relation to existing and proposed programs at the U.S. Department of Energy, namely the current Isotope Production & Distribution Program (IPDP) and the proposed Isotopes-USA consortium. There was a tacit expectation in the solicitation leading to this study, that several potential scenarios for structuring NBTF be analyzed. We consider this expectation to be untimely because of the many uncertainties regarding the final organization and administration for NBTF.

As suggested in the Institute of Medicine's recent report [Adelstein & Manning, 1994], there are several successful operating partnerships that can be used as a model for establishing NBTF. This model involves 3-way partnerships between government, universities, and the private sector. Atomic Energy of Canada (sponsored by the National Research Council of Canada), TRIUMF (a Tri-University Meson Facility), and Nordion (a private company) provide a successful operating example of this 3-part government/university/industry model. In Switzerland, the operation of the Swiss Institute of Nuclear Sciences (SIN) provides support both to universities and to the private sector.

The Canadian and Swiss model was strongly considered as it clearly influences many of the parameters studied in this project. Analysis of this model leads to two optimized administrative infrastructures that we conclude would be appropriate for the United States: NBTF as a DOE-sponsored independent program, and NBTF as a DOE program.

(1) NBTF as a DOE Sponsored Independent Program

We concluded that the best approach is to establish NBTF as an independent program under DOE sponsorship, directly connected to either IPDP or Isotopes-USA. NBTF would then directly interact with a regional network of major research universities to establish research, education, and outreach programs; establish partnerships with the national and international radioisotope manufacturing private sectors; and be in direct contact with the national and international scientific communities via a National Research Steering Committee. An operating partnership should be developed with a host research university and with the private sector.

For administrative and management efficiency, NBTF should have its own local independent administration, which shall operate the facility in compliance with all applicable regulations, guidelines, and policies, and be responsible for its financial well-being. NBTF administration should also be responsible for marketing its products, establishing partnerships for research and educational activities, and assigning priorities for the research and production (service) activities. NBTF administration should work closely with a National Research Steering Committee representing the scientific, educational, and private sector communities with which NBTF will collaborate. This administration should then be fully responsible for NBTF and be assigned the requisite decision-making authority.

General administrative oversight for NBTF should be established through an operating contract, similar to the ones for the national laboratories, with the University of California, Davis on behalf of the Regents of the University of California. UC Davis and DOE would then establish the administrative/management infrastructure for NBTF.

(2) NBTF as a DOE Program

A slightly different administrative infrastructure is possible for NBTF if it is established as a DOE facility under the direct administrative responsibility of either the existing IPDP or the proposed Isotopes-USA consortium. In this model, all other duties and responsibilities are the same as those proposed for

the DOE-sponsored independent organization; the only change is the level of DOE's administrative involvement.

Several potential drawbacks can be anticipated if this structure is established, mainly related to DOE's own policies and procedures that would presumably be applied to NBTF. These restrictions have already been evident at DOE's Isotope Production and Distribution Program, which by policy has not been able to meet competition (mostly foreign) in the radioisotope market. This situation can be avoided if NBTF is established as an independent organization in partnership with the private sector, as suggested above.

1.0 ACCELERATOR DESIGN

A dual-accelerator capability is proposed. Two accelerators — one covering the energy range from 10 to 40 MeV, the other covering the energy range from 30 to 100 MeV — will produce all the isotopes required, while maintaining maximum up-time and efficient utilization of facility and capital equipment resources.

A number of accelerator options were considered in selecting the machines best suited to accomplish the NBTF mission. Four configurations were studied: a 3 MeV high-current linac, a 40 MeV cyclotron, a 100 MeV cyclotron, and a 100 MeV linac.

The linacs were eventually ruled out as being too expensive, in part because of the disproportionately high cost of targets and target development they would require.

1.1 REVIEW OF ACCELERATOR OPTIONS

The technical parameters of the four accelerator options are summarized in Table 1-1. The first is a compact electrostatic quadrupole (ESQ) dc accelerator for neutron production. The accelerator itself would be similar to the high-current heavy ion beam injector designed at LBL for the DOE fusion program. The accelerator is described in a paper attached as Appendix C.

The lithium neutron target for this accelerator would require considerable development, and is considered expensive and risky, especially in light of the projected neutron yield — a relatively modest $10^9 \text{ n/cm}^2/\text{sec}$ thermal and epithermal. For the same projected cost, a tungsten target could be developed for the 100 MeV accelerator that could achieve $10^{13} \text{ n/cm}^2/\text{sec}$ in the reactor-equivalent energy range ($<0.625 \text{ eV}$).

The second accelerator option is a commercially available 1 mA, 40–10 MeV adjustable-energy cyclotron. This energy range could, in principle, be covered by a single accelerator — the high-energy 100 MeV linac — by shutting off the high-energy drift-tube sections during acceleration of low-energy beams, but this has to be considered a poor use of expensive capital equipment.

Moreover, the timeline for commissioning the NBTF facility and for beginning large-scale isotope production is significantly shortened by including the medium-energy cyclotron

Table 1-1. Major Parameters of Four Accelerator Options

PARAMETER	LINAC 3	CYCLOTRON 40	CYCLOTRON 100	LINAC 100
ACCELERATOR COST	\$4 M	\$5 M	\$10-12 M	\$20 M
PORTS	1 port	2 ports	2 ports	2 ports
BEAM TIME STRUCTURE	dc	cw	cw	pulsed
AVERAGE CURRENT	10-100 mA	1-2 mA	1-2 mA	>2 mA
TARGETRY COST	\$3-4 M	\$3-5 M	\$5-10 M	\$20 M *
NEUTRON PRODUCTION (THERMAL & EPITHERMAL)	10^9 n/cm ² /sec at 10 mA†		10^{13} n/cm ² /sec at <0.625 eV	
SIMULTANEOUS ENERGIES	1	2	2	2
PRIME POWER	150 kW	100 kW	250-350 kW	750-1,500 kW
ENERGY RANGE	1-3 MeV (dc)	10-40 MeV (cw)	30-100 MeV (cw)	20-100 MeV (pulsed)
ENERGY SPREAD	<1%	<1%	≥1%	$\Delta E \pm 0.1$ MeV
RF SPARE TUBES COST (2)		\$0.1 M	\$0.25 M	\$1.0 M
ENERGY TUNABILITY	continuous	continuous	continuous	discrete

* Considerable R&D would be required to develop targets for the 100 MeV linac; no targets already exist that allow linacs to produce isotopes. Estimates started at \$20 M.

† Limited by presently available target technology.

in the plan. Either of the high-energy accelerators (100 MeV linac or 100 MeV cyclotron) would be new and unique in certain respects, and will have to be designed, configured, and proven for NBTF, while the 40 MeV, 1 mA accelerator is available from at least two commercial vendors, who assert that upgrading to 2 mA is not a problem.

The primary choice to be made is between the 100 MeV cyclotron and the 100 MeV linac. The cyclotron is shown to have a clear advantage overall. The capital cost, operating cost, and spare parts cost of the cyclotron are all substantially less than for the linac. The rf system costs for the linac are estimated at \$8M, with a total capital cost of \$20M.

The cyclotron capital cost is estimated at \$10M, with future upgrade to 2 mA adding another \$2M. The cyclotron will also require significantly less research and development, particularly for its associated targetry.

Two important technical factors weigh in favor of the cyclotron:

One factor is the degree of adjustability of the beam energy. Discrete 1 MeV steps in energy are proposed for the linac, while the cyclotron is continuously adjustable. This is important, as the energy of the beam must be precisely adjusted to minimize the cross sections for competing, contaminating reactions.

The second factor relates to the temporal structure of the beam. The linac produces a pulsed beam, while the cyclotron produces a continuous-wave (cw) beam. For a given time-averaged beam current, the pulsed beam imposes considerably more severe requirements on target heat transfer, beam window lifetime, etc., particularly for gas and liquid targets, as compared with a continuous beam. In the commercial isotope-production business, accelerator targets are designed and well-developed for cw beams. Commercial users will not be as likely to collaborate or to underwrite target development programs that are not immediately transferrable to their applications.

The Linac Physics and Special Projects Division at Los Alamos National Laboratory conducted an investigation of a suitable linac for this Phase I NBTF Project Definition Study; a summary of the LANL report is included as Appendix D.

Our conclusion overall is that the most prudent accelerator choices for NBTF are the 100–30 MeV and 40–10 MeV cyclotrons. Both machines are upgradable to 2 mA cw operation.

1.2 100 MeV CYCLOTRON

This is a sector-focused cyclotron that accelerates high intensity (up to 2 mA) H^- ions to a maximum energy of 100 MeV. The energy of the extracted beam can be set to any value between 30 and 100 MeV by adjusting the radial position of the extractor foil.

Two adjustable extractors and extraction ports are provided, one on either side of the accelerator. Each extractor is rated for 1 mA extracted beam current. Dual, simultaneous extraction at two different energies is possible by adjusting the axial as well as radial position of the lower-energy extractor. Each extraction port can be connected to a two-port switching magnet, thus providing for four beamlines.

The cyclotron is shown in Figs. 1-1 and 1-2, and its key parameters are summarized in Table 1-2.

Table 1-2. Key Parameters, 100 MeV Cyclotron

Beam energy	smoothly adjustable from 30–100 MeV
Beam current	2 mA maximum extracted beam current
Energy spread	< 1% FWHM
Magnet	
Number of sectors	4
Hill field	1.445 tesla
Hill gap	4 cm
Valley field	0.10 tesla
Valley gap	64 cm
Excitation	50,600 amp-turns
DC excitation power	14.5 kW
Weight (steel)	202 tons
Weight (copper)	4 tons
Yoke dimensions (diameter, height)	473 cm, 160 cm
RF system	
Number of dees	2 (driven in phase)
Harmonic mode	4
Power (copper losses)	120 kW

Figure 1-1: 100 MeV Cyclotron, Plan and Elevation Views

Figure 1-2: 100 MeV Cyclotron, Horizontal and Vertical Sections

1.2.1 Magnet Configuration

The cyclotron magnet employs a 4-sector, azimuthally-varying-field configuration, as shown in Fig. 1-2. The magnet gap is 4 cm in the hill regions and 64 cm in the valley regions. The radial increase in average field, required to accommodate the relativistic mass increase of accelerated ions, is realized by increasing the azimuthal extent of the hills as radius increases.

Vertical focusing is provided by the azimuthally-varying field, combined with the alternating-gradient focusing forces due to the spiral angles at the leading and trailing edges of the hills. Harmonic coils or radial profile coils are not required, eliminating considerable complexity of design and of system control.

Magnet excitation is provided by hollow-core, water-cooled copper coils protected against coolant failure with overtemp and flow interlocks.

The magnet is mounted over a recess in the floor that provides access for maintenance of the vacuum system, etc. The base support structure places the height of the median plane at 52 inches (1.3 m) above the finish floor.

Components inside the accelerator chamber that are "consumable" or require service on a scheduled basis are accessible/removable through vacuum-locked ports. In the event access to the interior of the accelerator chamber is required, the upper magnet assembly and vacuum tank top are raised by a hydraulic lift system.

1.2.2 RF System

Accelerating Structure

The accelerating structure operates at 59 MHz, which is four times the particle revolution (or "going-around") frequency. There are two accelerating electrodes, or dees, which are nominally 45 degrees wide (180 rf degrees) at the center, and 30 degrees wide (120 rf degrees) at the radius of extraction.

The dees are situated in two opposing valleys and are connected at the center of the accelerator. Each dee is mounted on water-cooled posts. The posts are attached, in turn, to the floor of the valleys. The dees and their support posts function as a capacitively-loaded half-wave resonator that is grounded at both ends.

Because the rf structure is grounded for dc, there are no insulators — thus eliminating entirely any concern about rf insulator failure.

Ion loading effects and rf sparking are minimized in this system by maintaining a tight tank at high vacuum, utilizing metal seals, and employing oil-free components (high-vacuum pumps and related apparatus) in the accelerator tank.

Dee Voltage and RF Power Requirement

In order to optimize acceptance of beam from the injection channel, the amplitude of the dee voltage that accelerates the particles has been chosen to match the injection energy: 100 kV (from 0–peak).

Substantial rf power is required to overcome copper losses in order to excite the resonator to 100 kV. One of the significant advantages of the dee-in-valley concept is that the rf power needed to overcome these losses is greatly reduced. The dee-to-ground capacitance of each dee is essentially due to the edges only: approximately 0.375 pF per linear centimeter along each dee edge (top and bottom included) for the design contemplated here.

The dee chosen for this design is nominally 140 cm along each edge. Thus, the capacitance is $2 \times 140 \times 0.375 = 105$ pF. The energy stored in one dee at the peak of the rf cycle is:

$$1/2 \times \text{dee capacitance} \times (\text{peak voltage})^2 = 0.525 \text{ joules}$$

The “efficiency” of a resonator is characterized by its “Q value”, defined as:

$$Q = 2\pi \times (\text{operating frequency}) \times (\text{energy stored at peak of cycle}) / \text{power dissipated}$$

Long experience in modeling, constructing, and operating cyclotron resonators of this type tells us that a practical, achievable, and reliably predictable “Q-value” for this structure is about 3,500. Thus the power dissipated in the resonator, which is required to overcome copper losses, is given by:

$$\begin{aligned} \text{Power (copper loss)} &= 2\pi \times (\text{operating frequency}) \times (\text{energy stored at peak of cycle}) / Q \\ &= 6.28 \times 62 \times 10^6 \times 0.525 / 3,500 \\ &= 58,404 \text{ watts per dee} \\ &= 117,000 \text{ watts for 2-dee system} \end{aligned}$$

Power Amplifier

In addition to providing power to replace copper losses, the rf system provides power to the beam. The rf power required to accelerate the maximum beam current to top energy is equal to the power in the beam: 200,000 watts plus beam losses.

Leaving some margin and allowance for other factors — such as efficiency of the coupling circuitry, ion loading, etc. — the main rf power amplifier must be rated for [copper losses + beam power + other factors] = 350,000 watts output rf power delivered to the load.

A wide choice of rugged, high-power, liquid-cooled-anode vacuum tubes used in broadcast service is available for this application.

The rf power amplifier is mounted directly at the accelerator. The anode of the output stage is capacitively coupled to the resonator in order to achieve the required 5:1 voltage step-up from anode-to-dee system. This concept has been proven in commercially-built cyclotrons; the variable load presented by the beam appears as a variable resistance at the anode of the final amplifier. Directly-coupled systems perform well, with substantially less complexity of operation than coupling a remotely situated amplifier through a high-power transmission line.

1.2.3 Ion Source and Injection System

The accelerator is required to extract beams reliably with intensities from 1–2 mA. Recent advances in multicusp ion sources make it possible to meet this requirement with an injection system that does not require a buncher, a device commonly used to maximize the beam that can be captured within the phase acceptance of the cyclotron rf pulse. In order to extract 1–2 mA from the cyclotron, an injection system (with no buncher) will be required to transport 10–20 mA at 50–100 keV and then inflect the beam into a matched stable orbit for acceleration.

The proposed injection system consists of an H⁺ ion source, a beam extraction and low energy beam transport system (LEBT) or matching system, a transport line approximately 2 meters long, and an electrostatic inflector.

Ion Source

The ion source is an rf-driven multicusp generator that has been operated successfully at Lawrence Berkeley Laboratory for efficient production of both positive and negative ion beams. Multicusp plasma generators are capable of producing large volumes of uniform and quiescent plasmas. The rf-driven volume ion source that LBL provided for the Superconducting Super Collider (SSC) routinely produced a 35 kV, >30 mA H^- beam with a normalized rms emittance $<0.1\pi$ mm-mrad. The source was operated with a 100 μ s pulse width at a 10 Hz repetition rate. To enhance H^- output, the ion source was modified with a dispenser system to introduce a trace amount of cesium into the collar region of the plasma electrode. Beam currents in excess of 100 mA and electron-to- H^- -current ratios close to one were achieved. Emittance measurements at 70 mA suggest only a 20% increase over the uncesiated emittance values, still much smaller than ECR source emittances that are routinely used for heavy-ion injection into cyclotrons. This output beam emittance increase is expected to improve when the extraction optics are optimized during the design phase.

We propose to develop the rf-driven source for the production of cw H^- beam of about 20–40 mA. The cesium-dispensing as well as the electron-dumping systems must be properly designed for dc operation. A schematic diagram of the rf ion source is shown in Fig. 1-3. The source chamber is a copper cylinder (10 cm diameter $\times$ 10 cm) surrounded by 20 columns of samarium-cobalt (SmCo) magnets that form a longitudinal line-cusp configuration. The magnets are enclosed by an anodized aluminum cylinder with cooling water circulating between the magnets and the inner housing. The back flange has four rows of magnets cooled by drilled water passages in the copper. In order to enhance the H^- yield, a pair of water-cooled permanent magnet filter rods is installed near the extraction region. The filter rods provide a narrow region of transverse magnetic field which divides the entire source chamber into a discharge and extraction region. The filter field is strong enough to prevent energetic electrons from reaching the extraction chamber. Excitation and ionization of the gas molecules take place in the discharge chamber. Positive and negative ions, together with cold electrons, are present in the extraction region. They form a plasma with a lower electron temperature, which makes a favorable environment for the formation of H^- ions by dissociative attachment and their survival to reach the extraction aperture.

Figure 1-3. Schematic Diagram, RF Ion Source

The plasma is generated by inductive discharge via a three-turn antenna. The rf antenna is fabricated from 4.7-mm diameter copper tubing and is coated with a thin layer of hard porcelain material, which is slightly flexible and resistant to cracking. Clean, low duty (<5%) pulsed plasmas have been operated for periods of several months without any antenna degradation. The antenna is connected in series to a matching network consisting of an inductor and a variable capacitor used for resonant tuning. Rf power is transferred to this LC series circuit via a step-down isolation transformer, isolating the rf equipment from the high voltages of extraction and matching the 50Ω output impedance of the amplifier to the lower plasma impedance. A 2 MHz signal is generated by a wave synthesizer, gated by a pulser, and sent to the preamplifier which then triggers the main amplifier. Maximum efficiency is achieved when the output voltage and current from the rf amplifier are in phase and the load impedance is 50Ω .

Injection System

The extraction and LEBT systems will be designed using LBL's 2-D and 3-D ion optics computation codes. A preliminary design of the beam extraction and LEBT system was done for the SSC injector. The extracted beam contains both H^- ions and electrons. Because of the low duty factor operation, the electrons in the exit beam could be deflected by the magnetic field (generated by a pair of permanent magnets embedded in the first electrode) and are collected at full energy at the second accelerator electrode.

For cw beam operation, however, both heat-loading on the electron dump will pose serious problems. We propose to employ an accel/decel scheme in which the electrons are deflected in the second accelerator gap and are collected on the third electrode with almost zero energy. The H^- ions will be accelerated and guided along a single-channel, axially-symmetric focusing/defocusing system consisting of a series of electrostatic ring washers as illustrated in Fig. 1-4.

Fig. 1-4 shows the result of a computational study demonstrating the feasibility of transporting a 100 keV, 200 mA H^- beam. In principle, there is no limitation on the length of this transport system, provided that the vacuum condition is favorable to avoid the loss of the H^- ions due to stripping. For normal operation, only two dc power supplies are required. The final beam energy as well as the beam parameters such as the diameter, convergent angle, emittance, etc., can be adjusted by means of the last Einzel lens system. The H^- beam will then enter axially into the cyclotron through the hole in the iron yoke. The H^- ions will be deflected and enter into the proper orbits by means of a standard electrostatic inflector. LBL has recently designed, built, and installed electrostatic inflector systems in its 88-Inch Cyclotron, and in a C-permanent magnet "Cyclotrino," a tabletop cyclotron designed and built for accelerator mass spectroscopy (AMS) applications.

Figure 1-4. Beam Trajectories in 100 kV, 200 mA H⁻ Injector

1.2.4 Beam Extraction

Extraction by Charge Exchange

In an H^- cyclotron the beam is extracted by passing it through a thin carbon foil that removes both electrons from the H^- ion, converting it to an H^+ ion. Because the polarity of the ion changes from (-) to (+), the force on the ion changes from radially inward to radially outward, and the ion is extracted at essentially 100% extraction efficiency.

The binding energy of the excess electron attached to form an H^- ion is only 0.7 eV, and the binding energy of the atomic electron is about 14 eV. Both electrons are easily removed by passing the beam through a thin foil.

Carbon, in the form of pyrolytic graphite, is used as the foil material because it has desirable physical properties including high heat transfer coefficient (in the plane of the foil), high melting point, low sublimation rate, and reasonable mechanical strength. Carbon also has the advantage of imparting far less rms scatter to the ion beam than do refractory materials of higher atomic number.

Foil Lifetime

The choice of foil thickness is determined by a number of factors such as foil heating and lifetime, the allowable emittance growth due to scatter in the foil, and practical issues such as ease of handling and maintenance.

Data from the field suggest that lifetime for a 25 micron foil is of the order of 50 hours at 40 MeV, 200 μ A [Burgerjon, LANL, 1984]. The failure is not due to material loss through sublimation, but rather to radiation damage upsetting the uniformity of crystalline structure, causing the foil to curl and warp.

Some cooling of the extraction foil is achieved via conduction to the foil mount. Most of the cooling, however — especially at high beam current — is via thermal radiation at incandescent temperatures. For a given beam current, the power lost in a 5 micron foil at 100 MeV is approximately a factor of ten lower than the power lost in a 25 micron foil at 40 MeV.

A foil thickness of 5 microns provides the best overall performance considering both physical ruggedness (including ease of handling) and emittance growth. Based on the data

above, the service life of a 5 micron foil extracting 1 mA at maximum energy is projected to be ≥ 100 hours. The extractor mechanism has several foils mounted on a carousel so that operation need not be interrupted for more than a moment to change foils when they show signs of wear.

**Table 1-3. Scatter and Power Loss
as a Function of Foil Thickness and Beam Energy**

BEAM ENERGY (MeV)	5 μm FOIL		25 μm FOIL	
	RMS SCATTER (mrad)	POWER LOSS @ 100 μA (W)	RMS SCATTER (mrad)	POWER LOSS @ 100 μA (W)
30	1.64	1.92	3.66	9.60
40	1.23	1.52	2.75	7.60
50	0.98	1.27	2.20	6.35
60	0.82	1.10	1.83	5.50
70	0.70	0.97	1.57	4.85
80	0.61	0.88	1.37	4.40
90	0.54	0.82	1.22	4.10
100	0.48	0.75	1.12	3.80

Beam Spot Size

Some scatter is imparted to the beam as it goes through the foil. The root-mean-squared (rms) scatter depends on foil thickness and beam energy, as shown in Table 1-3. If a Gaussian beam distribution is assumed at the point of extraction, 63% of the beam will lie within (+) and (-) the rms scattering angle as listed in the table; 98% of the beam will lie within (+) and (-) twice the rms scattering angle.

Beam extracted at the lowest energy (30 MeV) must drift approximately 1.9 meters to reach the outside of the accelerator, where it is focused and steered down the beamline in the correct trajectory.

A 25 micron carbon foil would produce a beamspot (containing 98% of the beam) that is contained within a diameter of $1900 \times 4 \times 0.00366 = 28$ mm at the outside of the magnet yoke. A 5 micron carbon foil would produce a beamspot that is contained within a diameter of

$1900 \times 4 \times 0.00164 = 12.5$ mm. These data obviously demonstrate in favor of using thin carbon foils — no greater than 5 microns — for extraction.

The spot size at the exit, cited above for the lowest energy beam, includes only the effect of scatter, and does not account for lens effects. After passing through the extraction foil, the low energy beam must cross a hill boundary at an oblique angle to reach the exit port. This has the effect of focusing the beam in the vertical dimension and defocusing the beam in the horizontal dimension. In order to maintain a round beam spot that can be further steered, focused, and transported, the lens effect induced by the hill edge will be corrected before the beam exits the vacuum chamber, using an appropriately configured magnetic channel.

