DOE/ER/61874--T1-Pt.1

Project Definition Study for the National Biomedical Tracer Facility

Developed for the U.S. Dept. of Energy
by the
University of Alabama at Birmingham

Funding provided by the U.S. Dept. of Energy
and the State of Alabama

Feb. 15, 1995

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

Table of Contents

Project Definition Study

A.	Executive Summary	Page 1
B.	Introduction	Page 4
C.	Equipment Selection	Page 6
D.	Facility Design — Budget information removed — pp. 67-79	Page 56
E.	Environmental, Safety and Health Considerations	Page 82
F.	Operational and Organization Issues	Page 95
G.	Business Plan	Page 115
H.	Conclusions and Recommendations	Page 122
I.	Glossary	Page 124
J.	References	Page 125
K.	Advisory Committees	Page 126

Project Definition Study
for the
National Biomedical Tracer Facility

Developed for the U.S. Dept. of Energy
by the
University of Alabama at Birmingham

Funding provided by the U.S. Dept. of Energy
and the State of Alabama

Kenneth Roozen, Ph.D., Principal Investigator
Robert Atcher, Ph.D., Project Coordinator

Feb. 15, 1995

A. Executive Summary

The University of Alabama at Birmingham (UAB) has conducted a study of the proposed National Biomedical Tracer Facility (NBTF). In collaboration with General Atomics, RUST International, Coleman Research Corporation (CRC), IsoMed, Ernst & Young and our advisory committees, we have examined the issues relevant to the NBTF in terms of facility design, operating philosophy, and a business plan. We have utilized resources within UAB, CRC and Chem-Nuclear to develop recommendations on environmental, safety and health issues.

The Institute of Medicine Panel's Report on Isotopes for Medicine and the Life Sciences took the results of prior workshops further in developing recommendations for the mission of the NBTF. The IOM panel recommends that the NBTF accelerator have the capacity to accelerate protons to **80 MeV** and a **minimum of 750 microamperes** of current. The panel declined to recommend a cyclotron or a linac. They emphasized a clear focus on **Research and Development for isotope production** including target design, separation chemistry and generator development. The facility needs to emphasize **Education and Training** in its mission. The facility must focus on **Radionuclide production for the research and clinical communities**. The **formation of a public-private partnership** resembling the TRIUMF-Nordion model was encouraged. An **advisory panel** should assist with the NBTF operations and prioritization.

Project Definition Study Conclusions

Physical Parameters

In our analysis of an extended list of radionuclides of interest, we found no example of a reaction that required an energy of 80 MeV. In fact, we recommend a **maximum energy of 70 MeV** for the accelerator. Our initial impression was that specifying a beam current of >750 μA was too ambitious. In discussing this problem with accelerator vendors, we believe that specifying a **beam current of 1000 μA** for routine operation is warranted and technically sound. This current should satisfy production needs now and in the future. In order to provide the greatest precision in isotope production as well as analytical experiments and data generation for nuclear physics studies in reaction cross sections, we determined that the beam should be reproducible to within **±1.5 MeV** through the entire energy range **reproducible to ≤ 1 %**.

Based on the universal use of cyclotrons in the radionuclide production industry, the larger number of commercial vendors of cyclotrons, and the greater experimental flexibility, we have specified that a **negative ion proton cyclotron** be used for the accelerator. This decision was also driven by the potential for technology transfer to both the commercial vendors of radionuclides and the accelerator manufacturers. We also recommend that a second cyclotron that can accelerate He-4 be installed. It would be used to produce Astatine-211, an alpha emitting radionuclide that has great promise in therapy. This cyclotron would have a maximum energy of 30 MeV and beam current of at least 100 μA for internal and external targets.

The **cost of the NBTF is $82,000,000**, if housed in a 2 story structure, . This estimate is based on 1995 cost of construction in Birmingham with no cost escalation during the construction phase. Other sites around the country can be estimated with the appropriate cost increases for their higher cost of construction. The time of construction is approximately 36 months. This is primarily driven by the time required to design and construct the accelerators.

The NBTF should **operate 24 hours a day, 52 weeks per year**. Given the fact that this is a unique facility with a single accelerator, we strongly recommend that a **regular schedule of preventive maintenance** be undertaken to minimize unscheduled outages.

Environmental, Safety and Health (ES&H) Issues

We developed our recommendations on ES&H matters after extensive discussions with our contractors, members of our advisory committee from National Laboratories, and the commercial vendors.

Waste Disposal - **Waste minimization** is required including supercompaction. Storage has to be adequate to enable the NBTF to operate on a **decay and discard** principle, rather than disposing of all radioactive trash as low level radioactive waste. Given the current status of waste disposal in the U.S., we concluded that **the Southeast Compact is the only region in which the NBTF could be located** as it is the only region with a functioning disposal site.