Variable Energy Extraction

Extraction at a particular energy is accomplished by inserting the extractor foil at the appropriate radius. The foil is positioned at the proper position in the hill-gap so that after charge exchange takes place, the particle travels the necessary distance in the high magnetic field to achieve the correct curvature and trajectory toward the exit port.

The extractor mechanism is movable in both degrees of freedom in the horizontal plane. In addition, the foil itself is mounted on a rotatable carousel that holds a total of three foils to provide quick back-up and replacement as the operating extractor foil wears out. Incremental adjustment of the carousel rotation, under closed-loop feedback control from beam position sensors downstream, is used to steer the beam along the correct trajectory.

Dual Simultaneous Extraction

Dual simultaneous extraction is implemented using two extractor mechanisms, inserted on opposite sides of the cyclotron. Dual extraction is possible due to the fact that the beam within each orbit turn has a finite cross-sectional area. When the beam reaches the radius where the extractor foil is positioned, only the portion of the beam that is intercepted by the foil is extracted. That which has not quite reached the extraction radius will continue to circulate.

Another foil, positioned to intercept the remainder of the beam, will extract it. The ratio of beam currents extracted by the two foils is adjustable by fine-tuning the respective radial positions of the foils.

Dual Extraction at Different Energies

Simultaneous extraction at two energies means that the two extractors must operate at different radii. The extractor foil that operates at the lower energy (smaller radius) has an extra degree of mechanical motion: its position is adjustable in the vertical dimension so that a selected amount of beam can be intercepted from below the plane of acceleration.

Neutral Beam and Its Effect on Machine Design and Performance

Any cyclotron that accelerates H^- will suffer some loss of beam prior to extraction due to neutralization of negative ions. Some beam is lost due to dissociation of H^- ions by gas stripping, and some is lost at the highest energies due to electromagnetic dissociation. In any case, the resulting neutral beam is intercepted by specially-designed neutral beam baffles that minimize problems of overheating or activation of components in the accelerator tank.

Dissociation of H^- Ions by Gas Stripping

A portion of the accelerated beam is lost due to gas stripping. This can occur when an H^- ion passes too close to a gas molecule in the acceleration chamber. The resulting coulomb forces couple energy to the weakly-bound electron, breaking its bond and neutralizing the ion. The resulting neutral ion immediately exits the accelerating region in a straight path.

The probability of neutralization depends on the density of gas molecules (pressure), and the species of gas molecule: the larger the molecule, the more electrons (higher coulomb force), and the greater the stripping effect.

For a well-pumped, tight, but unbaked system, after being opened for maintenance, the principal residual gas component will be water vapor. Table 1-4 shows cumulative survival of beam out to energy, E , for various indicated pressures (as read on the vacuum gauge), assuming, pessimistically, that water vapor predominates — i.e., that the “effective” pressure for stripping is greater than the indicated pressure by a factor of 5.

**Table 1-4. Cumulative Survival of Beam Out to Energy, E,
for Various Indicated Pressures, Assuming the Effective Pressure
to Be 5 Times the Indicated Pressure**

ENERGY, E (MeV)	CUMULATIVE SURVIVAL @ pressure 1×10^{-8} Torr	CUMULATIVE SURVIVAL @ pressure 5.0×10^{-8} Torr	CUMULATIVE SURVIVAL @ pressure 1×10^{-7} Torr
10	0.9990	0.9954	0.9908
20	0.9987	0.9935	0.9871
30	0.9984	0.9921	0.9844
40	0.9982	0.9910	0.9821
50	0.9980	0.9900	0.9802
55	0.9979	0.9896	0.9793
60	0.9978	0.9892	0.9785
65	0.9977	0.9888	0.9777
70	0.9976	0.9884	0.9770
75	0.9976	0.9880	0.9763
80	0.9975	0.9877	0.9756
85	0.9974	0.9874	0.9749
90	0.9974	0.9871	0.9743
95	0.9973	0.9868	0.9737
100	0.9973	0.9965	0.9731

This table shows that the largest percentage loss of beam due to gas stripping occurs at the lower energies, and that the indicated vacuum should be maintained in the low-to-mid 10^{-8} torr range to limit overall gas stripping losses to a nominal 1% or less. The design of the accelerator vacuum system incorporates high-capacity, oil-free cryopumping to maintain the operating vacuum below 5×10^{-8} torr.

Electromagnetic Dissociation of H⁻ Ions

A charged particle traversing a magnetic field at high velocity experiences a force as if it were being acted upon by an equivalent electric field. This field can cause a negative ion — with its weakly bound electron — to dissociate, as described by a “decay” law of the form:

$$P \text{ (dissociation in time, } t) = 1 - e^{-(t/\tau)}$$

For a given computation interval (i.e., a selected range of radius, energy, etc.) the time, t , that the particle spends in the interval is proportional to the average path length in the orbit during which the particle sees the peak magnetic field, and inversely proportional to the energy gain per turn. The mean life, τ , is a very strong function of the equivalent electric field seen by the particle which, in turn, is a function of peak magnetic field and particle velocity [ref. Judd, *Nucl. Instrum. Methods* **18, 19** (1962)].

Unlike negative ion dissociation due to gas stripping, most of the electromagnetic dissociation takes place at the highest energies, as shown in Table 1-5.

Table 1-5. Cumulative Electromagnetic Survival of Negative Ions Out to Energy, E, for the Magnet and Acceleration Parameters Described Herein

ENERGY, E (MeV)	CUMULATIVE SURVIVAL	CUMULATIVE DISSOCIATION
60	0.99997	0.00003
70	0.9998	0.0002
80	0.99903	0.00097
90	0.9961	0.0039
95	0.9925	0.0075
100	0.9863	0.0137

The amount of beam loss due to electromagnetic dissociation at the highest energy governs critical cyclotron design parameters — most notably the peak magnetic field. This fixes the size of the magnet which, in turn, has a major impact on system cost. Some beam loss

due to gas stripping is inevitable. A limit of 2.5% total loss due to stripping provides a reasonable compromise between beam loss and overall cost.

Neutral Beam Baffle

Neutral beam must not be allowed to strike any components that could suffer damage due to overheating, or which could become highly radioactive. The design of the cyclotron includes a liner, or baffle, that absorbs the neutral beam in such a way as to minimize the potential for damage or activation.

If we assume acceleration of full current (2 mA) at top energy (100 MeV) the beam power lost to the perimeter is the sum of the components due to gas stripping and electromagnetic dissociation. If we assume 5×10^{-8} torr operating pressure in the tank, then

$$\begin{aligned} \text{power in neutral beam} &= 293 \text{ watts due to gas stripping} \\ &= 2740 \text{ watts due to electromagnetic dissociation} \\ &= 3033 \text{ watts total, distributed around the perimeter of the vacuum chamber} \end{aligned}$$

The power density of neutral beam, assuming a beam height of 1 cm around the perimeter, is approximately 4 watts per cm^2 . This power is converted to heat, which must be carried away to prevent an increase in temperature of the wall of the vacuum tank which, in turn, would lead to outgassing, pressure rise, and further increasing beam-loss.

The neutral beam baffle should be made of a material that produces as few prompt neutrons as possible (to minimize activation of nearby machine parts) and a minimum of long-lived radionuclides from direct proton bombardment. Attractive candidates are oxygen (in the form of pure water) and carbon — preferably depleted of ^{13}C — in the form of graphite. In either case the most prolific nuclear reactions result in short-lived activation products, but both materials also yield a relatively long-lived spallation product, 53.3 day ^7Be . The saturation yield for protons on water is approximately 0.5 Ci for 25 μA beam loss at 100 MeV. The saturation yield for protons on carbon is approximately 2.0 Ci for the same beam conditions. Beryllium-7 decays via electron capture, but also has a 477 keV (10.4% abundant) gamma ray emission.

Pure water flowing inside thin aluminum tubing would have the requisite heat transfer properties, but the range of 100 MeV protons in water is almost 76 mm. Water flowing behind

a thin membrane at the perimeter of a large cyclotron is also problematic from an overall reliability point of view. For these reasons, solid material is preferred for the beam baffle. Depleted ^{12}C carbon graphite material is available as a byproduct of separation of 1.10% abundant ^{13}C for applications in biomedical research, MRI imaging, etc. Removal of the ^{13}C component leaves a material with substantially reduced cross-section for neutron production.

The range of 100 MeV protons in carbon is approximately 38 mm. The ^{12}C graphite, in the form of 3 cm wide $\times$ 4 cm high rectangular rods, will be plated for good heat transfer to water-cooling channels on the wall that remove most of the heat from the neutral beam baffles. The graphite rods will also be sheathed in thin aluminum tubing to prevent outgassing into the tank as the rods warm up. Passages inside the tubing will allow flowing helium gas to further cool the graphite rods and to sweep out any gaseous products resulting from high-energy proton bombardment.

The neutral beam baffle helium-cooling system will include gas supply cylinder(s) with regulators, valves and controls, a 500 liter/minute bellows-pump, a reservoir, trap and gas/water heat exchanger rated to remove 2.0 kW.

The system is designed to ensure there will be no release of radioactivity.

1.2.5 Power Supplies

Magnet excitation is provided by a high-efficiency, switching-type power supply. The power requirement is modest enough that compact, commercial-grade supplies, ganged together to achieve the necessary current capacity and slaved to a common reference, will serve very well. The use of proven, commercial power supplies reduces cost and increases system reliability.

The required short-term current stability of 5 parts in 10^6 is not available in standard, off-the-shelf, commercial-grade supplies, but is easily achieved with the addition of an out-board precision reference, ultra-low-drift summing amplifier, and water-cooled, temperature-compensated shunt.

The rf system main amplifier cavity is housed directly adjacent to the cyclotron. The high-voltage anode power supply (20 kV DC at 12 amperes) plus a low-level pre-driver, intermediate power amplifier, and control circuitry are housed in an adjacent room.

The beamline steering and focusing quadrupole magnet power supplies are all standard, high-efficiency switching-type units.

1.2.6 Accelerator Control System

Before applying beam to the selected target, the accelerator is tuned to deliver the required beam current at the chosen energy to a beamstop upstream from the target. When stable operation is confirmed, the beamstop is opened and target bombardment commences.

The accelerator is one component in an overall control system network comprising beamlines and beamline vacuum systems, switching and focusing magnets, profile monitors, beamstops, collimators, targetry, etc.

The accelerator operates under computer control, using its own dedicated processor. Once the desired target and bombardment conditions are entered, the normal, routine operation of the accelerator is fully automatic. However, two or more appropriately-trained personnel will be on the premises as required by institutional, state, or federal safety and regulatory requirements.

All fast-response power supply regulation and safety interlock functions are hardwired into the supplies themselves. Thus, the computer system that controls the accelerator need not include real-time, closed-loop control of individual power-supply regulators.

The main accelerator computer control system turns the accelerator subsystems and components on and off as required; pre-sets correct operational parameters; fine-tunes certain parameters such as main magnet current, ion source current, extractor position, etc., in order to maintain stable operation over time; and is configured to read and display system status, control, and engineering parameters.

The operator console displays appropriate warning messages to invoke operator intervention if certain parameters drift outside correct limits.

Maintenance and troubleshooting of the accelerator and its subsystems is facilitated by a comprehensive command language that allows step-by-step control and monitoring of system states and parameters, including subsystem on/off functions and analog variables.

The command language provides "hands-on" control of all process variables. The functionality and power of the maintenance command language is such that only qualified, authorized personnel are allowed password access.

1.2.7 Vacuum System

The main tank vacuum must be maintained below 5×10^{-8} torr indicated pressure to satisfy the requirement for $\leq 1.0\%$ beam loss due to gas stripping. Six cryopumps with a combined pumping capacity of 96,000 liters/second for water, 36,000 liters/second for air, and 72,000 liters/second for hydrogen will be employed.

After closing the main tank and initiating pumpdown, the dominant component of residual gas will be water vapor. The amount of water vapor adsorbed by metal surfaces inside the acceleration chamber is minimized by opening the tank to dry nitrogen rather than room air whenever main tank vacuum must be broken.

Components which must be serviced on a scheduled basis, such as ion source and extractors, will be vacuum locked to minimize or eliminate the intrusion of room air during routine maintenance procedures.

After remaining closed and pumping for an extended period of time the dominant residual gas component will be hydrogen, most of which is slowly desorbed from metal surfaces, along with a small quantity that enters the main tank via the ion source injection channel.

Because the cryopumps are "capture" pumps rather than "throughput" pumps, they eventually saturate with hydrogen and require regeneration. A gradual increase in pressure in a blanked-off pump occurs as a pump approaches its limit for pumping hydrogen. The partial pressure for H_2 will be approximately 5×10^{-8} torr when a pump has accumulated 15 standard liters (50% of its total capacity), and 5×10^{-6} torr when saturated.

The regeneration process entails three stages — warm-up/purge, evacuation, and cooldown — and takes several hours. The frequency of regeneration is a function of overall gas load, system cleanliness, and vacuum system integrity, and can be scheduled on a regular basis.

Each cryopump is operated in conjunction with its own helium compressor. Power required for each compressor is 5 kW (30 kW total for six pumps).

1.2.8 Cooling

Closed-Loop Water System

Heat is removed from the accelerator and its components by a recirculating closed-loop water system. Cooling water channels inside the accelerator are kept out of the plane of acceleration to eliminate any possibility of direct proton activation. Neutral beam baffles, for example, are cooled with helium which, in turn, is passed through a water-cooled heat exchanger.

Secondary, neutron-induced activation of the cooling water is minimized by control of purity and cleanliness. Maintaining low electrical conductivity in the water is also essential in order to minimize leakage currents, which in turn could cause electrolytic action and erosion of water channels and fittings in the isolated, high-voltage ion source and rf amplifier anode cooling circuits.

The closed-loop recirculating water system, rated to remove heat from the various accelerator subsystems, is specified in Table 1-6.

Table 1-6. Closed-Loop Recirculating Water System Budget

RF accelerating structure	125 kW
RF amplifier anode	200 kW
Main vacuum system	30 kW
Magnet and magnet power supply	15 kW
Ion source and related subsystems	25 kW
Neutral beam baffle cooling	3 kW
TOTAL	400 kW

Assuming a short, large-diameter, low-loss supply and return, this translates to a ten horsepower pump, delivering 200 gallons per minute at a pressure drop of 80 pounds per square inch across the load.

Primary Cooling

Heat from the secondary loop that cools the accelerator must be removed through a heat exchanger to a primary heat sink cooled by running water, refrigeration, evaporative cooling towers, or a combination of the above and supplied as part of the facility. The total accelerator heat load to the environment, including pump losses and efficiency factors (but not including power consumed by the primary loop refrigeration system), is on the order of 425 kW.

Target and Beamline Cooling

The power deposited in the target(s) at full energy and full current is 200 kW. The cooling water for the targets and beamlines must be isolated in a separate closed-loop system (not included within the scope of this Phase I study). This is an important safety topic that will be addressed in Phase II.

Short-lived activation products are allowed to decay, while long-lived activation products must be trapped in the appropriate columns and then removed for storage and disposition.

1.2.9 Accelerator Engineering and Development

Powerful tools are available to the accelerator designer, enabling data to be imported directly from CAD drawing files into programs that analyze (1) magnetic and electric field properties of the magnet and rf accelerating structures, and (2) beam optics properties such as space charge, orbit trajectories, focusing, emittance growth, beam transport, etc., as the accelerator and its subsystems are being designed.

All salient aspects of the accelerator will be modeled by well-accepted finite-element computer software to validate concepts, work in progress, and finished designs prior to committing to large-scale construction.

1.3 40 MeV CYCLOTRON

The 40–10 MeV cyclotron will be a commercially produced cyclotron, similar to the somewhat lower energy Cyclone-30™ manufactured by Ion Beam Applications (IBA), Louvain-la-Neuve, Belgium. More than a dozen IBA machines are operating around the world today, and they are proven workhorses for radioisotope production. Another possible supplier is EBCO Technologies, Inc., in Vancouver, BC. Their TR30, for example, is comparable to the IBA machine. A Request for Quotations will be issued to these and other suppliers, with specifications detailing a 40 MeV version of these 30 MeV machines. It must be able to handle high-intensity H^- ions (beams of up to 2 mA), and the energy of the extracted beam must be adjustable to any level between 10 and 40 MeV.

As with the 100–30 MeV cyclotron, two adjustable extractors and extraction ports are provided, one on either side of the accelerator. Each extractor is rated for 1 mA extracted beam current. Simultaneous extraction at two different energies is possible. Each extraction port can be connected to a two-port switching magnet, thus providing for four beamlines.

For this Phase I Project Definition Study, the price of the IBA Cyclone-30™ was pro-rated for estimating the cost of NBTF's 40 MeV cyclotron.

2.0 NBTF FACILITY DESIGN

This section describes the NBTF facility design, and also discusses possible siting options for the facility.

2.1 PHYSICAL DESCRIPTION OF PROPOSED FACILITY

The facility comprises a $\approx 60,000$ sq.ft. building housing the two accelerators; shielding; target areas (8) and an independent neutron beam area; control rooms; production and research laboratories; machine and electronic shops; instrumentation (QC); environmental & health, physics, and computer rooms; and storage and waste management rooms. In addition, the facility is complemented with a library, a conference room, classrooms, administration and staff offices, and other services.

A preliminary layout of the proposed NPTF facility is shown in Fig. 2-1, and its key features are briefly described below.

2.1.1 Accelerators, Beamlines, Target Areas

Two accelerators are proposed: a 100–30 MeV cyclotron and a 40–10 MeV cyclotron. Both are negative H^- machines, to be operated initially at intensities up to 1 mA; each, however, is designed to be upgradable to 2 mA operation as new ion-source and target technology becomes available. The accelerators are housed in individual vaults, 34 ft. $\times$ 34 ft. for the larger cyclotron, 30 ft. $\times$ 30 ft. for the smaller.

Two extraction ports are located on each accelerator. Each extraction port is connected to a two-port switching magnet, thus providing for a total of 8 beamlines (4 per accelerator). The two beamlines on opposite sides of each accelerator can be operated simultaneously.

Eight target rooms, or “caves” — four per accelerator — are arranged as shown. Beamlines from the 100 MeV cyclotron go to Target Rooms A, B, C, and D; each of these caves is 20 ft. $\times$ 20 ft. In addition, the beamline to Target Room C continues on to the Neutron Target Area, which is 16 ft. $\times$ 16 ft. From the 40 MeV cyclotron, beamlines go to Target Rooms E and

F (14 ft. $\times$ 14 ft.) and G and H (14 ft. $\times$ 22 ft.). Beamlines in each of the target rooms can be split to two targets, as shown in Target Rooms C and G.

Commercially proven low-power target systems will be upgraded to withstand NBTF's higher beam levels. New high-power targets will be designed and developed as needed.

2.1.2 Shielding

A major shielding structure provides fully adequate worker, public, and environmental protection and safety from photon and particle radiation to be generated by NBTF. The walls, flooring, and ceiling are concrete of 12 ft. thick around the 100 MeV cyclotron vault and its target caves, and 8 ft. thick around the 40 MeV cyclotron vault and its target caves. Advanced shielding materials (boron-loaded concrete, borated polyethylene, water blankets) are strategically placed. Tunnels in the concrete accommodate the beamlines as well as conduits for supplying basic services (electricity, HVAC, water). A permanent overhead crane is used to lower the equipment into the vaults, and then to position the cast shielding blocks that form the ceiling.

Each vault and cave is accessed through a plug door resting on a 3-wheeled trolley, which slides along three tracks embedded in the floor; the plug doors and tracks are shown in the facility layout drawing.

Robotic target handling via a subterranean rail system was considered. This system would automatically move targets from the irradiation cells to the hot cells without human involvement. However, this option was discarded as too costly, in terms of both the additional construction and the complexity needed for its implementation. Further, in considering likely failure scenarios, it became apparent that a failure of the subterranean system (for example, a leaking target) could seriously contaminate the automated system and result in needless human exposure in order to repair the system. We therefore propose instead a shielded forklift-type vehicle to transport the targets from the irradiation cells to the hot cells. This vehicle could either be robotic or, with adequate shielding, human-operated. Engineered and administrative controls provide an acceptable level of safety against radiation exposure.

2.1.3 Neutron Production Area

The neutron production area uses beams from the 100 MeV cyclotron striking a proton-to-neutron conversion metallic target. By developing high-intensity proton-to-neutron conversion targets, we plan to produce research amounts of current and new neutron-rich (β -emitting) radioisotopes that are now only available from reactors. Research in this field has been conducted by various national laboratories for the Department of Defense; much of this work will be directly transferable. By integrating efforts being conducted at the national laboratories, we intend to develop accelerator-based technologies as alternatives to reactor-based technologies as sources of intense neutron beams for a variety of defense and non-defense purposes.

2.1.4 Radioisotope Production Facilities

The planned radioisotope production facilities will allow rapid processing, separating, controlling, and distributing of radioisotope products throughout the United States. An array of nine heavily shielded hot cells (150 mm walls) is equipped with manipulators to handle highly radioactive targets. A safe, optimized production facility will be designed, based on existing isotope-production facilities; this design will benefit from the accumulated experience of the commercial sector. Commercial, off-the-shelf equipment will be used. It is possible that existing DOE inventory from the national laboratories may also be usable, under long-term loan agreements, to help us pursue research topics of mutual interest.

2.1.5 Production and Research Laboratories

Production and research laboratories ($\approx 9,000$ sq.ft. total) will be designed in compliance with Good Laboratory Practices (GLP) and — where applicable — Good Manufacturing Practices (GMP) standards. These laboratories will provide a safe, appropriate setting for radioisotope production and for research in nuclear physics, radiochemistry, materials sciences, instrumentation, etc. The planned Satellite GMP in Sacramento will connect NBTF's research facility to the resources available at the UC Davis Medical Center, allowing for an effective collaboration in the development of new radiopharmaceuticals.

2.1.6 Education and Outreach Facilities

A library, conference room, and classrooms are provided in the facility building. Because we propose to locate NBTF within a larger institution (UC Davis, UC Davis Medical Center in Sacramento, or LLNL), there is no need to incorporate large public spaces appropriate for seminars, workshops, etc., into the facility building itself; such spaces will be readily available at any of the three host institutions.

2.2 LOCATION OF THE FACILITY

This study is predicated on NBTF being located in Northern California. The assumed site, where a single site is assumed, is the main campus of the University of California, Davis. Other siting options in Northern California are the campus at UC Davis's Medical Center in Sacramento, and the Lawrence Livermore National Laboratory in Livermore.

Northern California provides access to a population base of some 10 million people. This is important in terms of providing a substantial regional market for PET & SPECT radioisotopes, and also in terms of the overall resources available in such a well-developed area (see Appendix A).

3.0 DESIGN AND CONSTRUCTION COSTS

Design, engineering, construction, installation, licensing, and commissioning costs have been estimated for the proposed dual-cyclotron, high intensity proton and neutron beam NBTF facility described in Section 2 and shown in Fig. 2-1. These preliminary cost estimates were developed by staff, engineers, and consultants from the Titan Corporation (Titan Beta Division) and in consultation with collaborating scientists at Lawrence Berkeley Laboratory, Lawrence Livermore National Laboratory, and Los Alamos National Laboratory. Major equipment vendors were also consulted and asked to provide estimates.

A preliminary design and construction cost estimate is included as Table 3-1. Our estimated capital costs for a fully operational NBTF total just under \$50 million. This estimate includes all costs associated with designing, constructing, installing, licensing, and commissioning NBTF at one of the proposed sites: at the UC Davis Campus in Davis, at an already designated expansion site of the UC Davis Medical Center in Sacramento, or at the Lawrence Livermore National Laboratory. Land costs are not included, as the land would be provided at no cost by UC Davis or LLNL. The budget estimates were made in U.S. dollars at the early 1995 value.

Budget estimates have been included for major items essential for the commissioning and the initial operation of NBTF. These essential items include targets and enriched materials to be used as production and research targets. Budgets for these items are necessary and are included as capital costs as they are absolute requirements to operate NBTF and should be interfaced with its construction phase.

Shielding materials available in the region could be used at NBTF, reducing the total cost of the shielding for the new facility. For example, the DOE owns some 25 tons of shielding left over from the decommissioned Bevatron at LBL, even after the bulk of the shielding from this accelerator was shipped to Brookhaven. Similarly, shielding from the DOE's former rotating target neutron source at Livermore could be re-used. There is also a surplus inventory of high-density engineered materials at Crocker Nuclear Laboratory at UC Davis. The estimated shielding cost in Table 3-1 (\$6 million) does not take into consideration the savings that could be realized by incorporating some of this existing shielding into the shielding design.

Operating licenses for the facility are expected to be a subset of existing licenses at the University of California, Davis and at Lawrence Livermore National Laboratory. Licensing costs have been estimated accordingly.

The design and construction phase of NBTF has been estimated to require three and a half years, leading to initial operations during the fourth year of the project. Full commissioning of NBTF is expected by the end of the fifth year. A preliminary project schedule is provided in Fig. 3-1.

The estimated A&E costs (\$3.1 million) include project administration for the 3½-year design and construction phase. Once construction is complete, at the middle of the fourth year, it is expected that funds for the operational phase of NBTF will be used to support project administration through the completion of the commissioning phase.

At the end of the 5-year design, construction, and commissioning process, NBTF will be fully capable generating the revenue detailed in the business plan (Chapter 6).

NOTE: Construction cost sharing by non-Federal partners was not considered during this early stage (Phase I) of the NBTF Project Definition Study. In order to attract cost-sharing partners, a more clearly defined plan (including a site commitment) will need to be available. It is likely — because of NBTF's critical mission and its projected regional impact — that State and/or private resources will indeed be available for this project. Cost-sharing possibilities could better be explored during a later phase of the study.

Table 3-1. Preliminary NBTF Capital Cost Estimates (\$ Million, 1995 dollars)

Accelerators	
Cyclotron 100–30 MeV (1 mA, upgradable to 2 mA)*	12.0
Cyclotron 40–10 MeV (1 mA, upgradable to 2 mA)*	5.0
	<u>17.0</u>
Accelerator Ancillary Facilities and Equipment	
Beamlines (8) (4 per cyclotron)	2.0
Target Caves (8) (4 per cyclotron)	1.2
Targetry Systems and Enriched Target Inventory	2.5
	<u>5.7</u>
NBTF Facility	
Building for NBTF (excluding shielding)	5.0
Shielding for NBTF (3m and 4m vault walls; borated concrete)†	6.0
	<u>11.0</u>
Research, Production, and Other Laboratories	
Production Labs (\$300/sq.ft × 15 people × 300 sq.ft/person = 4,500 sq.ft)‡	1.4
Hot/Cold Research Labs (\$300/sq.ft × 15 people × 300 sq.ft/person = 4,500 sq.ft)‡	1.4
Hot Cells (9) (150 mm walls), with Manipulators	2.3
Safety Systems for Labs (ventilation/filtration, interlocks, alarms, monitors)	2.0
Target Preparation and Recycling Labs (1,000 sq.ft × \$300/sq.ft)	0.3
Quality Control Labs and EHS Labs (1,000 sq.ft × \$200/sq.ft, plus monitors)	0.5
Packaging/Holding/Distribution Lab (1,000 sq.ft × \$200/sq.ft)	0.2
Radioactive/Chemical Waste Handling Room (2,000 sq.ft × \$250/sq.ft)	0.5
Special R&D Equipment	2.5
	<u>11.1</u>
Support Facilities	
Machine/Electronic Shops	0.8
Computer Facility Room	0.2
Personnel (Offices); Administration	0.4
Reception/Visitor Area	0.2
Library, Conference Room, Classrooms	0.4
	<u>2.0</u>
Other Capital Costs	
Land (10–12 acres) (UCD or LLNL will provide land at no cost)	0.0
A&E (design, administration, professional fees, agency & environmental reviews and approvals, licensing, project staff)	3.1
	<u>3.1</u>
TOTAL ESTIMATED CAPITAL COST (\$ MILLION)	<u><u>49.9</u></u>

* Designed and built for 2 mA operation; upgrade from 1 to 2 mA requires higher-current injection system.

† Shielding designed and built for 2 mA operation for each cyclotron.

‡ A fraction of these costs may be used for a GMP satellite laboratory.

Figure 3-1. NBTF Design, Construction, and Commissioning Schedule

4.0 PERMITS

Staff at UC Davis' Crocker Nuclear Laboratory and at Lawrence Livermore National Laboratory are thoroughly familiar with all regulatory aspects associated with siting, constructing, and operating the proposed NBTF. The regulatory requirements for such a facility are extensive, but comparable to those already in effect at these two institutions.

The Crocker Nuclear Laboratory's Radioisotope Program has been operating successfully since 1977 with all appropriate Federal, State, Local, and University permits in place. These include, for example, Drug Master Files within the FDA as well as State of California Drug Manufacturing and Pharmacy licenses. Radioisotope packaging materials and containers have been developed and used in strict accordance with Nuclear Regulatory Commission, Department of Transportation, and all other Federal, State, and University regulations. Some 7,000 radioisotope shipments have been made by the CNL Radioisotope Program since 1977; none has resulted in a violation, citation, or sanction.

The major regulatory agencies with authority over NBTF are:

U.S. Department of Energy (if NBTF is a DOE facility)
U.S. Nuclear Regulatory Commission (if NBTF is <u>not</u> a DOE facility)
U.S. Food and Drug Administration
State of California Department of Health Services
U.S. Department of Transportation
International Air Transporters Association
Environmental Protection Agency (Federal and State)
Occupational Safety and Health Administration (Federal and State)
Regional Water Quality Control Board
Regional Air Quality Control Board
Local ordinances

The major regulations with which NBTF must comply are:

ANSI Standards

Code of Federal Regulations, Title 10, Energy

Code of Federal Regulations, Title 40, Protection of Environment

RCRA (Resource Conservation and Recovery Act)

NEPA (National Environmental Protection Act)

CAA (Clean Air Act)

CWA (Clean Water Act)

SDWA (Clean Drinking Water Act)

TSCA (Toxic Substances Control Act)

NESHAPS (National Emission Standards for Hazardous Air Pollutants)

CERCLA* (Comprehensive Environmental Response, Compensation & Liability Act)

SARA Title III (Superfund Amendments and Reauthorization Act)

Code of Federal Regulations, Title 49, Transportation

HMTA (Hazardous Materials Transportation Act)

California Code of Regulations, Title 26, Toxics

California Medical Waste Management Act

California Proposition 65†, which mandates full disclosure of hazards

U.S. Nuclear Regulatory Commission Regulation Guides†

* Only if NBTF is located at a Superfund site (e.g., LLNL)

† Only if NBTF is not a DOE facility

Because of staff familiarity with the applicable regulations, we do not anticipate project delays due to the permitting process. Operating licenses for NBTF are expected to be a subset of existing licenses at the University of California, Davis and at Lawrence Livermore National Laboratory. We expect all necessary permits and licenses to be obtained within the project design-and-build schedule (see Fig. 3-1), although we do suggest that EIRs be started in anticipation of contract award. Permit and licensing costs, estimated at \$300,000, are included as capital costs in the Design and Construction Cost Estimate (Table 3-1).

5.0 WASTE MANAGEMENT

This Phase I Project Definition Study was conducted under the assumption that NBTF would be sited (1) within the Davis Campus, (2) at the UC Davis Medical Center in Sacramento, or (3) at the Lawrence Livermore National Laboratory. Chemical, radioactive, and biological materials are essential to the continued operation of the UC Davis, its Medical Center in Sacramento, and LLNL; the existing (and currently under-construction) waste management facilities at these sites are more than adequate for NBTF's waste management.

The total yearly level of waste disposal materials from NBTF is anticipated to be <30 cubic yards (segregated and compacted), including dry waste, liquid waste, and glassware.

Several waste minimization strategies will be employed. Production methods that generate minimum amounts of waste will be used whenever feasible. Where possible, radioactive byproducts (potential hazardous waste) will be converted into useful, marketable products, such as ^7Be (53 d) and ^{22}Na (2.6 y). Waste will be segregated, characterized, and compacted to minimize volume.

5.1 WASTE MANAGEMENT PLAN AT UC DAVIS LOCATIONS

This plan is based on an existing and fully operational Health Physics Program at the University of California, Davis. The program has overall responsibilities for waste management derived from the general education and research activities at the UC Davis Campus as well as the education, research, and clinical activities of the UC Davis Medical Center in Sacramento (UCDMC-Sacramento). The Health Physics Program involves the Offices of Environmental Health & Safety (EH&S) at Davis and Sacramento, which are directly responsible for these matters at each location.

UC Davis's Health Physics Program has overall responsibilities for more than 350 Radioisotope Use Authorizations, involving nearly 1,200 research and teaching laboratories, and the participation of approximately 3,000 researchers. The extent of the basic, applied, and clinical R&D using radioactive materials at UC Davis amounts to nearly \$200 million per year [UC Davis Office of the Vice Chancellor of Research, January 1995].

Currently, the Health Physics Program and the EH&S offices in Davis and Sacramento operate a landfill facility located at the UC Davis Campus and a storage facility at UCDMC-Sacramento.

In 1993 the UC Davis administration, recognizing the essential role of the Health Physics Program in supporting the academic mission of UC Davis and UCDMC-Sacramento, approved the expansion of these facilities as a means to comply with new regulations and overcome new restrictions in waste management and disposal. By 1998, a new \$14 million (30,000 sq.ft) Environmental Services Facility (ESF) will be added and be assigned to the EH&S Office at the Davis Campus.

It is our plan to rely on the new ESF to handle all waste management and disposal requirements derived from NBTF — including handling, storage, and shipping of hazardous, radioactive, and mixed wastes. The new ESF will provide this resource to either of the two potential UC Davis sites being considered for NBTF (i.e., Davis and Sacramento).

5.1.1 UC Davis Environmental Services Facility (ESF)

As described in the UC Davis ESF Operational Plan [UC Davis Environmental Services Facility, Project Description, March 31, 1994], handling and storage of hazardous, radioactive, and mixed waste at ESF will be accomplished by using dedicated areas for radioactive waste operations, mixed waste operations, and hazardous waste operations. Floors are designed to accommodate drum storage and forklift loads. Continuous air monitoring for all radioactive and mixed waste stacks is provided through an isokinetic sampling system. Redundant exhaust fans with dual DOP treatable HEPA filters will also be installed.

The facility will be provided with a security system requiring card key access gates to the service yards and card key access doors to the administration area. Intruder alarms will be set to turn on after work hours and on weekends and holidays. This alarm system will be controlled from a central panel. There will be a one-alarm zone for the entire facility.

NBTF's anticipated <30 cubic yards per year of waste should be easily handled by UC Davis's new ESF facility.

5.1.2 Compliance Regulations for the UC Davis Environmental Services Facility

The regulations governing the approval and commissioning of the new UC Davis ESF are summarized here, divided into (a) codes, standards, and publications, and (b) references.

(A)	Codes, Standards, and Publications
1.	29 CFR Part 1926, Safety and Health Regulations for Construction, Department of Labor
2.	29 CFR Part 1910, Occupational Safety and Health Standards, Department of Labor
3.	National Fire Codes (NFPA), 1991 edition
4.	National Electrical Safety Code (ANSI C2)
5.	National Electric Code, NFPA 70, 1993 edition
6.	Lists of Inspected Appliances, Equipment, and Materials (Underwriters Laboratories, Inc.)
7.	Approval Guide of Equipment, Material, Services for Conservation of Property (Factory Mutual Engineering Corp.)
8.	Safety Code for Building Construction, ANSI A10 Series
9.	California Administrative Code, Title 8, General Industry Safety Orders, Construction Safety Orders, 1992 edition
10.	California Administrative Code, Title 19 and Title 24, 1992 edition
11.	Uniform Building Code (UBC), 1991 edition
12.	Uniform Mechanical Code (UMC), 1991 edition
13.	Uniform Fire Code (UFC), 1991 edition
14.	Uniform Plumbing Code (UPC), 1991 edition
15.	Federal, state, and local air pollution and water pollution control regulations
16.	Standards of the American Society for Testing of Materials (ASTM)
17.	American National Standards Institute (ANSI) Standards
18.	American Concrete Institute, Building Code Requirements (ACI 318-89) and Commentary (ACI 318R-89)
19.	Manual of Steel Construction, American Institute of Steel Construction (AISC), Allowable Stress Design (ASD), ninth edition

Figure 2-1. NBTf Facility Layout

TITAN Beta

CYCLOTRON OPERATION
SPACE = 33700 SQ. FT.

SHIELDING AREA = 9968 SQ. FT.

OFFICE SPACE = 2911 SQ. FT.

(B)	References
1.	Standards and Codes of the American Society of Mechanical Engineers (ASME)
2.	American Water Works Association (AWWA) Standards
3.	American Welding Society Handbook and Standards (AWS)
4.	National Electric Manufacturers Standards (NEMA)
5.	Insulated Cable Engineer's Association (ICEA) Standards
6.	State of California Department of Transportation, Highway Design Manual
7.	State of California Department of Transportation, Standard Specifications, latest edition
8.	Building Code Requirements for Reinforced Concrete (ACI 318-89)
9.	Guidelines for Seismic Restraints of Mechanical Systems and Plumbing Piping Systems, 1990 edition, published by the Sheet Metal Industry Fund of Los Angeles (SMACNA)
10.	Suspended Ceiling System Survey and Seismic Bracing Recommendations for the Lawrence Livermore National Laboratory, UCRL-15714, August 1985
11.	Americans with Disabilities Act (ADA)

5.2 WASTE MANAGEMENT PLAN AT LLNL LOCATION

Lawrence Livermore National Laboratory has operated for many years resources and facilities that greatly exceed the scope of operation intended or planned for NBTF. If NBTF is located at LLNL as part of the existing academic linkage between UC Davis and LLNL, we propose that all of the physical handling, storage, and disposal of hazardous materials as well as the administrative responsibility for waste management generated from NBTF be incorporated into LLNL's existing health physics programs. LLNL has a fully permitted RCRA (Part B) Treatment, Storage, and Disposal Facility [ref. UCAR-10275-93]. In addition, a new large-scale waste handling facility is currently being developed.

6.0 NBTF BUSINESS PLAN

This business plan has been prepared to provide estimates of annual revenue and operating expenses, in order to evaluate the economic viability of NBTF.

6.1 NBTF REVENUE FROM RADIOISOTOPE PRODUCTION

6.1.1 Data Sources for Estimating NBTF Revenue from Radioisotope Production

Radioisotope sales revenue and market data were obtained from the U.S. Department of Energy's Isotope Production and Distribution Program for FY1990, 1991, 1992, and 1993. Additional data were provided by the Radiopharmaceutical Market (Diagnostic Nuclear Medicine) and Radiochemical Market Studies conducted by the Technology Marketing Group [TMG Study, 1994] and reported in August 1994. Other assumptions and estimates were based on information obtained through direct consultation and discussions with marketing and sales representatives from U.S. and foreign commercial suppliers and radiopharmaceutical companies, and by direct consultation with scientists involved in radioisotope production in national laboratories, universities, and private-sector institutions. Revenue data from the operation of the Crocker Nuclear Laboratory's Radioisotope Program were also used to estimate the extent of existing and potential research radioisotope markets and demand levels.

6.1.2 Underlying Assumptions about NBTF Operations, Management, and Policies

The following assumptions were made in generating these estimates:

- (1) NBTF would supply, whenever possible, the entire radioisotope market covered by the operation of DOE's Isotope Production & Distribution Program currently based on the operation of LANL and BNL radioisotope production programs.
- (2) NBTF would match and greatly exceed all technical capabilities currently available in the commercial and non-commercial radioisotope production sectors.
- (3) NBTF would match or greatly exceed all quality attributes of the desired radionuclides and, therefore, no marketing or research-use restrictions would exist.

- (4) NBTF would be designed and staffed to operate on a continuous or a scheduled basis to fulfill the needs of the user community.
- (5) NBTF would not compete with the commercial sector by producing Thallium-201, Gallium-67, or Indium-111 as these isotopes are readily available and in sufficient amounts from many commercial sources. That is, NBTF would not serve a backup role to the commercial sector, as it appears that this function is not needed.
- (6) NBTF would produce Iodine-123 for research purposes only and as a partial exception to the non-competition statement (see 5, above). Although Iodine-123 is produced commercially, it is not readily available for research. NBTF would supply labeling-quality, high concentration Iodine-123 in various radiochemical forms to be used only for radiochemistry (labeling) and radiopharmaceutical research (pre- and clinical tests), primarily in the United States.
- (7) The production of large batches of Fluorine-18 is included as it appears that regional market distribution networks will be highly desirable under certain conditions to serve the expected demands for Positron Emission Tomography in large population centers.

We propose that these conditions and guidelines form part of a set of operational and programmatic guidelines and policies applicable to all management and operational strategies likely to be instituted to allow effective operation of NBTF.

6.1.3 Criteria for Estimating NBTF Revenue from Radioisotope Production

Revenue estimates for NBTF were developed for three different levels of expectation: firm, likely, and optimistic. The "firm" (very likely) estimate was established first, using data from the DOE's Isotope Production and Distribution Program and from Crocker Nuclear Laboratory. The next levels ("likely" and "optimistic") were then extrapolated on the basis of research and marketing information made available to the project team. The rationale behind the extrapolated "likely" and "optimistic" estimates is based on market demands and on the superior operational and throughput capabilities designed for the operation of a dual-cyclotron NBTF facility dedicated primarily to radioisotope production.

The rationale and the specific boundaries behind these categories are as follows:

Firm: These estimates are based on existing market data from DOE's FY1990 to 1993 sales of radioisotopes produced at LANL and BNL. These estimates were updated to expected FY1994 and FY1995 levels by assuming a conservative 10% per year increase. In addition, based on revenue data from the UC Davis Crocker Nuclear Laboratory, projected sales of Cobalt-57, Palladium-103, Iodine-123, and Fluorine-18 — which were not produced or included in the DOE's database — were also included in developing these estimates.

Likely: These estimates are based on the expectation that once NBTF is fully operational, the increased availability and reliability of supply will lead to an increase in the existing radioisotope markets. The "likely" estimates include a 30% increased market for the major research and industrial isotopes included in the "firm" estimates.

Optimistic: These estimates are based on the best-case scenario that may develop on the basis of a fully operational NBTF supplying radioisotope needs in the United States as well as abroad. However, a conservative approach was used by assuming that even in the best-case scenario, the technology available to NBTF requires utilization of less than 50% of its full production capacity. This is necessary to allow executing and supporting all of NBTF's other research and educational activities.

In all cases where extrapolated ("likely," "optimistic") estimates were established, only reasonable levels of market growth rates and demand levels were used. As an additional constraint for these estimates, we did not include increases in radioisotope prices which did in fact occur each year from 1990 to 1994. We therefore consider these estimates to be conservative and well within the conditions specified.

6.1.4 Analysis of Revenue Data from DOE's Radioisotope Production Programs

A number of biomedical research isotopes have been produced primarily and in large Curie quantities at DOE facilities at the Los Alamos National Laboratory and the Brookhaven National Laboratory. The production and revenue levels of these isotopes during FY1990–1993 were reported by the DOE Radioisotope Production and Distribution Program; these data are summarized in Tables 6-1 (Los Alamos), 6-2 (Brookhaven), and 6-3 (total DOE).

Table 6-1. Radioisotopes Produced and Sold by the Los Alamos National Laboratory

Radioisotope	Sales, in \$K and (Production Level, in mCi)			
	FY1990	FY1991	FY1992	FY1993
Aluminum-26	10.8 (0.001)	22.4 (0.003)	18.5 (0.05)	36.8 (0.99)
Arsenic-73	5.1 (30)	3.8 (22.1)	4.8 (23)	10.4 (66)
Beryllium-7	n/a	2.8 (5.6)	3.9 (9.5)	3.4 (7)
Bismuth-207	n/a	n/a	5.9 (0.4)	3.7 (0.2)
Cadmium-109	111 (2851)	121 (3039)	175.1 (3604)	198 (3564)
Copper-67	37.6 (1795)	33.1 (1615)	106 (2686)	30 (408)
Gadolinium-148	n/a	n/a	4.6 (0.01)	9.2 (0.02)
Germanium-68	184 (1068)	165 (1095)	236.9 (1132)	405.9 (1554)
Rubidium-83	5.8 (35)	1.8 (6.2)	4.3 (20)	n/a
Selenium-75	n/a	n/a	n/a	2.3 (204)
Silicon-32	n/a	1.5 (0.001)	39.0 (0.04)	21.8 (0.02)
Sodium-22	46.8 (1311)	49.0 (1645)	82.3 (1369)	147.4 (1702)
Strontium-82	301 (4615)	633 (9016)	482 (5826)	391 (4255)
Strontium-85	n/a	n/a	0.4 (1)	n/a
Technetium-95m	n/a	n/a	3.3 (3)	7.4 (7)
Vanadium-48/49	n/a	0.8 (4.2)	0.9 (3)	2.6 (10)
Yttrium-88	20.4 (85)	19.2 (79)	17.8 (64)	15.1 (61)
Zinc-65	n/a	n/a	n/a	2.3 (0.1)
Zirconium-88	1.2 (5)	0.6 (2)	n/a	0.5 (0.1)
Total	723	1,053	1,185	1,287

Source: DOE Radioisotope Production & Distribution Program.

Table 6-2. Radioisotopes Produced and Sold by the Brookhaven National Laboratory

Radioisotope	Sales, in \$K and (Production Level, in mCi)			
	FY1990	FY1991	FY1992	FY1993
Beryllium-7	10.7 (57)	0.2 (1)	n/a	3.0 (12)
Copper-67	10.4 (224)	13.9 (258)	14.7 (258)	27.9 (382)
Germanium-68	110.6 (601)	143.9 (805)	198.6 (838)	100.4 (398)
Magnesium-28	4.4 (10)	12.3 (21)	4.4 (0.4)	n/a
Rubidium-83	n/a	0.8 (10)	n/a	n/a
Ruthenium-97	n/a	n/a	n/a	5.8 (100)
Strontium-82	183.4 (2321)	318.0 (4350)	309.4 (3436)	612.0 (4539)
Technetium-96	1.4 (n/a)	0.2 (64)	4.2 (44)	3.5 (30)
Xenon-127	32.4 (3220)	1.3 (90)	4.4 (195)	1.6 (65)
Total	353.3	490.7	535.6	754.2

Source: DOE Radioisotope Production & Distribution Program.

Table 6-3. Total Radioisotopes Produced and Sold by the DOE, FY1990-93

Radioisotope	Sales, in \$K and (Production Level, in mCi)			Percent of Total Sales
	LANL	BNL	Total DOE	
Aluminum-26	88.5 (1.0)	—	88.5 (1.0)	1.4
Arsenic-73	24.1 (141.1)	—	24.1 (141.1)	0.4
Beryllium-7	10.1 (22.1)	13.9 (70)	24.0 (92.1)	0.4
Bismuth-207	9.6 (0.6)	—	9.6 (0.6)	0.2
Cadmium-109	605.1 (13058)	—	605.1 (13058)	9.5
Copper-67	206.7 (6503)	66.9 (1122)	273.6 (7625)	4.3
Gadolinium-148	13.8 (0.03)	—	13.8 (0.03)	0.2
Germanium-68	991.8 (4849)	553.5 (2642)	1,545.3 (7491)	24.2
Magnesium-28	—	21.1 (31.4)	21.1 (31.4)	0.3
Rubidium-83	11.9 (61.2)	0.8 (10)	12.7 (71.2)	0.2
Ruthenium-97	—	5.8 (100)	5.8 (100)	0.1
Selenium-75	2.3 (204)	—	2.3 (204)	†
Silicon-32	62.3 (0.061)	—	62.3 (0.061)	1.0
Sodium-22	325.5 (6027)	—	325.5 (6027)	5.1
Strontium-82	1807 (23712)	1422.8 (14646)	3,229.8 (38358)	50.6
Strontium-85	0.4 (1)	—	0.4 (1)	†
Technetium-95m	10.7 (10)	—	10.7 (10)	0.2
Technetium-96	—	9.3 (138)	9.3 (138)	0.2
Vanadium-48/49	4.3 (17.2)	—	4.3 (17.2)	0.1
Xenon-127	—	39.7 (3570)	39.7 (3570)	0.6
Yttrium-88	72.5 (289)	—	72.5 (289)	1.1
Zinc-65	2.3 (0.1)	—	2.3 (0.1)	†
Zirconium-88	2.3 (7.1)	—	2.3 (7.1)	†
Total	4,251.2	2,133.8	6,385.0	≈100

† negligible
(less than 1/10th
of 1 percent)

Source: Tables 6-1 and 6-2.

The combined DOE radioisotope revenue (FY1990–1993) from both LANL and BNL amounted to \$6,385,000 — for a yearly average of nearly \$1.6 million. Revenue data for FY1994 are not available at this time, but if a conservative increase of 10% is assumed revenue can be estimated at \$2.25 million for FY1994 and \$2.5 million for 1995 (see Fig. 6-1). The 10% increase is considered a conservative and realistic estimate based on yearly growth in excess of 10% from FY1990–93.

Figure 6-1. DOE Radioisotope Production Revenue

6.1.5 NBTF Revenue from Production of Radioisotopes Currently Produced by DOE

Further extrapolations to the existing revenue data from DOE markets were made under the following rationale and market conditions:

- (a) Revenue sales are largely dominated by four long-lived radioisotopes (i.e., Cadmium-109 (462.3 d), Germanium-68 (271 d), Sodium-22 (2.6 y) and Strontium-82 (25.6 d), amounting to nearly 90% of the total revenues over the FY1990-93 period (see Fig. 6-3);
- (b) The market needs for these isotopes will continue and be increased when supplied by NBTF because of their greater availability which will result from a fully operational and dedicated facility; and
- (c) Production efficiencies, in contrast to LANL and BNL programs, can be increased by incorporating modern cyclotrons capable of augmenting production yields.

Under these conditions, we conclude that the total revenue projections for NBTF can reasonably be increased by another 10% (a conservative level) to \$2.75 million a year.

The analysis of DOE revenue sources provides, then, the basis for the "firm" estimate of \$2.75 million used in the financial analysis of NBTF during its first year of full operation, under the above-mentioned operating assumptions. A "likely" estimate would amount to \$3.5 million for this first year if the actual annual growth rates for DOE sales during FY1990-1993 are used. The "optimistic" estimate was set at \$4.5 million, and assumes the growth of Sr-82 (Rb-82) for PET studies continues and market demand increases by 50%.

NBTF revenue from radioisotopes currently produced by DOE:

FIRM	\$2.75M	LIKELY	\$3.5M	OPTIMISTIC	\$4.5M
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6.1.6 Additional Revenue from Production of Co-57 and Pd-103

Additional expectations for revenue can be justified if Cobalt-57 (271.2 d) and Palladium-103 (16.97 d) are also added to the production plan for NBTF. These two isotopes have well-defined markets that have recently been estimated by the Technology Marketing Group study (August 1994) at \$1,000,000 annually apiece.

We are proposing that NBTF be built as a dual-cyclotron facility, with each cyclotron (and its shielding) capable of operating initially at 1 mA, upgradable to 2 mA. The multiple target capabilities (4 target areas per cyclotron) can then be used to readily enhance production levels for both of these isotopes. Today, Cobalt-57 and Palladium-103 are each best produced with low energy protons (20–30 MeV) on metallic targets. However, higher energy reactions in the 40–60 MeV range have been studied and could be used to supplement yields via parasitic bombardments, dual targets, or other approaches — thus taking advantage of the proposed dual-cyclotron NBTF.

Production of Cobalt-57 for the U.S. market is now being conducted mostly abroad. One U.S. company (Theragenics, Norcross, GA) is currently producing Palladium-103. Theragenics has expressed interest in increased availability of Palladium-103 and is planning to commission another cyclotron for its production [TMG Study, 1994]. Higher production capacity appears to be needed even after Theragenics' planned expansion, because the market for therapeutic radiopharmaceuticals is expected to grow significantly.

Given this rationale, it can be assumed that a 30% market share for each of these two isotopes can be readily accomplished by a fully operational NBTF. This would add \$600,000 in revenue to the "firm" estimate from DOE sales of \$2.75 million (see above) for a combined total of \$3.35 million per year. "Likely" and "optimistic" estimates for Cobalt-57 and Palladium-103 were established at \$800,000 (40% market share) and \$1,000,000 (50% market share) respectively. No foreign sales have been included, although some should be expected and are considered likely.

NBTF revenue from Co-57 and Pd-103:

FIRM	\$0.6M	LIKELY	\$0.8M	OPTIMISTIC	\$1.0M
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6.1.7 Additional Revenue from Production of I-123 and F-18

Many of the needed biomedical research radioisotopes are not readily available to U.S. researchers. Many others are not used simply because, although they are potentially available, their production and routine availability — important factors in planning and coordinating re-

search — are questionable. It is therefore difficult to elaborate a solidly based projection of the research market for such radioisotopes, and hence to estimate their impact on the revenue basis for NBTF. An example is the research needs related to the production of Xenon-122 and its distribution as a Xenon-122 (20 h) → Iodine-122 (3.6 min) generator for PET research and applications [Thomas F. Budinger, Lawrence Berkeley Laboratory, private communication]. Although Xenon-122 has been investigated and shows promise as a useful tool in R&D in diagnostic nuclear medicine, further research is impaired because of routine availability problems and cost [Adelstein & Manning, 1994, p. 9].

A few exceptions do exist in the United States, with the operation of the Crocker Nuclear Laboratory (CNL) at the University of California, Davis. CNL currently produces research quantities of Bismuth-205/206, high-specific activity Lead-203, and research quantities of Technetium-99m, and also has production capabilities to produce Iodine-123, Xenon-122 (Iodine-122), Cobalt-55, and Fluorine-18 via many different routes. The operation of Crocker Nuclear Laboratory and its Radioisotope Program is the only example in the United States of an accelerator operated as a self-supporting academic unit. The extent of the CNL Radioisotope Program is illustrated in Table 6-4 and its outreach in the United States and abroad is summarized in Appendix B. Clearly, this is a good model for projecting revenue and for evaluating the financial viability of NBTF. CNL and the proposed NBTF share similar missions and the expectation of financial self-sufficiency.

Over the last 15 years, CNL has accumulated market data for the sales of radioisotopes, radiochemicals, and radiopharmaceuticals. We have used this information to estimate with some degree of certainty the existence and extent of these potential markets for NBTF.

Since the 1980s, CNL's Radioisotope Program has produced Ci quantities of Iodine-123 (5 days a week) and Fluorine-18 (twice a week) for radiopharmaceutical uses and small tens-of-millicurie amounts of many research radionuclides including Cobalt-55, Xenon-122, Lead-203, Ruthenium-97, and Bismuth-205/206. The total income produced by these activities amounted to approximately \$5,000,000 in 7 years (average \$714,000 per year). Nearly 70% and 15% of this income, respectively, were derived solely from the sales of Iodine-123 and Fluorine-18. Indeed, the CNL cyclotron — which is a 70 MeV isochronous cyclotron with limited ($<25 \mu\text{A}$) external proton beams — averaged as much revenue ($\approx \$714,000$) as BNL and for many radioisotopes had revenue levels comparable to LANL. Crocker Nuclear Laboratory's

Table 6-4. Radioisotopes, Radiochemicals, and Radiopharmaceuticals Produced at the Crocker Nuclear Laboratory's Radioisotope Program, University of California, Davis (1975-present)

Radioisotopes	
<i>SPECT Radioisotopes</i>	
Iodine-123	Technetium-99m
Gallium-67	Thallium-201
<i>PET Radioisotopes</i>	
Barium-128→Cesium-128	Nitrogen-13
Carbon-11	Rubidium-81
Chlorine-34m	Strontium-82→Rubidium-82
Cobalt-55	Tellurium-118→Antimony-118
Fluorine-18	Xenon-122→Iodine-122
<i>Research Radioisotopes</i>	
Astatine-211	Lead-203
Bismuth-205/206	Molybdenum-99
Cobalt-56	Palladium-100
Cobalt-57	Palladium-101
Cobalt-58	Rhodium-101m
Iodine-124	Ruthenium-97
Iodine-131	Xenon-125
Lead-201	
Radiochemicals; and SPECT- and PET-Radiopharmaceuticals	
¹²³ I-HPDM	<i>Supplied certified for human use:</i>
¹²³ I-Fibrinogen	¹²³ I-Sodium Iodide
¹²³ I-Bleomycin	¹²³ I-Sodium o-Iodohippurate
¹²³ I-Iodine Mono-Chloride	²⁰¹ Tl-Thallous Chloride
⁵⁵ Co-Bleomycin	¹⁸ F-Fluor-deoxyglucose

Total revenue from production and distribution of these products (1983-89) ≈ \$5,000,000

Average annual revenue (1983-89) \$714,000

average annual revenue from Iodine-123 (5 years) was \$500,000. For Fluorine-18 (8 years) it reached \$110,000 while serving three PET research centers in Northern (UC Berkeley, Stanford University) and Southern (UC Irvine) California.

The major reason for this financial record is that CNL operated routinely for 48 weeks each year and achieved >95% reliability of supply for both Iodine-123 and Fluorine-18. In addition, CNL established scheduling priorities to meet the demands imposed by the production schedules, by the physical parameters (i.e., half lives) of Iodine-123 (13.2 h) and Fluorine-18 (110 min), and by the distribution network. Clearly the programmatic focus and guidelines established at CNL contributed largely to the financial success of the Radioisotope Program.

It is anticipated that the Fluorine-18 research and clinical markets in Northern and Southern California that have been served by CNL over the past 8 years will be served in the future by NBTF. Nevertheless, we have adopted a conservative approach in estimating the additional NBTF potential revenue from Iodine-123 and Fluorine-18 sales. A "firm" estimate was projected at \$300,000/year (\$150,000 each). The "likely" estimate of \$600,000/year (\$200,000 for Iodine-123 and \$400,000 for Fluorine-18) is well within past performance at CNL. The "optimistic" estimate is \$800,000/year (\$250,000 for Iodine-123 and \$550,000 for Fluorine-18). These estimates are reasonably achievable if larger demands for research quality Iodine-123 and a regional supply of Fluorine-18 for PET clinical programs — through a regional radiopharmacy system — are adopted as NBTF support activities.

No foreign sales for Iodine-123 have been included in these estimates, although some should be expected and are considered likely in Central and South America.

NBTF revenue from I-123 and Fl-18:

FIRM	\$0.3M	LIKELY	\$0.6M	OPTIMISTIC	\$0.8M
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6.1.8 Summary of NBTF Revenue Estimates from Radioisotope Production

From the preceding projections and estimates, the annual revenue for NBTF derived from the production and distribution of both biomedical research and noncommercial biomedical/industrial radioisotopes is summarized in Table 6-5.

Table 6-5. NBTF Annual Revenue Estimates from Radioisotopes

Radioisotope	Revenue Estimate (\$ million)		
	Firm	Likely	Optimistic
Biomedical Research	2.75	3.50	4.50
Co-57 and Pd-103	0.60	0.80	1.00
I-123 and F-18	0.30	0.60	0.80
Total	3.65	4.25	6.30

*Sources: For biomedical research radioisotopes, DOE data;
for Co-57 and Pd-103, TMG data; and
for I-123 and F-18, CNL data. See text.*

6.2 NBTF REVENUE FROM OTHER SOURCES

6.2.1 Research & Development

Research and development activities are to be a major focus of NBTF's mission. R&D has been strongly considered in this project and has influenced all of the design and operational plans for NBTF. We recommend (see Sec. 6.6.2) that some portion of the basic research and development activities be funded directly by DOE. Such funding would directly support NBTF's broad interdisciplinary research mission:

- (1) The operation of the proposed NBTF will develop into a Center of Excellence and will allow R&D to be conducted with the best technology available and supported by a leading group of advisory scientists from a variety of scientific disciplines interacting with the investigating scientists;
- (2) The R&D to be conducted at NBTF would include the use of several of NBTF's unique features, such as the broader proton energy range available by using two cyclotrons and the accelerator-based neutron production area, which will provide neutron reaction research capabilities and the possibility of producing small amounts of neutron-rich isotopes as an alternative to reactors.

Despite the general consensus and clear definition of scope for NBTF, it is difficult at this time to project the extent of core support that will be needed for NBTF research and development. For the purpose of this Phase I study, we have estimated \$1 million per year would be provided to support a diverse group of research activities at NBTF. These R&D activities would be conducted under set criteria, using a peer-review system for evaluating the merit of basic and applied R&D proposals generated by NBTF in collaboration with the overall scientific community. Core support of \$1 million per year to supplement other income seems adequate, and is used as the "firm" revenue estimate in this analysis. "Likely" and "optimistic" revenue estimates from R&D activities have been set at \$1.5 and \$2.0 million per year.

The core support for NBTF R&D activities and programs is summarized in Table 6-6. The fractional support for R&D from these core funds has been set somewhat arbitrarily (but consistent with NBTF's mission) at 30% for basic R&D and 70% for applied R&D.

Table 6-6. NBTF Annual Revenue Estimates from Core Support of R&D

Radioisotopes	Revenue Estimate (\$ million)		
	Firm	Likely	Optimistic
Basic R&D (Nuclear Sciences; Life & Environmental Sciences; Food & Agriculture)	0.3	0.5	0.7
Applied R&D (Radioisotope Production Radiochemistry: Targetry, Clinical Trials, Biotechnology Product & Instrumentation Testing, Beam Services)	0.7	1.0	1.3
Total	1.0	1.5	2.0

Sources: See preceding text.

6.2.3 Intellectual Property and Licensing Fees

No revenue from intellectual and industrial properties (patents and trade secrets) or licensing fees is forecast for the first five (5) years of full operation. This allows a reasonable period of basic and applied R&D activities in which to build the foundations for developing new patentable results. Projections beyond the initial 5-year phase cannot be justified at this time because of the many uncertainties regarding the final operational infrastructure for NBTF.

However, it is recommended that provisions to establish guidelines leading to the development of patentable results be set from the beginning, as NBTF is likely to become the focus of many technological innovations.

6.2.3 Education Programs and Outreach Activities

NBTF is chartered by the nuclear and biomedical science community with being a driving force in education and outreach activities to be performed through the establishment and support of various programs and activities.

Programs for nuclear scientists and technicians; graduate and under-graduate students; and professional, industrial, and academic scientists and engineers from the United States and abroad are expected to be an important part of NBTF. The organization of workshops, seminars, symposia, and conferences — in collaboration with other institutions — is also expected to be a function of NBTF. As part of NBTF's education and outreach missions, Federal and State scientists and technical staff of the regulatory agencies can be introduced and trained in all aspects of nuclear sciences and applications.

Financial support for many of these activities can be obtained from other DOE sources; the National Academy of Sciences; Federal and State agencies; and professional societies such as the Society of Nuclear Medicine, the American College of Nuclear Physicians, the American Nuclear Society, the American Chemical Society, the American Physics Society, and many others. Further support for these education and outreach activities may be obtained from private sources, including the major radiopharmaceutical manufacturers, the biotechnology industry, and the major instrument manufacturers — through the establishment of grants and fellowships. Ultimately, most of these groups are expected to benefit from the presence and educational focus of NBTF.

Due to the critical mission to be played by NBTF, it is reasonable to expect that funding will be available to support a small but permanent core of programs. Therefore, while we believe that significant funding is definitely available for these activities, we have adopted once more a cautious (conservative) approach and have established a "firm" annual revenue estimate of only \$100,000 for these activities. The "likely" estimate has been established at \$200,000 per year, which is especially reasonable when averaged over a longer operational period, once NBTF has established a scientific reputation and a good record of scientific, technical, and educational achievements. Finally, the "optimistic" estimate was set at \$300,000 per year.

6.2.4 Summary of NBTF Revenue Estimates from Other Sources

From the preceding projections and estimates, the annual revenue for NBTF derived from sources other than the production and distribution of radioisotopes is summarized in Table 6-7.

Table 6-7. NBTF Annual Revenue Estimates from All Other Sources

Source	Revenue Estimate (\$ million)		
	Firm	Likely	Optimistic
Research & Development	1.0	1.5	2.0
Intellectual Property and Licensing Fees	—	—	—
Education Programs and Outreach Activities	0.1	0.2	0.3
Total	1.1	1.7	2.3

Sources: See preceding text.

6.3 SUMMARY OF ESTIMATED NBTF REVENUE FROM ALL SOURCES

The total estimated NBTF revenue is presented in Table 6-8 and in Fig. 6-2.

Table 6-8. Total NBTF Annual Revenue Estimates from All Sources

Source	Revenue Estimate (\$ million)		
	Firm	Likely	Optimistic
Radioisotope Production & Distribution	3.65	4.25	6.30
All Other Sources	1.10	1.70	2.30
Total	4.75	5.95	8.60

Sources: Tables 6-5 and 6-7.

Figure 6-2. Total Estimated Annual NBTF Revenue

6.4 NBTF EXPENSES

6.4.1 Assumptions and Data Sources for Estimating Expenses

The annual cost for operating the proposed NBTF is estimated based on projected expenses for personnel (management and staff) and for operation of the facility. It is assumed that NBTF will be operational for 52 weeks ($\approx 8,736$ h) each year, with $\approx 80\%$ use factor ($\approx 6,990$ h) for both accelerators. These are extreme operational goals, and they are used in order to provide a very conservative maximum operational cost. This approach is consistent with the conservative estimates made for revenue sources.

Cost data associated with the operation of Crocker Nuclear Laboratory's 76-in. cyclotron along with its ancillary research and maintenance facilities were also used in estimating and projecting NBTF annual expenses.

6.4.2 Management and Staff Expenses

The level of personnel (full-time equivalent, FTE) necessary to operate and maintain the NBTF facility and fulfill its programmatic objectives is estimated at 45 FTE. A general distribution of FTE classifications is given in Table 6-9.

It is assumed that salaries plus benefits (at 20-30%) average \$60,000/year/FTE, for a total annual management and staff expense of \$2.70 million. Current (FY1994/95) salary levels for faculty and professional staff at the University of California, Davis, were used in these estimates.

6.4.3 Other Operational Expenses

All other expenses — including power consumption, site and equipment maintenance and repairs, and S&E — to support NBTF are itemized in Table 6-10. The estimates were based on the operation of the Crocker Nuclear Laboratory and extrapolated to the proposed NBTF facility. These estimated "other" operational expenses total \$2.53 million/year.

Table 6-9. NBTf Personnel Classification and Annual Cost Estimates**(A) Management, Administration, Clerical**

Management (Director, Associate Directors [2], Chief Financial Officer)	4 FTE
Administration (Clerical)	3 FTE
Public Relations/Customer Service	2 FTE
Chief Custodian	1 FTE
Subtotal	10 FTE

(B) Research Scientists

R&D Scientific Leadership Staff	5 FTE
R&D and Technical Staff	10 FTE
Sponsored Visiting Scholars, Scientists & Students	5 FTE
Subtotal	20 FTE

(C) Technical Operation and Support Staff

Accelerator Operation	8 FTE
Environmental Health & Safety Staff	2 FTE
Technical Staff (Electronic, Mechanical, Computer)	5 FTE
Subtotal	15 FTE

TOTAL STAFF	45 FTE
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TOTAL ESTIMATED ANNUAL PERSONNEL COST	\$ 2.7 million
(Avg. \$60,000 Salary & Benefits / Y / FTE)	

Table 6-10 NBTF Estimated Other Annual Expenses (\$ Million)**(A) NBTF Operation**

Communications (telephone, fax, etc.)	0.04
Computers (software, repair, and maintenance)	0.06
Security, Site Maintenance, Repair	0.30
Transportation (3 cars, 3 trucks)	0.05
Site Equipment Rental and Services	0.25
Subtotal	0.70

(B) NBTF Utilities

Power Utilities	0.61
(1,200 kWh for accelerators $\times$ 50 weeks $\times$ 0.8 duty factor; and 250 kWh for facility $\times$ 52 weeks $\times$ 1.0 duty factor)	
Water/Gas	0.02
Waste Management (storage, disposal)*	0.15
Subtotal	0.78

(C) NBTF Supplies & Expenses

Supplies and Expenses (45 FTE $\times$ \$10,000/yr.)	0.45
Subtotal	0.45

(D) NBTF Program Support

Education Expenses	0.20
(conferences, seminars, lecture series, travel to scientific/technical meetings, business travel)	
Outreach Program (travel, publications, brochures)	0.10
Legal Services, Patents, Publications	0.10
Library Expenses (books, journals)	0.05
Promotion, Advertisement, Newsletters	0.04
Licenses	0.01
Insurance (not covered by host institution)	0.10
Taxes (Non-Profit)	0.00
Subtotal	0.60

TOTAL ESTIMATED OTHER ANNUAL EXPENSES**\$ 2.53**

* Assumes waste management through the
Environmental Services Facility at UC Davis.

6.4.4 Summary of Estimated NBTF Expenses

The total estimated cost of operation amounts to \$5.23 million (\$2.70 million for personnel plus \$2.53 million for other expenses).

6.5 SUMMARY OF REVENUE AND EXPENSE ESTIMATES

The total projected revenue and expense estimates for NBTF are presented in Table 6-11. This summary includes projection of annual revenue generated from radioisotope sales, research and development activities and programs, and educational and outreach activities. Expenses include annual cost of management and staff (salaries and benefits) as well as other operational expenses derived from accelerator operation, utilities and site maintenance, supplies and expenses, and program support.

Table 6-11. Summary of Total Annual NBTF Revenue and Expense Estimates

Revenue Sources	Revenue Estimate (\$ million)		
	Firm	Likely	Optimistic
Radioisotope Production	3.65	4.90	6.30
R&D Activities	1.00	1.50	2.00
Education & Outreach	0.10	0.20	0.30
Total Annual Revenue	4.75	6.60	8.60

Expense Sources	Expenses Estimate (\$ million)
Management & Staff	2.70
Other Expenses	2.53
Total Annual Expenses	5.23

Sources: Tables 6-8, 6-9, and 6-10.

6.6 CONCLUSIONS AND RECOMMENDATIONS

6.6.1 NBTF Prospects for a Balanced Budget

From this financial analysis, potential annual revenue estimates range from \$4.75 million ("firm") to \$6.60 million ("likely") and \$8.60 million ("optimistic"). Annual expenses were estimated at \$5.23 million. Therefore we have concluded that, after its construction and commissioning, NBTF would be financially viable with minor adjustments to this income/expense analysis. The existing market data from DOE and the experience of other U.S. facilities — such as Crocker Nuclear Laboratory at UC Davis — clearly indicate that self-sufficiency is likely.

The "firm" revenue estimate of \$4.75 million/year is based on existing market data and extremely conservative market demands and market share scenarios. It assumes (as do the "likely" and "optimistic" estimates) that the operation of DOE's radioisotope production programs at both LANL and at BNL are phased out and are absorbed by NBTF. It includes a core support allocation from DOE of \$1 million/year to fund the research and development activities and programs at NBTF (see Recommendations below).

The "likely" revenue estimate of \$6.60 million/year assumes that NBTF management closely follows and quickly responds to rapid changes in market forces; the incremental increase over the "firm" estimate is largely based on projecting an increased market. In the "likely" estimate, the support allocation for R&D activities is increased to \$1.5 million. We do not discuss whether this fund should come entirely from DOE or be shared with NBTF self-generated support. Some R&D funds could be generated from NBTF-led initiatives, outside the traditional funding sources (e.g., collaborative research with the private sector).

The "optimistic" revenue estimate of \$8.60 million/year requires that NBTF use most of its potential for radioisotope production, with its marketing activities being coordinated and executed with direct participation in national, regional, and even international markets.

Once NBTF is fully operational, it is very likely to produce a net financial gain. Mechanisms should be in place to allow NBTF to invest any financial gains, although the possibility that core support be eliminated or reduced should also be included. Financial flexibility is highly desirable because NBTF will be involved in research programs that can quickly change as they are affected by new developments in many areas (i.e., medicine, life sciences, biotechnology, etc.).

6.6.2 Recommendations

Typically, the type of engineering and technological research required in the development of radioisotope production technologies is not a high priority and it is therefore not included in the programmatic objectives of most research funding sources. Direct funding of R&D by DOE (and/or the private sector) will allow NBTF to fulfill its expected role of supporting basic and applied nuclear science. Such funding would allow R&D to be planned on a long-term basis and focused on areas that are of broad interest and of high priority to the research community. Benefits from this approach may be significant in increasing national resources and reducing the cost of radiotracer-based R&D in many other scientific and technical disciplines.

We consider this core R&D funding to be part of the DOE mission, corresponding to the current funding (at much higher levels) of the radioisotope production programs at Los Alamos National Laboratory and Brookhaven National Laboratory.

We believe that NBTF should be considered as a national program requiring a combination of steady core support (including funding for its own research, at \$1 million/year) and self-generated financial resources from its service/support missions. We are confident that NBTF — once it becomes a fully operational and mature institution — will be capable of generating most if not all of its needed financial resources. We urge the U.S. Department of Energy, as the agency chartered with administering the nation's educational and research resources in the nuclear sciences, to provide a long-term plan and a commitment to core support of NBTF's research program.

7.0 OPERATING PLAN

As proposed in this study, NBTF has throughput capability far beyond what is required to meet all the goals set forth in the business plan (Section 6) and the radioisotope production plan (Section 8). Criteria for the operating plan will be dictated by the needs of the market — which, for radioisotopes, is a year-round market. NBTF will be committed to producing whatever is needed, whenever it is needed.

NBTF is being designed, and will be adequately staffed and managed, to maximize operations flexibility. Schedule will vary within the year, and from year to year, in response to varying market and research needs. New radioisotope production technologies will be developed by NBTF in order to take full advantage of its in-house capabilities (100 MeV cyclotron, neutron beam area, etc.); these new technologies will also impact the operating plan.

NBTF has been designed to be able to accommodate future increased throughput needs (as required by a potentially greatly expanded market) — for decades to come. For example, new targetry to be developed at NBTF will allow the use of more intense beams; the accelerators have been designed to be upgradable from 1 mA to 2 mA operation to provide these beams, and the shielding is designed for 2 mA operation.

Periods of non-stop operation will be interspersed with appropriate periods of “down” time as required, for example, for routine target maintenance and for scheduled preventive maintenance on the accelerators.

The operating schedules of the two cyclotrons will be staggered so that one or both is always on. This means that the 30–40 MeV energy range is always available.

Timing is critical for several of the very short-lived products, which require “just in time” delivery. The operating schedule will be arranged so that short-lived radioisotopes can be shipped for Monday delivery.

We have arbitrarily defined an operating schedule of 6-days-on, 1-day-off, for 50 weeks out of the year. The six 24-hour days total a 144-hour production week; 50 of these weeks in turn total a 7,200-hour production year. This arbitrary 300-day year is used in the analysis of the radioisotope production plan (Section 8). This schedule is roughly equivalent to that suggested

in several NBTF workshops [Holmes, 1991; Kliwer & Green, 1992], which was 24 hours/day, 7 days/week, for 42 weeks/year ($24 \times 7 \times 42 = 7,056$ hours/year). Commercial radioisotope producers typically have 100-hour weeks, 50 weeks/year (5,000 hours/year).

Indeed, NBTF as planned could meet the current market needs in under 25 weeks (both accelerators, two simultaneous targets each, see Section 8.4), thus being available more than 50% of the time to fulfill its research and development mission.

8.0 RADIOISOTOPE PRODUCTION & DISTRIBUTION PLAN

This plan demonstrates that the proposed NBTF, as described in Section 1 (Accelerator Design) and Section 2 (Facility Design), is capable of accomplishing the stated radioisotope production objectives, routinely and safely, while at the same time supporting its other missions — which include research, education, and outreach programs.

Although the subsequent distribution of radioactive materials from NBTF is important, it is not addressed in detail in this plan. The University of California at Davis' Crocker Nuclear Laboratory has shipped over 7,000 packages of radiochemicals and radiopharmaceuticals for research and medical uses without incident and in full compliance with all applicable regulations. Although new regulatory guidelines may appear in the future, we have sufficient experience and "know how" to continue our unblemished record of meeting safe distribution standards. Further, several commercial companies involved in the commercial manufacturing and distribution of radioactive materials have expressed interest in collaborating with us to distribute NBTF radioactive products (see letter from DuPont, in Appendix E).

The resulting NBTF inventory list contains isotopes with existing uses and isotopes with perceived potential uses. It contains isotopes with low-level and sporadic demands and isotopes whose current needs require a high level of commitment to routinely establish and execute production regimes. The production of these latter isotopes requires dedicated target bombardment areas, highly specialized target handling facilities, and dedicated radiochemical systems for processing and separating the desired products. Yet because of the programmatic emphasis of NBTF, most isotopes to be produced and distributed would require commitment to small-scale production regimes with general purpose facilities and routinely scheduled distribution.

The challenge is to formulate a plan that meets both of these drastically different production and distribution requirements: small-scale production of the more esoteric isotopes on the one hand, and large-scale routine production of established isotopes on the other hand.

8.1 SELECTION AND CLASSIFICATION OF NBTF RADIOISOTOPES

We have selected and classified an inventory of radioisotopes to be produced by NBTF, on the basis of previous reports and also in consideration of the business plan proposed in this report (see Section 6).

Extensive discussions and detailed analyses of the nation's needs for research radioisotopes have recently been made via NBTF workshops at the Los Alamos National Laboratory [Moody & Petersen, 1989] and at Purdue University [Kliwer & Green, 1992]. Additional inventory lists and rationales have been reported by the Society of Nuclear Medicine and the American College of Nuclear Physicians [Holmes, 1991] and more recently by the Institute of Medicine [Adelstein & Manning, 1994]. We do not address or challenge the rationale behind the selection and choices of NBTF radioisotopes reported elsewhere. Instead, we focus on analyzing how to utilize and manage the proposed NBTF resources to best achieve its dual goal of providing an adequate radioisotope supply at a reasonable cost while at the same time supporting its research mission.

In addition, existing DOE commitments to the research community and to the private sector call for the production and supply of many radioisotopes from DOE's programs at Los Alamos and Brookhaven. All these isotopes have been identified as having important roles in fulfilling critical technical needs in medical and clinical research and in industrial applications. Several of these radioisotopes are special cases because they are being produced only through the DOE's programs at LANL and BNL. If NBTF is to replace these programs, it must assume responsibility for the supply of these radioisotopes.

The current radioisotope market is being affected by the appearance of new inventories from international sources, especially Russia and Canada. These foreign sources have already had an effect on DOE's Isotope Production and Distribution Program (IPDP) market share. During FY1994 [unofficial data], the expected revenue levels from radioisotope production at LANL and BNL were not met, despite the production of adequate levels in a reduced schedule of operation. The market was especially affected by the introduction of new inventories of Strontium-82 and Germanium-82, two of the most profitable radioisotopes produced at LANL and BNL. Clearly new market forces are in place and need to be considered.

In the scientific literature as well as the news media, radioisotopes are variously classified, on the basis of their intended use (broadly or narrowly defined) and on the basis of their

production source, resulting in a hodgepodge of overlapping categories — e.g., “research,” “industrial,” “commercial,” “medical,” “PET,” and “labeling” isotopes, etc. For this Project Definition Study, we have divided the proposed NBTF radioisotopes into two basic groups:

- (a) **NBTF Research Radioisotopes** are isotopes for basic and applied research, selected after careful review by the NBTF National Research Steering Committee. The selected isotopes are to be produced on a scheduled basis in generally small batches in sub-Curie amounts. The research radioisotopes include both neutron-deficient isotopes normally produced via proton-induced nuclear reactions and neutron-rich isotopes produced via neutron-induced nuclear reactions (capture and fission). Both of these particle beam capabilities are design features of our proposed NBTF.
- (b) **NBTF Revenue Radioisotopes** are those isotopes selected to provide large, long-term revenue for NBTF. These isotopes are to be produced routinely for existing markets, and have been identified in the business plan (Section 6) as annual revenue sources at “firm,” “likely,” and “optimistic” levels. These isotopes would be produced with high-intensity proton beams from either or both of the two proposed NBTF cyclotrons. The specific isotopes selected for revenue production, like those selected for research, may change over time to keep pace with changing markets. NBTF management would be responsible for prudent selection of these “cash cow” isotopes.

8.2 PRODUCTION PLAN FOR RESEARCH RADIOISOTOPES

The research isotope inventory is based primarily on the NBTF Isotopes List reported at the Purdue University workshop [Kliwer & Green, 1992], and subsequently incorporated into the Institute of Medicine's *Isotopes for Medicine and the Life Sciences* [Adelstein & Manning, 1994]. However, we have extended the list to include additional research radioisotopes.

Specific research isotopes will be added and subtracted from the inventory as research needs change. Research interest has been expressed for many isotopes not included in this list and in some cases the interest has been curtailed by lack of availability and cost. A major part of NBTF's mission is research into radioisotope production technologies, and this emphasis can be expected to lead to many new isotopes being made available as new production methods are developed.

8.2.1 NBTF Research Radioisotopes via Proton-Induced Nuclear Reactions

Neutron-deficient radioisotopes intended for a wide variety of research purposes are listed in Table 8-1. Because accelerator-based production methods for both Molybdenum-99 and Technetium-99m have been investigated at the University of California, Davis [Lagunas-Solar et al., 1991; Lagunas-Solar, Jungerman & Castaneda, 1993; and Lagunas-Solar et al., 1994], they are included in Table 8-1.

The neutron-deficient radioisotopes listed in Table 8-2 are parent/daughter generator systems. These generators have been identified as candidates for Positron Emission Tomography [Adelstein & Manning, 1994].

8.2.2 NBTF Research Radioisotopes via Neutron-Induced Nuclear Reactions

NBTF as designed and proposed in this study has research facilities that would provide access to intense ($>10^{10}$ n/cm²sec) neutron fluxes to be generated by a proton-to-neutron conversion target. This would allow the production of small research quantities of neutron-rich isotopes including β -emitting isotopes of interest for research into new therapeutic (cancer therapy) radiopharmaceuticals. Many neutron-rich isotopes would be potentially available from neutron-induced reactions at NBTF. These isotopes are listed in Table 8-3, together with their intended end-uses (i.e., cancer therapy, biomedical R&D, diagnostics, treatment of disease).

The rationale for this approach is based on the fact that the future operation of many reactors is uncertain, and therefore the supply and availability of a broad spectrum of reactor-produced isotopes is also in question. Reactor-produced radiotracers have demonstrated usefulness in almost all fields of scientific and technical R&D.

It would certainly be appropriate for NBTF, as part of its assigned role in radioisotope production R&D, to be instrumental in facing this challenge. We suggest that NBTF should be a center of coordination for R&D into alternative methods for producing neutron-rich isotopes, integrating efforts already in motion at several national laboratories. The potential outcome of this area of research would be an assessment of alternatives to reactor-produced radioisotopes, based on using NBTF as a test bed for future technological solutions to this rapidly evolving scenario of reactor shutdowns.

Table 8-1. NBTf Research Radioisotopes from Proton-Induced Nuclear Reactions

Arsenic-73	Copper-64	Scandium-47
Arsenic-74	Copper-67	Technetium-95m
Beryllium-7	Gold-195m	Technetium-96
Bismuth-205	Indium-114m	Technetium-99m [†]
Bismuth-206	Iodine-123	Tungsten 178
Bismuth-207	Iodine-124	Vanadium-49
Bromine-76	Lead-203	Xenon-127
Bromine-77	Magnesium-28	Yttrium-88
Bromine-80m	Molybdenum-99 [†]	Zirconium-89
Cobalt-56	Palladium-103	
Cobalt-57	Ruthenium-97	

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

[†] Radioisotope added to the Adelstein & Manning list.

Table 8-2. NBTf Research Radioisotopes from Proton-Induced Nuclear Reactions, Potentially Useful for PET Parent/Daughter Generator Systems

Barium-128 → Cesium-128	Tellurium-118 → Antimony-118
Germanium-68 → Gallium-68	Titanium-44 → Scandium-44
Iron-52 → Manganese-52m	Xenon-122 → Iodine-122
Selenium-72 → Arsenic-72	Zinc-62 → Copper-62
Strontium-82 → Rubidium-82	

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

Table 8-3. NBTf Research Radioisotopes from Neutron-Induced Nuclear Reactions**CANCER THERAPY**

Arsenic-77	Holmium-166	Rhenium-186
Californium-252	Iodine-125	Samarium-145
Copper-67	Iridium-192	Scandium-47
Dysprosium-166	Lutetium-177m	Silver-111
Einsteinium-253	Osmium-194	Strontium-90 (Y-90)
Fermium-255	Palladium-103	Tungsten-188 (Re-188)
Gadolinium-159	Phosphorus-32	
Gold-199	Phosphorus-33	

BIOMEDICAL R&D

Bromine-82	Osmium-191	Selenium-75
Calcium-47	Phosphorus-32	Strontium-85
Cerium-141	Phosphorus-33	Sulfur-35
Chromium-51	Platinum-195m	Tellurium-123m

DIAGNOSIS

Cobalt-58
Copper-64
Iridium-191

TREATMENT OF DISEASE

Californium-252	Gold-199	Rhenium-188
Dysprosium-165	Holmium-166	Samarium-153
Erbium-169	Rhenium-186	

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

8.3 PRODUCTION PLAN FOR REVENUE RADIOISOTOPES

The improvement of the current radioisotope production and distribution system in the United States is the subject of much review and deliberation among all concerned government and private sectors (see "U.S. Department of Energy National Isotope Strategy," prepared by the Isotope Production and Distribution Program, August 1994). The eventual transition from current DOE strategies and operational infrastructure to the planned NBTF must be carefully planned.

Several key assumptions about revenue were made in the business plan (Section 6). These assumptions were based on a financial and market rationale, and resulted in the identification of a group of isotopes considered essential for the economic viability of NBTF.

In the following analysis, we look at the current DOE programs — in which we have identified five isotopes as major sources of income— and then at the expanded program at NBTF for large-scale radioisotope production.

8.3.1 The DOE's "Big Five" Radioisotopes

During FYs 1990 to 1993, a large fraction (> 93%) of the combined annual revenue generated from sales of radioisotopes produced at LANL and BNL was derived from only five of the nearly thirty radioisotopes available from these facilities. Summary information about DOE's "Big Five" radioisotopes is presented in Table 8-4, which lists the revenue level for each and their combined effect on the overall level of income to DOE's radioisotope production laboratories. Ranked by their fractional contribution to revenue, the DOE's "Big Five" isotopes are:

(1)	Strontium-82	(25.6 d)	50.61%
(2)	Germanium-68	(271 d)	24.21%
(3)	Cadmium-109	(462 d)	9.48%
(4)	Sodium-22	(2.61 y)	5.10%
(5)	Copper-67	(61.9 h)	4.13%

Table 8-4. Sales of DOE's "Big Five" Radioisotopes, FY1990-93

Radioisotope	Brookhaven		Los Alamos		Combined DOE	
	Total Sales (\$ K)	Fraction of Total Sales (%)	Total Sales (\$ K)	Fraction of Total Sales (%)	Total Sales (\$ K)	Fraction of Total Sales (%)
Cadmium-109	—	—	605.1	14.24	605.1	9.48
Copper-67	56.9	2.67	206.7	4.86	263.6	4.13
Germanium-68	553.5	25.94	991.8	23.34	1,545.3	24.21
Sodium-22	—	—	325.5	7.66	325.5	5.10
Strontium-82	1,422.8	66.68	1,807.0	42.54	3,229.8	50.61
Total					5,969.3	93.54

DOE "Big Five" radioisotopes (FY1990-93) = \$ 5,969,300
 All DOE radioisotopes (FY1990-93) = \$ 6,381,800
 "Big Five" Radioisotopes as a fraction of total sales = 93.54%

Source: DOE Radioisotope Production & Distribution Program.

The combined income from the "Big Five" radioisotopes amounted to 93.54% (\$ 5,969,300) of DOE radioisotope revenue for FY1990-93. Production of these isotopes is critical for the financial structuring of DOE's radioisotope production programs, and will also be critical for the success of NBTF.

8.3.2 The "Big Ten" NBTF Commercial Radioisotopes

Based on the current market and on the technical capabilities of the proposed NBTF, ten radioisotopes (the "Big Ten") that are expected to provide a critical financial base for the operation of NBTF have been identified. These include the DOE's Big Five, along with another five that show excellent promise for large-scale production. They are:

(1)	Cadmium-109 (Ag-109)	(462 d)
(2)	Cobalt-57	(271.8 d)
(3)	Copper-67	(61.9 h)
(4)	Fluorine-18	(2 h)
(5)	Germanium-68 (Ga-68)	(271 d)
(6)	Iodine-123	(13.2 h)
(7)	Palladium-103	(17 d)
(8)	Sodium-22	(2.61 y)
(9)	Strontium-82 (Rb-82)	(25.6 d)
(10)	Xenon-127	(36.4 d)

The production methods, beam parameters, and yields for these radioisotopes are summarized in Table 8-5. Yield estimates are projected yields per mA of beam per day of bombardment. Proportional adjustments to this comparison can easily be made.

Table 8-5. Proposed Methods for Large-Scale Production of NBTF "Big Ten" Radioisotopes

Radioisotope	(Half Life)	Nuclear Reaction	Proton Energy (MeV)	Yield (mCi/μAh)	NBTF Yield × 1 mA (Ci/Day)
Cd-109	(462 d)	$^{109}\text{Ag}(p,n)^{109}\text{Cd}$	30–10†	0.038	0.91
			10–3	0.010	0.24
			30–3	0.047	1.13
Co-57	(271.8 d)	$\text{Ni}(p,xn)^{59}\text{Co}$	23	0.004	0.10
		$^{59}\text{Co}(p,3n)^{57}\text{Ni} \rightarrow ^{57}\text{Co}$	40	0.002	0.05
Cu-67	(61.9 h)	$^{68}\text{Zn}(p,2p)^{67}\text{Cu}$	40	0.020	0.48
I-123	(13.2 h)	$^{124}\text{Xe}(p,x)^{123}\text{I}$	26	14	336
		$^{127}\text{I}(p,5n)^{123}\text{Xe} \rightarrow ^{123}\text{I}$	70–48	23	552
F-18	(2 h)	$\text{Ne}(p,x)^{18}\text{Ne} \rightarrow ^{18}\text{F}$	70–40	600	360*
		$\text{Na}(p,x)$	70–40	100	60*
Ge-68	(271 d)	$^{69}\text{Ga}(p,2n)$	30–15	0.03	0.72
		$\text{Ge}(p,pxn)$	70	0.05	1.20
Na-22	(2.61 y)	$^{26}\text{Al}(p,3p3n)^{22}\text{Na}$	100–26	0.018	0.43
			68–26	0.013	0.31
		$\text{Mg}(p,xn)^{22}\text{Al} \rightarrow ^{22}\text{Na}$	80–26	0.014	0.34
			68–26	0.010	0.24
Pd-103	(17 d)	$^{107}\text{Ag}(p,5n) \rightarrow ^{103}\text{Pd}$	80–40	10	240
		$^{103}\text{Rh}(p,n)$	20–3	6	144
Sr-82	(25.6 d)	$\text{Rb}(p,xn)$	80–40	0.20	4.8
Xe-127	(36.4 d)	$^{127}\text{I}(p,n)$	20–8	0.08	1.9
		$^{133}\text{Cs}(p,2p5n)$	100	0.11	2.6

* With 6 h bombardment and 0.1 mA beams; for references, see text.

† Incident and exit energy.

The rationale behind the choice of each of the "Big Ten" radioisotopes is as follows. In these analyses, we arbitrarily define a year as consisting of 24 hours/day, 6 days/week, for 50 weeks/year — in other words, 7,200 hours (or 300 days).

(1)	Cadmium-109 (Ag-109)
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Cadmium-109 (462 d) is used as an x-ray fluorescence source in industrial processes. Interest has also been expressed in exploring the use of its Silver-109 (39.8 sec) for heart flow studies in pediatric nuclear medicine [Holmes, 1991]. The market is estimated at 20 Ci/year [TMG Study, 1994], and prices range from \$50–60 per mCi.

The projected production rate ranges from 0.24 to 1.1 Ci/day, depending on the production route. These yields represent a potential income of \$12,000 to \$55,000 per day to NBTF, using the lower price of \$50/mCi. Assuming a 50% market share (10 Ci/year), \$500,000 per year income would be realized. This volume could be produced in 9 to 42 days, depending on the production route chosen. Clearly, NBTF's capacity greatly exceeds the current market of 20 Ci/year. It is possible that NBTF's excess capacity could be used to induce market demand by lowering prices, thus competing more favorably with alternative x-ray tube technologies.

(2)	Cobalt-57
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Cobalt-57 (271.8 d) is used in nuclear medicine as an energy source for calibration purposes (i.e., for imaging systems) and for transmission imaging. Annual market demand has been estimated at 8 Ci/year [Holmes, 1991] to 50 Ci/year [TMG Study, 1994]. Current prices fluctuate between \$35–55 per mCi.

The production rate projected at NBTF ranges from 0.05 to 0.10 Ci/day (at 1 mA), representing a potential income of \$1,750 to \$3,500/day, if we assume the lower \$35/mCi price. If Cobalt-57 is produced at a relatively low rate of \$2,000/day for 300 days, the potential annual income amounts to nearly \$600,000, representing a 30% share of the larger estimated market of 50 Ci per year

(3) Copper-67

Copper-67 (61.9 h) is a research isotope being investigated as a monoclonal antibody label with potential diagnostic and therapeutic applications. Research demand was estimated at 600 mCi/year in 1991 [Holmes, 1991] and reached approximately 800 mCi in 1993 [DOE data]. If the expectation of success with Copper-67 labeled monoclonal antibodies materializes, market demand is expected to reach 2 Ci/month, or 20–24 Ci/year [Holmes, 1991; TMG Study, 1994] — a potential market 25 to 30 times the volume of the present market. NBTF could become a sole source for this isotope — as LANL and BNL are now.

The production rate projected at NBTF is 0.5 Ci/day (at 1 mA), representing a potential income of approximately \$25,000/day, assuming a price of \$50/mCi. If Copper-67 is produced at this rate, only 48 days of NBTF operation are needed to satisfy the entire estimated annual market demand (24 Ci). The potential income at 100% market share would amount to \$1,200,000 per year.

(4) Fluorine-18

Fluorine-18 is used for the synthesis of several radiopharmaceuticals. In particular, the use of F-18 fluorodeoxyglucose (FDG) for brain, heart, and tumor studies is expected to grow significantly. It also appears that FDG's production and availability are excellent opportunities for centralized facilities located in highly populated regions. The market in these regions can be served through regional radiopharmacies.

If PET-FDG is clearly established and reimbursement issues are solved, a reliable regional source can be very competitive and secure ready availability at reduced costs. We therefore propose that NBTF serve this function and become a regional asset for the supply of Fluorine-18.

Fluorine-18 production and supply is now limited to a small number of high-capital-cost research & clinical centers. The current practice of operating self-sufficient PET medical centers with on-site low-energy medical cyclotrons is economically questionable. After years of operation, such PET centers (≈ 70 in the United States) are yet to be fully recognized as the best approach [Conti, Keppler & Halls, 1994]. Many of the existing clinical PET programs are facing financial difficulties due to the large operating expenses and to the complexities of operating dedicated accelerators.

Many of these accelerators are now being reevaluated largely due to economics and some are even being considered for potential shutdown.

It appears that a solution to the economic and operational problems of these PET centers would be the establishment of centralized radiopharmacy operations. The large production capacity of NBTF could then provide one such centralized regional operation and produce large, daily quantities of Fluorine-18 with >70 MeV protons either on Ne gas targets or on Na targets (see Table 8-6). Tens of Curie batches are expected with this new approach [Lagunas-Solar et al., 1992; Lagunas-Solar & Carvacho, 1995].

The production rate projected at NBTF ranges from 60 Ci per batch with Na targets (6-hour bombardments at 0.1 mA) to over 300 Ci per batch with thick Ne gas targets at end of bombardment (EOB). Assuming three half lives (≈ 6 h) decay and 50% radiochemical yields, batches containing nearly 4 Ci of an F-18 radiopharmaceutical could be delivered throughout Northern California.

If six PET cameras with 5 patients per day are serviced via this system, NBTF would be required to supply approximately 30 doses per day (20 mCi/dose) at an estimated price of \$100/dose for a daily income of \$3,000. Projected yearly estimate (using a conservative 50 weeks $\times$ 6 days per week) could reach \$630,000 per year.

This income scenario may be drastically increased if SPECT systems are utilized via high-energy collimators to conduct similar diagnoses. The regional market may then reach 5 times the above projection (\$3,000,000 per year) or more.

As designed, NBTF would only need 1–2 hours/day to accommodate, as an example, the Northern California regional market (population base = 10 million). Expanding the market radius can be accomplished with the development of Ne and Na targets for mA-level beam operation.

(5)	Germanium-68 (Ga-68)
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Germanium-68 (271 d) is produced only at LANL and BNL. It is used as a calibration source for PET scanners. The market has been estimated at 12 Ci/year [TMG Study, 1994], and the current price is \$125 per mCi.

The production rate projected at NBTF ranges from 0.72 to 1.20 Ci/day, representing a potential income of \$1,500,000/year to NBTF (at \$125/mCi).

Producing the entire annual market supply of Germanium-68 at NBTF would represent only a 12 day operational commitment (at 1 mA on a single target, or 0.5 mA on each of two targets). There is considerable leeway to adjust prices to compete with potential (or existing) foreign sources.

(6)	Iodine-123
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Iodine-123 (13.2 h) is a commercially available isotope now being produced both in the United States and Canada. While it appears that the commercial market is well supplied, the use of Iodine-123 for research has been limited by cost and quality (i.e., radiochemical purity) factors. Current commercial market estimate is 200 Ci/year [TMG Study, 1994] (≈ 1 Ci/day at calibration), divided almost equally between thyroid applications (capsules) and labeled compounds. This market can be satisfied with daily batches ($5 \text{ days/week} \times 50 \text{ weeks} = 250 \text{ days/year}$) of 12–14 Ci.

If NBTF participates in this market, production levels of up to ≈ 15 Ci/day are well within the proposed technical features of NBTF. If a simultaneous double target is operated at 0.2 mA per target (already demonstrated in the commercial sector), yields per hour of bombardment (2 h combined) would range from 6 Ci (Xe-124 target) to 8 Ci (I-127 target). Thus a two hour per day scheduled commitment for NBTF could easily satisfy the entire market. The production rate could reach up to 360 to 550 Ci/day if high power targetry is developed.

The research market for labeling quality Iodine-123 is expected to be 1–2 Ci/year and to provide approximately \$150,000/year. NBTF should easily be able to supply this market with <1 h bombardment per day. Iodine-123 in different radiochemical forms and in high radioactivity concentration ($>500 \text{ mCi/mL}$) would facilitate R&D on new iodinated radio-pharmaceuticals. When reaching the pre- and clinical trials test phases, NBTF should supply Iodine-123 in support of these trials.

(7)	Palladium-103
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Palladium-103 (17 d) is a “cancer therapy” isotope already being produced by a U.S. company (Theragenics, Norcross, GA), with an estimated market of \$1,000,000/year (1 Ci/year at \$100/mCi). No hard market projec-

tions are available but it has been suggested that further demand exists [TMG Study, 1994].

NBTF projected production levels range from 144 to 240 Ci/day at 1 mA (24 h bombardment) depending on the method used (see Table 8-6). Clearly, NBTF would have excess capacity to supply this isotope.

NBTF could provide additional supplies of this isotope to the private sector if market demands are not covered by existing suppliers. Potentially, and based upon a 25% share of the market, NBTF could easily generate approximately \$250,000 through production and distribution of Pd-103 in collaboration with the private sector.

(8)	Sodium-22
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Sodium-22 (2.6 y) is used in fluid flow analysis and is now being produced at Los Alamos National Laboratory (sole U.S. source). A \$156,000 market existed in FY1993 [DOE data; TMG Study, 1994] at \$120/mCi. Total market demand (1993) amounted to 1.3 Ci.

NBTF production capabilities for this isotope are projected as 0.24 to 0.43 Ci/day at 1 mA. It is also available as a sub-product from Al used in target, collimator, and Faraday cup systems. Clearly NBTF can supply the entire yearly demand while committing minimal fractions of its operational schedule. NBTF projected revenue is \$200,000 per year.

(9)	Strontium-82 (Rb-82)
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In a generator form, Strontium-82 (25.6 d) is used to provide Rubidium-82 (1.27 min) for PET studies. This generator provides access to positron emitting radiopharmaceuticals without a cyclotron. The Sr-82→Rb-82 generator is therefore critical for the operation of approximately 15 PET cameras in the United States [TMG Study, 1994]. Each center requires a generator (150 mCi Sr-82 load per month) for a total demand of approximately 2.3 Ci/month (28 Ci/year). Because of losses and regulatory demands, the actual production level may reach 3–4 Ci/month.

Production levels at NBTF have been estimated as 9.6 Ci/day at 1 mA if high-power targets are developed. At current levels of operation of com-

mercial targets, a 0.15 mA level is routinely used. Based on today's technology, NBTF production levels would be approximately 1.4 Ci/day. Therefore, NBTF would be required to operate 3 days (72 h) to satisfy the monthly demand (15 generators). The projected income would be \$150,000/month (100 mCi generators at time-of-calibration) for a yearly total of \$1,800,000. Current market is estimated at \$2,700,000/year [TMG Study, 1994].

(10)	Xenon-127
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Xenon-127 (36.4 d) was used for pulmonary imaging when it was being produced with DOE facilities at the Brookhaven National Laboratory. Its market demand reached up to 3 Ci per year [DOE data; Holmes, 1991; TMG Study, 1994].

The production of Xenon-127 at NBTF can be accomplished in a parasitic mode with the production of Iodine-123 (via Xenon-123) with 70 MeV protons, with double targets, and/or independently with low energy beams (30–20 MeV). In addition, if the need for Xenon-122 (20 h)→Iodine-122 (3.6 min) generators for research materializes, it is possible to design and operate a target that would simultaneously produce these three xenon isotopes of interest. This production regime has been demonstrated at the University of California, Davis (see also Lagunas-Solar et al., 1986).

The projected yield for Xenon-127 at NBTF ranges from 1.9 to 2.6 Ci/day, which is clearly sufficient to produce several batches per month with minimal commitments of NBTF operational schedule.

Projected annual revenues from Xenon-127 may reach those of previous years if supply is restored. These projections amount to \$75,000 per year (\$25 per mCi).

8.3.3 Market and Income Potential for NBTF's "Big Ten" Radioisotopes

A summary of the operational strategies (targets, beam energies, and intensities) and financial objectives for NBTF's "Big Ten" radioisotopes is given in Table 8-6 and shown in Figure 8-1.

For each of these ten selected radioisotopes, NBTF will be able to improve production capacity significantly by employing a fully dedicated facility and taking advantage of proton

Table 8-6. Market and Income Summary Data for NBTF "Big Ten" Radioisotopes

Radioisotope	Total Market		NBTF Market	
	(Ci/year)	(million)	Share (%)	(million)
Cd-109	20	\$1.0	50	\$0.5
Co-57	50	\$1.8	33	\$0.6
Cu-67 (for R&D)	1	\$0.05	100	\$0.05
F-18* (for PET)	4 Ci/d	\$0.63	100	\$0.63
Ge-68	12	\$1.5	100	\$1.5
I-123 (for R&D)	1.5	\$0.15	100	\$0.15
Pd-103	1	\$1.0	25	\$0.25
Na-22	1.3 (1993)	\$0.15	100	\$0.15
Sr-82	28	\$2.7	66.6	\$1.8
Xe-127	3	\$0.08	100	\$0.08
Total Market		\$20.1		
Total Expected NBTF Revenue from Existing Markets				\$5.70

* Regional market in Northern California (≈ 10 million population base)

Sources: See preceding text for details.

NOTE: Table 8-6 includes only known, existing markets. Three other projected markets, not included in the conservative summary data in this table, were discussed in the text. If the anticipated success with ^{67}Cu -labeled monoclonal antibodies materializes, the market could leap to 20 Ci/year; NBTF's potential annual income at 100% market share (as sole source) would be \$1.2 M. If the regional market for ^{18}F for SPECT as well as PET grows as discussed, NBTF's annual earnings (at 80% market share) would be \$2.4 M. Finally, Table 8-6 includes ^{123}I only for R&D. If NBTF were to assume 10% of the commercial market, this would mean another \$0.7 M in annual revenue.

Figure 8-1. Market and Income Summary Chart for NBTF "Big Ten" Radioisotopes

energy beams especially tuned to maximize production yield and isotope purity while minimizing the production of radioactive waste.

DOE's "Big Five" isotopes are expected to be equally important to NBTF's financial health. The production of "long-lived" Cobalt-57 (271.8 d) can be easily incorporated because of the excess capability designed for NBTF. The production of "medium-lived" Palladium-103 (17 d) and Xenon-127 (36.4 d) can be accomplished by scheduling short but intense irradiations to peak production yields at fixed weekly or bi-weekly intervals. Finally, the production of "short-lived" radioisotopes such as Iodine-123 (13.2 h) and Fluorine-18 (2 h) must be conducted on daily schedules. Iodine-123 for national distribution must be scheduled on a daily basis (4-5 days/week) to peak production levels to be able to distribute with up to 1.5-2 days of pre-calibration (standard practice in commercial distribution). Fluorine-18 for regional distribution (i.e., Northern California) would have to be scheduled daily for early morning release to the distribution network with up to 8 hours pre-calibration.

8.4 NBTF PRODUCTION SCHEDULE

An example of an annual production schedule is presented in Table 8-7. This schedule illustrates the flexibility that is possible with the proposed NBTF and also the complementary features of its two proposed cyclotrons.

The schedule is based on a variety of assumptions about production volume and operations. Specifically, it:

- (1) Assumes 24-hour operation, 6 days per week, for 50 weeks per year for a total operational time of $24 \times 6 \times 50 = 7,200$ hours (300 days) per year per beamline per cyclotron. Because each cyclotron can use two beamlines simultaneously, each cyclotron has 600 operational hours/year.
- (2) Assumes the need to be able to satisfy the entire projected markets (not just NBTF's share) for I-123 and F-18 (i.e., 200 Ci/y for I-123, rather than 20 Ci/y; and 4,000 Ci/y for F-18, rather than 3,000 Ci/y).
- (3) Assumes that five isotopes are made with each cyclotron, although some isotopes could be produced with either one (i.e., I-123, Ge-68, and Xe-127 from parasitic targets for the production of I-123 and Xe-122). This is a well balanced complement of accelerator resources.

- (4) Assumes the following release schedules for the "Big Ten" radioisotopes. The producing accelerator (100 MeV cyclotron or 40 MeV cyclotron) is listed in parentheses.

Every Six Months:	Na-22 (100)
Every Three Months	Cd-109 (40), Co-57 (40), Ge-68 (40)
Every Month:	Pd-103 (40), Sr-82 (100), Xe-127 (40)
Weekly	Cu-67 (100)
Daily (5 days/week)	F-18 (100), I-123 (100 & 40)

The schedule demonstrates that operating with up to 1.0 mA (for Co-57) and with <0.4 mA for the other isotopes, NBTF can produce its entire inventory of revenue isotopes (the Big Ten) — plus cover additional markets for Cu-67, F-18, and I-123, should that prove necessary — and still be able to devote half its resources to its R&D mission.

Table 8-7. Production Schedule for NBTF "Big Ten" Radioisotopes

Radioisotopes	NBTF Market, Ci/year	NBTF Yield Estimates,* Ci/day (mA)	Schedule, beam days†
(1) Production with NBTF 100 MeV Cyclotron			
Cu-67 (61.9 h)	20‡	0.10 (0.4)	100
F-18 (2 h)§	4,000‡	Ne target: 6/h (0.1) Na target: 1/h (0.2)	(28) 84
I-123 (13.2 h)	200‡	I target: 55 (0.2)	44
Na-22 (2.61 y)	1.3	0.06 (0.4)	11
Sr-82 (25.6 d)	20	1.0 (0.2)	20
Total 100 MeV Cyclotron scheduled beam-days per year			259
(2) Production with NBTF 40 MeV Cyclotron			
Cd-109 (462 d)	10	0.26 (0.2)	38.5
Co-57 (272 d)	17	0.10 (1.0)	170
Ge-68 (271 d)	12	0.2 (0.4)	30
I-123 (13.2 h)	200‡	Xe target: 34 (0.2)	71
Pd-103 (17 d)	0.25	40 (0.2)	< 1
Xe-127 (36.4 d)	3	0.2 (0.1)	15
Total 40 MeV Cyclotron scheduled beam-days per year			326

* Yield estimates include production and decay losses to time of calibration.

† Schedule based on 24 hours/day, 6 days/week, 50 weeks/year, for total of 7,200 hours/year (300 days) per cyclotron, per beamline. The operational capacity of each cyclotron, with its dual simultaneous beam extraction capability, is $2 \times 300 = 600$ beam-days per year.

‡ These are total markets, not NBTF's share (see Note below Table 8-6). Total market is shown to demonstrate NBTF's capability to meet the entire market need for these radioisotopes, if necessary.

§ Assumes 5 d/wk, 50 wks/yr for 250 single batches/year. The less attractive scenario (84 d) based on the lower-yield Na target was used in estimating yearly scheduled bombardments.

8.4.1 Projected 100 MeV Cyclotron Share of "Big Ten" Production Schedule

The total bombardment scheduled for the 100 MeV cyclotron amounts to 259 beam-days (see Table 8-7). Because the cyclotron is designed to allow simultaneous extraction of two beams, the 259 beam-day schedule can be accomplished half that number of calendar days. In other words, the 100 MeV cyclotron's share of the "Big Ten" production schedule can be completed in just 130 calendar days. The days available for other NBTF activities (that is, for R&D) would then be >56% of the scoped operation for the 100 MeV cyclotron (see Fig. 8-2).

8.4.2 Projected 40 MeV Cyclotron Share of "Big Ten" Production Schedule

The total bombardment scheduled for the 40 MeV cyclotron amounts to 326 beam-days (see Table 8-7). Assuming a simultaneous bombardment regime is used, the number of calendar days committed to operating for the production of the "Big Ten" radioisotopes is 163 days. The available days for other NBTF activities (that is, for R&D) would then be >45% of the scoped operation for the 40 MeV cyclotron (see Fig. 8-2).

Figure 8-2. Ratio of "Big Ten" Production Schedule to R&D

8.5 CONCLUSIONS

The two NBTF cyclotrons are designed to maximize operating flexibility; each allows two extracted beams to be used simultaneously, at different energies, in multiple target areas. The preliminary analysis of NBTF's production capacity contained in this section shows that, as designed and proposed in this Phase I Project Feasibility Study, NBTF can:

- (1) Develop a competitive position for the production of the critical market-driven "Big Ten" radioisotopes. NBTF must be operated and managed with adequate priority and dedicated facilities given to this production goal. Routine availability must be achieved with a high degree of reliability.
- (2) Reach the revenue projections made for the "Big Ten" radioisotopes while operating well within the proposed technical and operating capabilities.

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9.0 RESEARCH AND EDUCATION PROGRAMS

Northern California is blessed with an infrastructure that will prove ideal for maximizing NBTF's potential. We propose to site the facility at the University of California, Davis, campus. Although NBTF itself is still a dream, the infrastructure to support it in Northern California is real and it is very solid.

Regional Support	University of California, Davis	Private Sector
<ul style="list-style-type: none"> • UCSF, and its Medical Center • UC Berkeley • UC Santa Cruz • Stanford University, and its Medical Center • UC Davis Medical Center in Sacramento • California State University, San Jose • Lawrence Berkeley Laboratory • Lawrence Livermore National Laboratory • Los Alamos National Laboratory (New Mexico) 	<ul style="list-style-type: none"> • College of Letters and Science • College of Agricultural and Environmental Studies • School of Medicine • School of Veterinary Medicine • Veterinary Medical Teaching Hospital • Regional Primate Center • Environmental Services Facility (state-of-the-art waste management) • UC Davis Medical Center in Sacramento, • Crocker Nuclear Laboratory 	<ul style="list-style-type: none"> • Radiopharmaceutical Industry • Biotechnology Industry • Health Care Industry • Computer & Electronics Industry • Food and Agriculture Industry • Environmental Technology
Population base of ~10 million. Excellent transportation within the region, as well as outside. UC Davis connects readily to Hwy 5, the major route to Southern California and another 30 million people. Half a dozen major airports.		

These resources are so extensive they will allow us to establish virtually any research or education program. In addition to this wealth of resources, NBTF as planned will have a wealth of real estate. It has been designed to accommodate current needs and also to provide for future expansion, including specialized physical facilities as required by future research needs. The present plan calls for locating the facility on 10–12 acres of land, of which only 1¼ acres (less than 15%) is committed to the proposed facility building described in Section 2.

For NBTF to be successful, it must be supported by already-established regional strengths. Its mission, however, is national in scope.

Research and education activities are an essential part of the programmatic objectives planned for NBTF. While many strategies may be possible for establishing guidelines for these programs, we agree with the generalized sentiments and direction that have been expressed and document in studies and reports [Holmes, 1991; Adelstein & Manning, 1994].

We strongly recommend that clearly stated guidelines be established to ensure that research and education/outreach activities at NBTF are conducted with a well-defined focus — that is, that they all be related to radioisotope production technologies.

9.1 BASIC AND APPLIED RESEARCH ACTIVITIES

Research activities should support, expand, and improve NBTF's radioisotope production capabilities. The primary research objectives must be related to advancing the accelerator-based radiation sciences: nuclear physics, nuclear chemistry, and radiochemistry. Other research objectives include improvements in accelerator technologies (beam transport, optics, diagnostics), radiation detection and assays, material sciences (targetry, shielding), system automation and robotics, and environmental health sciences.

Suggestions for proposed research projects may be generated internally by NBTF scientists or proposed to NBTF by external collaborators. However, acceptance and prioritization of research activities should be established in consultation and in agreement with the NBTF National Research Steering Committee, to be composed of a select group of the nation's leading scientists and NBTF staff members.

It would be premature in this Phase I report to outline a program of research. To illustrate the diversity and significance of the research that might appropriately be conducted at NBTF, however, the following are examples of research areas for which NBTF's unique blend of capabilities would be exceptionally well suited.

● Nuclear Reactions

Nuclear reactions must be well characterized by precise, high resolution excitation functions (cross sections vs energy) before a critical evaluation of radioisotope production techniques (including targets) can be made. Often, precise excitation functions for several reaction channels are needed. However,

most reports in the scientific literature do not provide adequate resolution. As radionuclide yields and purities depend on beam energy and target parameters (chemical identity, chemical purity, etc.) a set of precisely measured excitation functions is necessary. The study of proton- and neutron-induced reactions and their corresponding excitation functions should therefore be an important scientific objective of NBTF research.

● Targetry Technology

While accelerator technologies have evolved significantly over the last decade in many critical areas (e.g., ion sources, beam transport, beam extraction) the targets used for commercial radioisotope production with high beam intensity have not. Current commercial targets impose several limitations, such as beam power and stability. These limitations force industry to compromise their production schedules. Because they must operate their accelerators at beam levels lower than their operational capabilities, they must run for a longer time than would be necessary with improved targets.

Targetry research is scarce due to lack of ready access to research facilities operating accelerators similar to the ones used commercially. Part of the justification for NBTF's proposed 40–10 MeV cyclotron is that it provides commercial-like technologies that would clearly allow targetry research to be directed to existing target needs in the commercial sector. In addition, the proposed 100 MeV cyclotron would demand new targets to be designed and new materials to be used at NBTF, thus "accelerating" the development of the next generation of high-power targets.

NBTF, as planned, would be able to provide unique resources and facilities for target development and on-line testing.

● Beam Technology

The evolution of modern accelerators, both linacs and cyclotrons, capable of routine operation at mA beam levels has been driven by the development of new ion source technologies as well as an evolution in design and engineering in many other key components in the overall structure of an accelerator. The use of high beam power also requires better techniques (and materials) for beam transport and beam diagnostics. Integration and full utilization of these techniques is critical to properly manage and operate the high energy (100 MeV), high intensity (1 mA, upgradable to 2 mA) cyclotron being proposed.

NBTF's proposed 100 MeV cyclotron will be the first high-intensity, high-energy cyclotron to be built as a dedicated radioisotope production machine. As an operational test base for integrating new designs and materials, NBTF will be contributing to the advancement of beam technology even as it is being built.

● Target/Product Radiochemistry

Radiochemical separation and purification techniques have been developed by using — singly or in combination — several conventional chemical techniques (precipitation, ion exchange, solvent extraction, etc.) adapted to the specific product in mind. Rapid and efficient separation and purification methods are always needed to minimize losses by chemistry and by decay.

New methods in separation science and technology (e.g., microfiltration) should be investigated to continually improve radioisotope separation and purification techniques. NBTF inevitably must be involved in this area because radioisotopes will be developed there, and target/product separations must be developed accordingly.

NBTF could provide valuable assistance to the private sector by providing both a test bed and a source of raw (radioisotope) materials for testing and validating new processes. One of the problems confronting industry is that even after a method has been established and proven, it may become "frozen" by regulations. The cost of implementation usually is prohibitive as it requires new and extensive data in addition to a new evaluation by regulatory bodies. Industry is therefore generally reluctant to undertake these actions because of cost.

NBTF can support the private sector by researching modifications to existing protocols as well as by providing raw (radioisotope) materials for testing for regulatory purposes. New automated PC-controlled radiochemistry production systems enabling real-time controls of a separation or synthesis procedure may result from this activity. Many new methods would be amenable to full automation and controls (via computers). Therefore, target/product research should also be integrated with automation and computer techniques in order to provide new, routine, and safe alternatives.

● Applied Accelerator Technologies

Once established, NBTF will have unique resources in its scientific and technical staff as well as in its physical capabilities. Collaborative investigations in various areas of biomedical, physical, and analytical research based on the NBTF accelerators will be pursued. Potential topics include accelerator mass spectrometry, particle-induced material effects, and elemental analyses in medicine, food and agriculture, and the environmental sciences.

For example, because biological effects occur in natural systems at extremely small concentrations of parts per billion or less, the field of accelerator mass spectrometry (AMS) is receiving strong consideration as it has the potential to provide quantitation at attomole sensitivities [Vogel & Turteltaub, *Trends in Analyt. Chem* 11(4), 142–149 (1992)]. An NBTF-based AMS collaborative research program has the potential to support investigating the pharmacokinetics and genotoxicities of toxins and drugs at very low doses, as well as many other nutrition, toxicity, and elemental balance studies in human subjects. This area also has the potential to develop into an extremely sensitive new tool for medical diagnosis.

Using a reasonable fraction of NBTF's planned proton and neutron beam resources, collaborative research projects in material sciences effects induced by particle beams and new ultrasensitive analytical methods based on radioactivation or proton-induced x-ray fluorescence (PIXE) can be expanded to medical, food, agricultural (i.e., soils), and environmental analyses. NBTF can then be the incubator for several analytical applications of accelerated proton beams by establishing, with University-based scientists, a diverse set of interdisciplinary research projects.

● Instrumentation Testing and Standardization

Research in science and technology and the practice of nuclear medicine require testing and proper calibration of instruments and other measuring devices in many diverse environments. Space radiation simulation, for example, provides opportunities to test and modify instruments to be used in outer-space exploration, which is characterized by proton and neutron fluxes. Imaging instrumentation and radiation detection instrumentation also requires proper testing and calibration in many different hostile radiation environments. Because of its planned physical infrastructure, NBTF will be in a position to assist the instrumentation industry by generating many types of radiation fields for testing, modification, and calibration (standardization) purposes.

9.2 RESEARCH COLLABORATION

Research collaborations throughout the United States should be established with the scientific community at large. This 3-way partnership with academia and the private industrial sector should provide NBTF with a constant infusion of tasks for its research mission. Because we expect that NBTF will be located and operated as part of a major research university, these collaborations should result in many opportunities for extramural funding, while also involving faculty and staff, graduate students, and undergraduates in the midst of a highly stimulating environment.

With focused objectives, primarily in the applied sciences, NBTF should become a partner and not a competitor with the scientific research community, which in turn is expected to contribute basic innovations. Basic research activities, generally the domain of research universities and funded through a competitive peer-review system, must only be conducted when it is necessary and is related to the development of potential innovations in radioisotope production technologies. No deviations from these general guidelines should be permitted as any digression would result in generalization (lack of focus) and place NBTF in potential competition with the peer-review research institutions.

NBTF scientific staff, however, should be permitted and encouraged to seek extramural funding related to the research missions of NBTF.

9.3 EDUCATION PROGRAMS

The education activities should take full advantage of NBTF's unique leadership in nuclear and radiochemistry, accelerator technologies, and engineering related to radioisotope production and radiochemistry. Education programs should be established to provide formal academic training for the next generation of research and applied radiochemists, health physicists, and radioisotope production technicians.

A study commissioned in 1988 by the National Research Council* concluded that there was a serious shortage of trained nuclear chemists and radiochemists and that the demand would

* "Training Requirements for Chemists in Nuclear Medicine, Nuclear Industry, and Related Areas," Board on Chemical Sciences and Technology, Commission on Physical Sciences, Mathematics, and Resources (National Academy Press: Washington DC, 1988).

greatly exceed the supply over the next decade. It appears that this prediction has been proved correct, as today few U.S. universities and colleges contain academic programs intended for training students in the nuclear and radiation sciences. With the advent and growth of new medical technologies (SPECT and particularly PET) and the emergence of new accelerator (negative ion PET cyclotron) and radiochemical (synthesis automation) technologies, this shortage has become even more acute. Radiochemistry as a discipline is seriously threatened by the dearth of facilities. Lawrence Livermore National Laboratory has been one of the leading centers for radiochemical research; most of the radiochemists there are now approaching retirement age, and the next generation is not in place to replace them, or to learn from them.

NBTF can play a strong role in rebuilding the nuclear and radiation sciences in this country, by developing a Nuclear & Radiation Sciences curriculum in a major research university. Curricula developed collaboratively under the auspices of NBTF would be available for adoption by universities throughout the United States.

The Office of Research at UC Davis has already committed to a plan for developing such a curriculum; the Department of Chemistry will house this academic program. Livermore's Department of Chemistry and Materials Science has agreed to join forces with the University in developing the curriculum, and a collaboration agreement is being formulated. This is but one example of a collaboration based on existing institutional resources that could be integrated within the scope of NBTF.

UC Davis's Department of Applied Science has been located at LLNL for years, and is a further example of the well-established ties between these two institutions; this teaching and research facility has promoted interdisciplinary interactions between faculty, students, and visiting scientists.

Programs such as San Jose State University's Nuclear Chemistry Summer Program, which offers much-needed introductory courses, and UC Davis's Crocker Nuclear Laboratory Summer Fellowships in Radiochemistry & Radioisotope Production (offered with the support of the Associated Western Universities Summer Fellowship Program) would be supported and expanded. New programs based at NBTF — for undergraduate and graduate students and for visiting scientists — would also be instituted. It is essential, especially in light of the huge growth of new medical technologies, that education and training be provided not only in fields of scientific research, but also in the day-to-day techniques of radioisotope production, radio-

chemical separation and purification; radiochemical and radiopharmaceutical syntheses; and radiation protection and safety.

Conferences in the general radiation sciences as well as seminars and technical workshops devoted to key topics related to the mission of NBTF should be established in collaboration with neighboring research universities and under the auspices of the U.S. Department of Energy, professional societies, and industry. In order not to duplicate or create another forum for scientific and technical audiences already established in the traditional series of professional society meetings, these NBTF activities should be highly focused and directed to smaller audiences.

9.4 FACILITATING AND STREAMLINING RADIOPHARMACEUTICAL DEVELOPMENT

The operation of NBTF in direct collaboration with the private sector should provide numerous opportunities for supporting the private sector's commitment to the development and testing of new radiopharmaceutical drugs. Research and testing protocols would be established under strict confidentiality guidelines to protect patentable innovations and/or trade secrets. Initial testing, including supplying adequate amounts of radioisotopes as raw materials, can be achieved by establishing collaborative projects housed and directed by NBTF staff with the direct participation and guidance of private sector scientists.

A Satellite GMP facility to be located at the UC Davis Medical Center in Sacramento is proposed for this purpose. It would provide a direct liaison between NBTF and the medical/clinical research staff, as well as the necessary licensed resources to support this type of collaborative activity. Initial pre-clinical phase testing as well as the different research and clinical trials required under the Investigational New Drug (IND) system can be performed. The execution of New Drug Application (NDA) phase testing on a regional or national scope may also be facilitated.

Advantages of this collaboration are likely to include cost savings (due to higher efficiencies) and a significant reduction in the time required to bring new drugs to the market. A formal academic program to conduct IND trials may in fact be instituted at UC Davis on the basis of NBTF.

9.5 TECHNOLOGY TRANSFER

Because much of the research focus of NBTF deals directly with operational aspects of its cyclotrons, many innovations in high-power targetry and beam management technologies (transport, diagnosis, optics) are expected and should be directly transferred to the commercial sector. NBTF can serve as a testing facility for technologies with potential to directly impact the operations of commercial radiopharmaceutical companies.

NBTF's 40–10 MeV cyclotron will have production capabilities similar to those of most of the cyclotrons operating in the commercial sector. This means that research and technology development done with the 40–10 MeV cyclotron can be directly transferred to private companies operating cyclotrons with similar characteristics.

Innovations based on research on nuclear reactions and on new faster target/product radiochemical separation methods can also be directly transferred to the commercial sector. NBTF can provide assistance and support so that innovations applicable to the commercial sector can be developed; tested, validated, and approved by regulatory agencies without the direct involvement of dedicated commercial facilities.

APPENDIX A

REGIONAL RESOURCES

- ★ The UC Davis Radioisotope Program at Crocker Nuclear Laboratory has been developing new radioisotope production techniques while supplying a variety of research radioisotopes, radiochemicals, and certified SPECT & PET radiopharmaceuticals since the 1970s (*see App. B*). Also located at the UC Davis campus are the California Regional Primate Center and the Veterinary Medical Teaching Hospital; these facilities provide unparalleled access to animal models of human disease to be used in animal testing, as well as access to animal patients with spontaneously occurring cancers and other diseases.
- ★ Other proposed sites for NBTF are the UC Davis Medical Center in Sacramento, and Lawrence Livermore National Laboratory.
- ⊕ The UC Davis Medical Center in Sacramento is expected to be the nation's largest teaching hospital by the year 2005, and includes a world-class Cancer Center. In addition to the research and teaching hospitals at UC Davis, UCSF, and Stanford, the region contains several Veterans Administration Hospitals, the Alta Bates Hospital in Berkeley, Sutter Memorial and Mercy Hospitals in Sacramento, and a variety of other private hospitals that would provide a network of facilities for clinical studies and research.
- ◎ Three major branches of the University of California are located in the region — UC Davis, UC Berkeley, and UCSF — as is Stanford University. Campuses of the State University system are located in San Jose, Sacramento, Hayward, and San Francisco. Altogether, the area contains nearly 300,000 undergraduate and graduate students.
- ◎ The Berkeley campuses (UC Berkeley and Lawrence Berkeley Laboratory) have pioneered the use of accelerators for research and medicine since the 1930s. They continue to be in the forefront of nuclear medicine, with their PET research and clinical studies. Lawrence Livermore National Laboratory has unparalleled experience in nuclear and radiochemistry for processing and separating complex radionuclide mixtures. Los Alamos brings to the consortium its expertise in high-power targetry design. (Being in New Mexico, LANL is not physically "local" — but because it falls under the University of California administrative umbrella, it is usually considered to be one of "ours.")
- ✈ Northern California, which has a population base of approximately 10 million people, is well served by reliable transportation systems. UC Davis connects readily to Hwy. 5, a major north/south access route to nearly 30 million people. A small university airport is located a mile from campus, and the Sacramento Metropolitan Airport (an international facility) is only 16 miles away.

Figure A-1 Geographic Distribution of Major Regional Resources

APPENDIX B

UNIVERSITY OF CALIFORNIA, DAVIS CROCKER NUCLEAR LABORATORY RADIOISOTOPE PRODUCTION EXPERIENCE

Activities at UC Davis's Crocker Nuclear Laboratory (CNL) have supported local, regional, and national research and clinical use programs based on the production and distribution of many non-commercial isotopes and research radiopharmaceuticals. Collectively, these activities represent a regional version of the proposed nationwide scope and mission of NBTF.

Since the early 1970s, UC Davis and CNL have conducted nuclear & radiochemistry R&D associated with radioisotope production and radiopharmaceuticals, based primarily on the use of 68-MeV protons, dedicated target facilities and radiochemistry laboratories. This research includes all aspects of large-scale (0.5 to 4 Ci/batch) production of radioisotopes, including designing, constructing, and maintaining targets for ^{123}I , ^{201}Tl , and ^{18}F production; developing target chemistry processes and radiochemical processes for radioisotope processing and labeling (i.e., $^{201}\text{TlCl}$, ^{123}I -Fibrinogen, ^{123}I -Bleomycin, ^{123}I -Sodium o-Iodo-Hippurate, ^{123}I -HIPDM, ^{18}F -FDG); designing, constructing and operating remote-automated radiochemistry systems; hot-lab operation; and waste management.

Since 1977, under State and Federal regulatory approvals (including Drug Master Files and Drug Manufacturing and State Pharmacy Licenses) the Radioisotope Program at CNL has provided a steady supply of medical and research radioisotopes in California and nationwide. This included the supply of several certified SPECT (I-123 and Tl-201) and PET (F-18 FDG) radiochemical and radiopharmaceutical products for research and clinical uses.

In addition, numerous other research radioisotopes were developed and supplied for medical, agricultural, and environmental research applications in the United States, Canada, Japan, Australia, and in many European and South American nations. CNL has also successfully completed major technology transfer projects with several U.S. and foreign radiopharmaceutical companies.

UC Davis's Radioisotope Program at CNL has established a national and international reputation and leadership in many radioisotope production techniques, including the development of large-scale capabilities for ^{123}I produced via the $^{127}\text{I}(p,5n)^{123}\text{Xe} \rightarrow ^{123}\text{I}$ reaction ("Continuous Flow Radioactive Iodine-123 Production," U.S. Patent Certificate # 4,818,868; April 4, 1989). This continuous flow process provided the purest, labelable ^{123}I available in the United States for many years and the technique was later transferred to the U.S. radiopharmaceutical industry and to many foreign institutions. CNL's role in providing ^{123}I was largely responsible for prompting the U.S. private sector to develop large-scale production capabilities and a national supply.

In the late 1970s, after developing targets, radiochemical techniques, and automated systems, CNL was the first non-profit accelerator used in the large-scale production of ^{201}Tl , which was supplied in California and to the western United States weekly and for many years when commercial sources were scarce and being developed. In the early 1980s, when PET imaging was established in the UC system (Donner Laboratory, UC Berkeley; Brain Imaging Center, UC Irvine), CNL and the Donner Laboratory jointly established the techniques to produce radiopharmaceutical-quality ^{18}F -FDG (in compliance to all State/Federal regulations) for research and clinical uses throughout California. For nearly ten years, CNL was the only facility able to produce and supply this radiopharmaceutical, year around, to many research/clinical collaborating institutions. The research conducted at CNL includes the systematic study of proton-induced nuclear reactions and the experimental measurement of reaction cross sections for a broad spectrum of research radionuclides. In many instances, CNL made available for the first time to nuclear medicine researchers in the United States and abroad, research radionuclides not available from other commercial or national laboratory sources (i.e., ^{18}F [1972]; pure ^{123}I [1973], ^{81}Rb [1976], ^{201}Tl [1976]; ^{203}Pb [1977], ^{55}Co [1978], ^{101}Pd [1979], $^{101\text{m}}\text{Rh}$ [1981], ^{97}Ru [1982]; $^{128}\text{Ba}/^{128}\text{Cs}$ [1983]; $^{122}\text{Xe}/^{122}\text{I}$ [1986]; $^{205/206}\text{Bi}$ [1987], ^{100}Pd [1988], $^{118}\text{Te}/^{118}\text{Sb}$ [1990]), $^{34\text{m}}\text{Cl}$ [1991] and ^{99}Mo - $^{99\text{m}}\text{Tc}$ [1992].

Table A-1. Institutions Receiving R&D Support with Radioisotope, Radiochemical & Radiopharmaceutical Products from CNL's Radioisotope Program, 1977 to present

(1) ACADEMIC INSTITUTIONS	
Arizona, University of, Tucson, AZ	(I-123, Tl-201, Pb-203, Co-55)
California, University of - Berkeley, (LBL-Donner Lab.)	(I-123, Xe-122, F-18, Co-55, Rb-81)
California, University of - Davis	(I-123 Products, Rb-81, Tl-201)
California, University of - Irvine	(F-18 FDG)
California, University of - Los Angeles	(I-123 Products)
California, University of - San Francisco	(I-123 Products, Tl-201, F-18 FDG)
California, University of - Santa Cruz	(Pb-203)
Chicago, University of, Chicago, IL	(I-123, I-123 Hippurate)
Cincinnati, University of, Cincinnati, OH	(I-123, I-123 Hippurate)
Duke University Medical Center, Durham, NC	(I-123)
George Washington University, Washington, D.C.	(I-123 Products)
Harvard Medical School, Cambridge, MA	(I-123)
Indiana University Medical Center, Indianapolis, IN	(I-123, I-123 Hippurate)
Johns Hopkins University Hospital, Baltimore, MD	(I-123 Products)
Kentucky, University of	(I-123)
Loyola University Medical Center	(I-123)
Maryland, University of, Baltimore, MD	(Pb-203)
Miami, University of, Miami, FL	(I-123 Products)
Michigan, University of Medical Center, Ann Arbor, MI	(I-123, I-123 Hippurate)
Minnesota, University of Hospitals, Minneapolis, MN	(I-123)
New Mexico, University of, Albuquerque, NM	(I-123)
New York, State University of (SUNY), Brooklyn, NY	(I-123 Hippurate, Tl-201)
New York, State University of (SUNY), Buffalo, NY	(I-123, I-123 HIPDM)
New York, State University of (SUNY), Syracuse, NY	(I-123 HIPDM)
North Carolina, University of, Chapel Hill, NC	(I-123)
Ohio State University, Columbus, OH	(I-123)
Oklahoma, University of, Oklahoma City, OK	(I-123, I-123 Hippurate)
Pennsylvania University Hospital, Philadelphia, PA	(I-123)
Pittsburgh, University of (Presbyt. Hosp.) Pittsburgh, PA	(I-123)
Southern California, University of	(I-123 Products, Pd-101, Rh-101m)
South Carolina, Medical University of, Charleston, SC	(I-123)
Stanford University, Stanford CA	(I-123 Products, F-18 FDG)
Texas, University of, Dallas, TX	(I-123)
Texas, University of, Houston, TX	(I-123, I-123 Hippurate, Tl-201)
Washington, University, St. Louis, MO	(I-123 Products)
Washington, University of, Seattle, WA	(I-123 Products, Tl-201)
Wisconsin, University of, Madison, WI	(I-123, Tl-201)
Yale University, New Haven, CT	(I-123 Products)

(2) MEDICAL CARE INSTITUTIONS

Children's Hospital Medical Center, Boston, MA	(I-123 Products)
Children's Hospital of Los Angeles, Los Angeles, CA	(I-123 Hippurate)
Cleveland Clinic Foundation, Cleveland, Ohio	(I-123 HIPDM)
Coney Island Hospital, Brooklyn, NY	(I-123, I-123 Hippurate, Tl-201)
Good Samaritan Regional Medical Center, Phoenix, AZ	(F-18)
Henry Ford Hospital, Detroit, MI	(I-123 Products)
Kaiser Foundation Hospitals, Oakland, CA	(I-123)
Kettering Medical Center, Kettering, OH	(Tl-201)
Marshfield Medical Foundation, Marshfield, WI	(I-123)
Memorial Sloan-Kettering Cancer Center, New York, NY	(Co-55)
Mercy General Hospital, Sacramento, CA	(Tl-201)
Mercy San Juan Hospital, Carmichael, CA	(Tl-201)
Michael Reese Hospital, Chicago, IL	(I-123 Products)
New England Medical Center Hospitals, Boston, MA	(I-123)
Northwestern Memorial Hospital, Chicago, IL	(I-123)
Salem Memorial Hospital, Salem, OR	(I-123)
Sutter Community Hospitals, Sacramento, CA	(I-123, Tl-201)
Wesley Medical Center, Wichita, KA	(I-123 Hippurate)
William Beaumont Hospital, Royal Oak, MI	(I-123)

(3) FEDERAL GOVERNMENT INSTITUTIONS

Armed Forces Radiobiology Research Institute, Bethesda, MD	(I-123 Products)
Bureau of Radiological Health	(I-123)
Letterman Army Medical Center, Presidio of San Francisco, CA	(I-123, Tl-201, Pb-201)
National Institute of Standards & Technology (Formerly NBS)	(I-123)
National Institutes of Health	(I-123, Bi-205/206, Pb-203)
Naval Regional Medical Center, Oakland, CA	(I-123, Tl-201, Pb-201)
Veterans Administration Hospital, Gainesville, FL	(I-123)
Veterans Administration Hospital, Loma Linda, CA	(I-123)
Veterans Administration Hospital, San Diego, CA	(I-123)
Veterans Administration Medical Center, Lexington, KY	(I-123)
Veterans Administration Medical Center, Martinez, CA	(I-123 Products, F-18 FDG)
Veterans Administration Medical Center, Palo Alto, CA	(F-18 FDG, Tl-201)
Veterans Administration Medical Center, Portland, OR	(I-123)
Veterans Administration Medical Center, Sepulveda, CA	(I-123 Products)
Veterans Administration Medical Center, West Roxbury, MA	(I-123)

(4) STATE AND LOCAL GOVERNMENT INSTITUTIONS

Los Angeles, County of - Harbor General Hospital, L.A., CA	(I-123 Products)
Los Angeles, County of - M. L. King Jr. Gen. Hospital, L.A., CA	(I-123 Products, Tl-201)

(5) RADIOPHARMACEUTICAL INDUSTRY

Benedict Nuclear Pharmaceuticals, Inc., Golden, CO	(I-123 Products, Tl-201, Targets)
Coulter Immunology Division, Hialeah, FL	(Bi-205/206)
Diagnostic Isotopes, Inc. Bloomfield, NJ	(Tl-201)
Diagnostic Radio-Pharmacies, Inc., Buena Park, CA	(Tl-201)
Gammaceutics, Albuquerque, NM	(I-123, I-123 Hippurate, Tl-201)
ICN Biomedicals, Inc. (Irvine, CA)	(F-18 and F-18 FDG)
Mallinckrodt, Inc., St. Louis, MO	(I-123 Products)
Medi-Physics, Inc., Richmond, CA	(I-123 Products, Targets)
New England Nuclear Corp., No. Billerica, MA	(I-123 Products, Targets - Co-55)
Omni Medical, Paramount, CA	(I-123)
Pacific Radiopharmacy, Ltd., Honolulu, HI	(I-123 Products)
Proctor & Gamble, Ross, OH	(Bi-205/206)
Pro-Scan, Inc., Denver, CO	(I-123, I-123 Hippurate)
Radcal Corp., Monrovia, CA	(I-123, Tl-201)
Radpharm, Inc., San Francisco, CA	(I-123 Products, Tl-201)
Syncor Corp. (a.k.a. Pharmatopes, Inc.), Sacramento, CA	(I-123 Products)
Syncor Corp., Kansas City, MO	(I-123)

(6) FOREIGN INSTITUTIONS

Amersham Australia, Sydney, Australia	(I-123 Products)
Chedoke Hospitals (McMaster University), Hamilton, Ont., Canada	(I-123)
Daiichi Radioisotope Laboratory, Tokyo, Japan	(I-123 Products)
Dr. Mladen Stojanovic Hospital, Zagreb, Yugoslavia	(I-123, I-123 Hippurate)
Foothills Hospital, Calgary, Alberta, Canada	(I-123)
Jose J. Aguirre Hospital, Univ. of Chile, Santiago, Chile	(I-123, I-123 Hippurate)
Chilean Nuclear Energy Commission (La Reina), Santiago, Chile	(I-123, I-123 HIPDM)
Lund, University of, Lund, Sweden	(I-123 Hippurate, Tl-201)
Nihon Medi-Physics, Takarazuka, Hyogo, Japan	(I-123)
Nordion International, Inc., Kanata, Ontario, Canada	(I-123)
Pro-Scan Canada, Markham, Ontario, Canada	(I-123, I-123 Hippurate)
Radiochemical Centre, Ltd., Amersham, England	(Tl-201, Pb-201/Tl-201)
University Hospital, London, Ontario, Canada	(I-123)
Vancouver General Hospital, Vancouver, BC., Canada	(I-123, I-123 Hippurate)

APPENDIX C

A 2.5 MeV ELECTROSTATIC QUADRUPOLE DC ACCELERATOR FOR NEUTRON BEAM APPLICATIONS

*Based on J. Kwan et al. presentation at the Government Workshop
on Accelerator-Based Neutron Sources for Boron Neutron Capture Therapy (BNCT),
Sept. 11-14, 1994, Jackson, Wyoming.*

1. INTRODUCTION

In a recent paper, O.A. Anderson et al. [1] proposed to use a dc electrostatic quadrupole (ESQ) accelerator to deliver more than 100 mA of 2.5 MeV proton beam onto a lithium target for generating a neutron beam. The emerging neutron beam can be used for Radioisotope Production and Research and other applications like Boron Neutron Capture Therapy (BNCT) and neutron radiography.

Beam current ≥ 100 mA can only be achieved by electrostatic accelerators. We have been developing high-current ESQ accelerators as neutral particle beam injectors into tokamak fusion reactors, and as injectors for heavy ion induction linac drivers for inertial fusion reactors. While the beam dynamics in dc ESQ accelerators has been demonstrated in previous experiments, the remaining challenge is to develop a compact power supply system tailored to the accelerator.

Because of the inherent simplicity and efficiency of the design, the construction and operating costs of a high power ESD are relatively low.

2. BEAM FOCUSING USING ELECTROSTATIC QUADRUPOLES (ESQs)

In an ESQ system, the quadrupole electrodes have transverse electric field component to transverse focus the accelerator ion beam. The ESQ reverses polarity for each subsequent unit (alternating gradient) to achieve focusing in both planes. The key advantage of an ESQ system is that the transverse focusing can be very strong (useful for a high current beam) without incurring a longitudinal field near or exceeding the breakdown limit [2].

Another advantage in applying a strong transverse field is that the secondary electrons (or ions) generated within the accelerator column are quickly removed by the ESQ electrodes instead of being allowed to multiply into a column arc-down. High energy stray electrons are detrimental in a vacuum chamber because they produce unwanted x-rays.

3. ESQ ACCELERATOR DEVELOPMENT

In 1970, Abramyan et al. [3] reported the achievement of a 1.2 MeV hydrogen beam (50% H_1^+ , 30% H_2^+ , and 20% H_3^+) using an ESQ accelerator (a peak current of 80 mA and an average power of 10 kW). The recent development of ESQ accelerators has been driven by two separate needs in the US fusion program. Earlier tokamak reactors used high power (several MW) neutral beam injectors with particle energy up to 120 keV. In the next generation reactors (e.g., the International Thermonuclear Experimental Reactor, ITER), which are larger and have a hotter and more dense plasma, the required beam energy is ≈ 1.3 MeV. Fig. 1 shows a 1.3 MeV, 1.0 A D⁻ dc ESQ accelerator channel which was designed to be modular for low cost and easy construction [4]. (The average accelerating gradient is about 0.5 MV/m. The lower field makes the accelerator slightly longer, but with the gain in safety and reliability. A special feature of this design is the use of an acceleration gap between each set of quadrupoles thus providing a greater flexibility in varying the beam energy without changing the beam current.) A smaller prototype which contains five quadrupoles to match and accelerate 100 mA of He^+ to 100 keV was built and tested at LBL. In testing, almost no beam loss and very little degradation of beam optics were found [5].

In the inertial fusion program, heavy ion beams are being considered as drivers for pellet implosion. Here, the main acceleration will be done by a pulsed induction linac to reach beam energy as high as 10 GeV, but a MeV-ranged ESQ accelerator is needed as an injector. At LBL, a 2.0 MeV ESQ injector was successfully tested to deliver 800 mA of 1 μs K^+ beam [6]. The accelerator is powered by a Marx generator. Details of measured beam optics were reported to be in good agreement with 3-D simulations. Again, the experiment has shown no beam loss or aberrations. The injector, including the K^+ surface ionization source, the extraction diode and the ESQ accelerator, is shown in Fig. 2. The apparatus is enclosed by a 5-ft diameter steel tank. During operation, the tank is filled with 80 psig of SF_6 .

4. A CONCEPTUAL ESQ ACCELERATOR DESIGN FOR NEUTRON BEAMS APPLICATIONS

First, let us examine the required size of a 2.5 MeV ESQ accelerator. The most likely place for an arc-down is along the surface of an insulator. As a general rule, the insulator should not be subjected to more than 20 kV/cm on the vacuum side and 10 kV/cm on the air side. Since the air-side number can be raised to 58 kV/cm when air is replaced by 3 atm. of SF₆ the minimum length of a dc accelerator column is determined by the vacuum/insulator interface which allows a maximum accelerating gradient of 20 kV/cm, or 2 MV/m.

If we assume a very conservative acceleration gradient of 0.5 MV/m, a 2.5 MeV proton beam will have a column approximately 5 m long, operable in air. The ion source and extractor at the front end will take up another 0.5 m. Additional space (≈2 meters) must be allowed to prevent electrical arc-down to the surroundings. The system is more compact if the column is enclosed in a steel tank filled with SF₆. In this case, we can raise the gradient to 1.5 MV/m (still below the 2 MV/m vacuum/insulator limit), so that a 2.5 MeV column is 1.7 m long. Again after adding space for the ion source and the surrounding, the enclosure tank is approximately 3 m long. To save space, the power supply can be custom built alongside the accelerator column. The enclosure tank will therefore have a diameter of 2–3 m wide.

References

- [1] J. Kwan et al., 1st Government Workshop on Accelerator Based Neutron Sources for Boron Neutron Capture Therapy.
- [2] O.A. Anderson et al., *Nucl. Instrum. Methods* **B40/41**, 877 (1989).
- [3] E.A. Abramyan et al., *Atomnaya Energiya* **29**, 346 (1970).
- [4] O.A. Anderson et al., IAEA 13th Inter. Conf. on Plasma Physics and Controlled Nuclear Fusion Research, Washington, DC (1990).
- [5] J.W. Kwan et al., *Proc. 14th IEEE Particle Accelerator Conf.* **1995**, San Francisco, May 6–9 (1991).
- [6] S.S. Yu et al., *Proc. Inter. Symp. on Heavy Ion Inertial Fusion*, Frascati, Italy, May 25–28 (1993); LBL-33806, Lawrence Berkeley Laboratory (1993).

NOTE: This presentation has been developed into a report available from Lawrence Berkeley Laboratory: LBL-35540 (1994).

Figure 1. Schematic diagram of a proof-of-principle 1.3 MeV, 1.0 A D^- dc ESQ accelerator proposed for neutral beam injector for ITER.

Figure 2. Schematic diagram of a 2.0 MeV, 800 mA, $1\mu s$ K^+ beam ESQ injector developed for heavy ion fusion accelerator driver.

APPENDIX D

90 MeV LINEAR ACCELERATOR FOR NBTF ISOTOPE PRODUCTION

*Los Alamos National Laboratory
Accelerator Research Division
Linac Physics and Special Projects Section*

One of the accelerator options explored by the Northern California National Biomedical Tracer Facility Consortium was a 90 MeV linear accelerator. The linac design developed for this study by the Los Alamos National Laboratory is summarized here in Appendix D.

90 MeV LINEAR ACCELERATOR FOR NBTF ISOTOPE PRODUCTION

1.0 ACCELERATOR PERFORMANCE SPECIFICATIONS

Ion	proton
Final energy	90 MeV
Beam current (minimum average)	1 mA

- Four output beamlines to research/production targets
- Two concurrent beams having different energies
- Energy variation accommodating 2.5% steps from 30–90 MeV

2.0 ACCELERATOR REFERENCE DESIGN

2.1 Overall System Design

Ion	proton
Final energy	90 MeV
Beam current (average)	1 mA
Beam current (peak)	42 mA
Beam pulse length	200 μ sec
Beam macropulse frequency	120 Hz
Beam duty factor	2.4 %
Length (total)	40 m
Power required (total)	750 kW

2.2 Injector

Beam current (peak)	60 mA
Extraction voltage	45 keV
Emittance	$\leq 0.03 \pi$ cm-mrad

2.3 RADIOFREQUENCY QUADRUPOLE (RFQ)

Injection energy	45 keV
Final energy	12 MeV
Injected beam current	50 mA
Injected emittance	$\leq 0.03 \pi \text{ cm}\cdot\text{mrad}$
Transmission	$\geq 90 \%$
RF frequency	433 MHz
Surface field (peak)	$1.8 E_k$
Length	6 m

RFQ rf system

Frequency	433 MHz
Copper power (peak)	3.4 MW
Beam power (peak)	540 kW
Control and losses	15 %
Power required (peak)	4.0 MW
Power required (average)	100 kW
Klystron	TH2118
Power (peak)	6 MW
Power (average)	200 kW
Duty	3.3%
Pulse length	220 μsec
Number required	1 each
Efficiency	58 %

2.4 CCDDL (2 DRIFT TUBE LINACS PER CAVITY)

Injection energy	12 MeV
Final energy	90 MeV
Injected beam current	42 mA
Injected emittance	$\leq 0.03 \pi \text{ cm}\cdot\text{mrad}$
Transmission	100%
RF frequency	1300 MHz
Surface field (peak)	$1.75 E_k$
Power density (peak)	10 W/cm^2
Length (active)	22.5 m
Length (total)	31.4 cm
Number of accelerator cavities (total)	136
Accelerating gradient	5 MV/m
Number of quadrupoles (total)	68
Quadrupole gradient (maximum)	150 T/m
Quadrupole length (overall)	6 cm

CCDDL rf system

Frequency	1300 MHz
Copper power (peak @ $k=5\%$)	4.6 MW
Beam power (peak)	3.3 MW
Control and losses	15%
Power required (peak)	9 MW
Power required (average)	225 kW
Klystron	TH2104U
Power (peak)	10 MW
Power (average)	250 kW
Duty	2.5 %
Pulse length	250 μsec
Number required	1 each
Efficiency	45 %

3.0 LAYOUT

A schematic layout of the system is shown in Fig. 1. The total length of the entire linac including the ion source is about 39.8 meters. The entire CCDTL is powered by a single klystron tube. A proton (H+) as opposed to H- injector is used for better reliability and emittance.

4.0 RFQ

4.1 SSC RFQ

An RFQ for the Superconducting Super Collider (SSC) was built and successfully operated. This RFQ is 2.5 meters long with a design current of 50 mA (peak).

4.2 Higher-Energy RFQ

Since the fabrication of the SSC RFQ, a longer segmented RFQ was designed. An 8-meter-long waveguide coupled cold model was constructed and successfully tested for tunability, field uniformity, and stability. The design current is 100 mA and the design energy 7 MeV. Based on the same design principle, we have designed a 6-meter-long RFQ capable of delivering 20 mA at 12 MeV to be used for the NBTF linac.

4.3 RFQ Brazed Model

Traditionally, we have used electroforming techniques to assemble the entire RFQ from its constituent segments. However, this process while very robust is very costly. In order to economize on the fabrication cost, we have constructed a brazed model section of an RFQ designed at 500 MHz. This method is conventionally used in fabrication of other accelerating structures and is relatively inexpensive. The model has been successfully tested for mechanical, rf, and vacuum integrity. The field distribution before and after furnace brazing did not show any frequency change.

FIGURE 1

5.0 CCDTL

For the NBTF linac, we propose a CCDTL structure from 12 to 90 MeV. The entire accelerating structure will be powered by a single klystron. This structure combines features of the conventional DTL and CCL. It has high shunt impedance for velocity range of $0.2 \leq \beta \leq 0.5$. It has the inherent stability of a CCL at $\pi/2$ structure mode. In our design, two drift tubes are used inside each cavity.

5.1 Cold Model

A 7 cell cold model for the CCDTL at 1.4 GHz and for $\beta = 0.283$ has been built. Accelerating field profile and dispersion curves were measured and stem modes were investigated. The results of the cold model studies are in accord with the accepted behavior of the structures.

The cooling scheme of a CCDTL structure is similar to a coupled cavity linac structure with circumferential and web cooling. Additional ring and drift tubes with circumferential cooling are also provided.

5.2 Quadrupole Design and Specifications

A schematic of the quadrupoles for the CCDTL accelerating section is shown in Fig. 2. The specifications for the quadrupoles are as follows.

Inside diameter	1.2 cm
Outside diameter	8.8 cm
Length (total)	6.5 cm
Length (pole)	4.0 cm
Length (effective)	4.5 cm

FIGURE 2

Number of turns	7
Current	350 A
Conductor OD	0.477 cm SQ
Conductor ID	0.254 cm RD
Volts	1.4 volts
Power	500 watts
Coolant pressure	40 psi
Coolant flow	0.25 gal/min
Coolant temperature	8° C
Gradient	153 T/m
GL	6.88 T
Harmonics (r=4mm)	< 0.5 % of n=2

The quadrupole will occupy $\approx 2 \beta \lambda$ of drift space. It can be split into halves to allow it to be installed and removed from the beamline without breaking vacuum. The coolant flow rates and pressure drops are for all four coils in series.

5.0 METHOD FOR CHANGING BEAM ENERGY

The energy of a standing wave accelerator can be varied by switching off part of the accelerator. Using this method, the fields in part of a standing wave accelerator can be turned off in such a way that the beam current does not excite fields in the turned-off section. This would enable N different energies in successive macropulses. The successive beam pulses with different energies must be separated at exit. The concept has been verified experimentally, and is in the process of being patented.

6.0 BEAM TRANSPORT

A beam transport and expander system can be designed to produce a nearly uniform beam distribution at a production target. A typical system consists of quadrupole magnets to maintain

transverse focusing in order to transport the beam and to produce beam waists at desired locations for manipulation by the higher order magnets. Higher order magnets such as sextupoles and octupoles are used to transform the Gaussian or triangular output distribution from the accelerator. Both rectangular and circular distributions which are nearly uniform can be produced by this technique.

APPENDIX E

LETTERS OF SUPPORT

The National Biomedical Tracer Facility continues to draw warm support in Northern California. In this Phase I Project Definition Study report, letters are included from the Chancellor and the Vice Chancellor for Research of the University of California, Davis (see front of report) and also from:

J.M.R. Hutchinson, Radioactivity Group Leader, Ionizing Radiation Division, Physics Laboratory, National Institute of Standards and Technology

Carmen J. Marchetti, Materials Management Coordinator, DuPont NEN Products

Jeff Wadsworth, Associate Director, Chemistry and Materials Science, Lawrence Livermore National Laboratory

These letters supplement those in our original February 1994 proposal, which include:

Prof. Glenn T. Seaborg, Associate Director at Large, Lawrence Berkeley Laboratory

Stephen P. Meyer, Senior Vice President Finance & Chief Financial Officer, Titan Corporation

Anthony A. Zante, President, and Kenneth Whitham, Vice President, Titan Beta Division

William A. Barletta, Director, Accelerator & Fusion Research Division, Lawrence Berkeley Laboratory

Stanley O. Schriber, Director, Accelerator Operations & Technology Division, Los Alamos National Laboratory

Torben O. Brun, Operations Manager, Manuel Lujan Neutron Scattering Center, Los Alamos National Laboratory

Sidney Niemeyer, Division Leader, Nuclear Chemistry Division, Lawrence Livermore National Laboratory

Henry H. Kramer, Fellow American College of Nuclear Physicians, consultant

Prof. Kevin M. Smith, Chair, Department of Chemistry, University of California, Davis

George M. Segall, M.D., Director, Positron Emission Tomography, School of Medicine,
Stanford University

Prof. Peter A.J. Englert, Director, Nuclear Science, San Jose State University

Len Hendrikson, President, Isotope Products Laboratory

R.A. Greenwell, Director, Advanced Technology Division, Science & Engineering
Associates, Inc.

NIST

UNITED STATES DEPARTMENT OF COMMERCE
National Institute of Standards and Technology
Gaithersburg, Maryland 20899-0001

January 31, 1995

Dr. Manuel Lagunas-Solar
Crocker National Laboratory
University of California
Davis, CA 95616

Dear Dr. Lagunas-Solar:

This letter is written to express our interest in collaborating with the proposed National Biomedical Tracer Facility (NBTF) which, I understand from Dr. Kramer, you are presently planning. The National Institute for Standards and Metrology has a significant and long lasting interest in programs associated with present and future radiopharmaceuticals for diagnostic and therapeutic purposes. We have established national standards for such materials as a prerequisite for FDA licensing for many years. The development of national standards would require a close cooperative program between our two laboratories involving basic research into the physical and chemical characteristics of newly generated materials by the NBTF. I hope that this suggestion meets with your approval.

Yours sincerely,

A handwritten signature in cursive script, appearing to read "J.M.R. Hutchinson".

J.M.R. Hutchinson
Group Leader
Radioactivity Group
Ionizing Radiation Division
Physics Laboratory

E.I. DUPONT DE NEMOURS & CO. (INC.).
BIOTECHNOLOGY SYSTEMS

Dr. Manuel C. Lagunas - Solar, Chair
NOR - CAL Executive Committee
University of California, Davis
Crocker Nuclear Laboratory
#1 Bainer Hall Drive
Davis, California 95616-8569

February 6, 1995

Dear Dr. Lagunas - Solar,

It was a pleasure to speak to you recently and learn more of your efforts to develop a National Biomedical Tracer Facility at U. Cal., Davis and to share some thoughts about the project and its importance to research, medicine and industry. We at DuPont NEN Research Products, with our colleagues at the DuPont Merck Pharmaceutical Company have been supportive of the NBTF program since its inception. As we discussed, the recently published report on Isotope Availability by the Institute of Medicine made a strong case for the construction of an NBTF. In addition to this support a very strong argument was made for the presence of a private sector partner responsible for marketing, sales and distribution of products manufactured at the NBTF.

DuPont NEN Research Products has been a long time supplier of radioisotopes and radiolabeled chemicals for the research, medical and industrial communities. We have over the years developed a strong marketing sales and distribution organization in support of this business. We have also had a close relationship with the Missouri University Research Reactor(MURR), one of the most reliable major suppliers of reactor produced radioisotopes in the world. We are in the process of further strengthening this relationship through an alliance that will support the research, development and production of short lived isotopes for research and use in radiotherapy. The establishment of the NBTF as a source of accelerator produced radioisotopes would be a complement to this program. Should U. Cal, Davis be awarded funding beyond the Project Definition Phase, or be chosen as the site of the NBTF we at DuPont NEN Research Products would be willing to assist in any way possible with advice and consultation in regard to technical and business planning. In addition, should your site be chosen as the NBTF, we would like to have the opportunity to discuss and evaluate the feasibility of having DuPont NEN Products serve as the marketing, sales, and distribution organization for the NBTF production facility. We would also provide assistance where possible in technical issues beyond those that would have been addressed in your project definition study.

I hope that the above is of interest to you. It offers an opportunity to address the needs of our industry and its supportive research community in an effective manner utilizing two well established organizations. Please consider this possibility as you go forward with your proposal and I wish you the best of luck in your Project Definition submittal.

Sincerely,

Carmen J. Marchetti
Materials Management Coordinator
DuPont NEN Products

cc : R. Lucas
R. Perullo

BIOTECHNOLOGY SYSTEMS

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Jeff Wadsworth
Associate Director

February 8, 1995
95-17

Dr. Manuel Lagunas-Solar
Crocker Nuclear Laboratory
University of California, Davis
1 Bainer Hall Drive
Davis, CA 95616

Dear Dr. Solar:

Through my Department's Isotope Sciences Division, I have been following closely the NORCAL committee's progress toward its NBTF Project Definition Study Report. I believe that this facility would be a very valuable asset to the nuclear medicine community and I strongly support its goals of reliable isotope production, research applications, and educational opportunities. I wish to assure you that the Chemistry and Materials Science Department of the Lawrence Livermore National Laboratory will continue to be a willing and active participant in support of the NBTF.

If, as a result of the Project Definition Study, the Department of Energy does not feel that the private sector has the required capability to construct and operate the facility, my Directorate would look very favorably on performing siting studies for locating the NBTF at Livermore. I look forward to further cooperation with you and your committee on this very important and necessary project.

Sincerely,

Jeffrey Wadsworth
Associate Director

JW:cav

cc: R. W. Kuckuck
M. A. Krebs

APPENDIX F

REFERENCES

References to academic papers are provided, as appropriate, either within the text or at the end of the section in which they occur.

Abbreviated citations to the following basic sources used throughout the text are made in the form shown at the left in this list.

- [Adelstein & Manning, 1994] S.J. Adelstein and F.J. Manning, eds., *Isotopes for Medicine and the Life Sciences*, Institute of Medicine, National Academy Press, Washington, DC, 1994.
- [Holmes, 1991] R.A. Holmes, Principal Investigator, *National Biomedical Tracer Facility: Planning and Feasibility Study*, Society of Nuclear Medicine and U.S. Department of Energy Isotope Production Program, March 1991.
- [Kliwer & Green, 1992] K.L. Kliwer and M.A. Green, *Proceedings of the Purdue National Biomedical Tracer Facility Workshop*, Purdue University, West Lafayette, IN, April 28–30, 1992).
- [IPDP, 1994] U.S. Department of Energy *National Isotope Strategy*, Isotope Production and Distribution Program, Washington, DC, August 1994.
- [Moody & Petersen, 1989] D. Moody and E. Petersen, *Proceedings of the DOE Workshop on the Role of High-Energy Accelerators in Nuclear Medicine*, U.S. Department of Energy, Los Alamos National Laboratory (Conf. LA-11579-C), May 1989.
- [TMG Study, 1994] This refers to data presented in Appendix 7.2-a/-b ("Radiopharmaceutical Market Diagnostic Nuclear Medicine" and "Radiochemical Market Study"), prepared by Technology Marketing Group, Des Plaines, IL, copyright 1994; used for the purposes of this Phase I Project Definition Study by permission of the U.S. Department of Energy.

APPENDIX G

Attached is the list of 9 items to be addressed in the Phase I reports, as it appeared in the Supplemental Information (pp. 3-4) to the U.S. Department of Energy, Office of Energy Research, Office of Health and Environmental Research: Solicitation for a Project Definition Study.

C. NBTF Project Definition Study Report

Each applicant receiving an NBTF Project Definition Study award (hereinafter "Grantee") must include the following items in the NBTF Project Definition Study report:

- ① • A narrative discussion and sketch for a large proton accelerator to produce radioisotopes for medical and research purposes. This should include a description of the type of accelerator, the proton beam energy, and the proton beam current of the proposed accelerator. "Suggested" characteristics of an NBTF accelerator as described in the *NBTF Planning and Feasibility Study of the National Biomedical Tracer Facility Report, 1991*, and the *Proceedings of the Purdue National Biomedical Tracer Facility Workshop, 1992*, are as follows:

- (1) the accelerator may be a linear accelerator (Linac) or cyclotron
- (2) the extracted proton beam energies should range from 30 to 100 MeV step size
- (3) the energy should be reproducible to 1%
- (4) the beam energy spread should be < 1%
- (5) the beam current should be >0.75 mA, with an expectation of achieving 1.0 mA
- (6) the accelerator should provide two high-intensity beams and two low-intensity beams, at least two of which can be operated simultaneously with separately controllable energies

It is requested that the Grantee review the suggested characteristics for the NBTF accelerator and provide justification for these characteristics and any changes proposed.

- ② • Provide a narrative discussion and sketch for the radioisotope production facility. This should include a specific design of the target facility(s) and associated radioisotope separation facility(s) (hot cells). Specific items such as, the number of beam lines, the energy of the beams lines, and the utilization of existing facilities/equipment should be included. The number and design of the targeting facilities should adequately meet the expectations as reported in the *NBTF Planning and Feasibility Study of the National Biomedical Tracer Facility Report, 1991* and the *Proceedings of the Purdue National Biomedical Tracer Facility Workshop, 1992*. Provisions should also be included for the incorporation of radiochemistry laboratories meeting Good Laboratory Practice (GLP) standards. It is requested that the Grantee also provide justification and rationale for the proposed target facility design.
- ③ • Develop preliminary cost estimates for the design and construction of the NBTF. Include construction schedules for the accelerator and the associated radioisotope production facilities. Discuss potential for construction cost-sharing by non-Federal partners.
- ④ • Describe all Federal, State, and local permits required to construct and operate the NBTF. This should include cost estimates and time schedules for obtaining these permits.

- ⑤ • Develop a detailed plan for handling, storage, and disposal of radioactive wastes generated by the NBTF. Include in your discussion, the types of radioactive waste generated, estimated quantity and half-lives involved, and Federal, State, and local regulatory requirements.
- ⑥ • Provide a business plan for the operation of the NBTF. Include and fully describe:
- (1) anticipated sales of isotopes and identify potential purchasers
 - (2) expected annual income from sales
 - (3) all costs of operation associated with the facility
 - (4) annual costs of waste removal
 - (5) plan for reimbursing the Government for its contribution for the NBTF

If the total projected income is insufficient to cover operating costs, provide a method to avoid or recover these costs.

- ⑦ • Provide a detailed plan for operating the NBTF. It was suggested in the *NBTF Planning and Feasibility Study of the National Biomedical Tracer Facility Report, 1991* and the *Proceedings of the Purdue National Biomedical Tracer Facility Workshop, 1992*, that the facility should operate 24 hours/day, 7 days/week for a minimum of 42 weeks/year. It was also suggested that a normal operation/maintenance schedule could be 3 weeks of continuous accelerator operation followed by one 8-hour maintenance shift.
- ⑧ • Provide a detailed discussion on the types of proposed radiolabels to be produced annually, the quantity of radiolabels produced annually, production schedules, priorities, and any planned collaborations. The following radiolabels were suggested in the *Proceedings of the Purdue National Biomedical Tracer Facility Workshop, 1992*.

^{75}Br	^{24}Mg	^{45}Sc	^{46}V	^{54}Co	^{57}Co	^{65}Zn
^{64}Cu	^{67}Cu	^{68}Ga	^{75}As	^{76}Br	^{77}Br	^{82}Br
^{82}Sr	^{86}Y	^{88}Zr	^{94}Tc	^{96}Tc	^{97}Ru	^{108}Cd
^{114}In	^{125}Xe	^{124}I	^{127}Xe	^{132}Ba	^{199}Au	^{203}Pb
^{203}Bi	^{204}Bi	^{207}Bi	^{235}Np	^{236}Np	^{237}Pu	

It is requested that each Grantee review this list of candidate radiolabels and provide justification for their need and also evaluate the needs for additional radiolabels.

- ⑨ • Discuss your ability to provide an education and training program in radiochemistry and related areas or provide evidence that such capabilities can be obtained. Discuss potential for conducting research and training in the areas of target design, radiochemistry, etc.