ES&H Construction Regulatory Issues - We determined that, in Alabama, there is no significant regulatory hurdle at the State level. At the federal level, we determined that an Environmental Impact Statement is required. This will result in a substantial commitment of time and money.

ES&H Operational Regulatory Issues - This facility would be operated under the supervision of the state regulatory authority unless it was constructed at a national laboratory. We have determined that there are significant resources within the national laboratory system that could be drawn upon to construct an effective and efficient ES&H "culture" at the NBTF. The experience of the labs in coming into compliance with all applicable Federal, State and Local regulations has also provided us with a model for training of the workforce at the NBTF.

Organizational Parameters

The mission of the NBTF includes three major components: **isotope production; research and development; and education and training**. The first component can be accomplished nearly anywhere; it is driven primarily by shipping to the customer. The other two components of the mission are more sensitive to location. Our advisory committee was unanimous in recommending that the **NBTF be located at a University with a comprehensive program in basic science, engineering and clinical science all at the same location.** We are convinced that the interaction among faculty, students, staff, and others will be enhanced by proximity to the campus rather than offsite. This would enhance the NBTF as a center for nuclear medicine research and better integrate its activities and focus to radionuclides that have clinical utility. In addition, given its status as a national and international resource, the location should be within 20 minutes of a major airport to facilitate short term visits from interested users as well as same-day shipping.

The advisory committee was unanimous that **the NBTF not be located at a National Lab**. Their reasons included excessive regulation, micromanagement by DOE (both noted in the recent Galvin report as problems), and the lack of a business mentality in operations at the national laboratories.

We recommend that the NBTF be **organized along its mission components**. The primary component would be **Operations**. The operation of the accelerator and target areas; the processing of routine targets; the compliance with all Environmental, Safety and Health Regulations; the packaging and shipping of radionuclides and waste; and the marketing, order entry and other business activities would be handled by this section.

The second component would be **Research and Development (R&D)**. All work in this section would be focused on the NBTF activity, i.e. isotope production. The technical staff and equipment necessary to conduct a broad research program in targetry development is already in place at national laboratories and does not have to be duplicated at the NBTF. We advocate instead a strong link to industry and the national laboratories to utilize their resident expertise in targetry development.

The third component, **Education and Training (E&T)**, should be focused on three primary activities. The first is the training and education of the NBTF staff and workers, particularly with respect to environmental, safety and health regulations. The second is the education and training of students including those who are early in their career preparation (high school and undergraduate school) and those who are more advanced (graduate students and postdoctoral fellows). The third is training and education of those in career transition (scientists interested in radionuclide applications, technicians in industry, etc.).

Operational Parameters

In order to best define and delineate the activities, we recommend that the **operations division be run as a business**. Using this model, anyone who uses the facility will be treated as a customer, including those in the R&D and E&T components of the NBTF. Using this paradigm, priorities would be customer-driven. Production would take top priority at every juncture. We determined that the NBTF should never produce a retail product, either as a source radionuclide or as a radiopharmaceutical. We are convinced that the requirements for Good Manufacturing Practice (GMP), in the case of radiopharmaceutical manufacture, would be a drain on resources.

This is not an attempt to minimize compliance with established quality standards, however. We anticipate that several radionuclides produced at the NBTF would be produced under Drug Master Files(DMF). A DMF is used by the Food and Drug Administration (FDA) to insure certain quality standards are met. In order to insure that the quality standards are met for international users, we have examined implementing ISO 9000 standards. These standards provide for certifiable methods and procedures to insure that quality is part of the production process. We recommend that the **NBTF comply with ISO 9000** standards in order to ensure the greatest commitment to quality in the operation of the NBTF. This international standard would also insure that operations would be done under Good Laboratory Practice (GLP) guidelines.

We endorse the IOM panel's **recommendation for an advisory panel.** The panel will insure that the NBTF is run in a manner that meets the needs of the user community. The Advisory Panel would be useful in establishing priorities for isotope production, particularly for those that would be produced at less than full cost recovery. The panel would also provide guidance on NBTF research programs.

Business Plan

We have concluded that the **NBTF is not economically feasible as a private undertaking**. Our most conservative estimates are that a privately built and operated NBTF would run at an annual deficit of greater than $3 million per year when financing for the facility was included. Under these circumstances, it was impossible to construct a scenario in which the government was paid back for its investment. In contrast, we have determined that industry is quite capable of contributing to some aspects of the NBTF. The accelerator industry is well equipped to produce and maintain an accelerator that meets the specifications of this study.

We have determined, however, that **several opportunities exist for industrial participation** in the NBTF. The most direct would be if the operations function were outsourced to industry. A second mechanism for public-private partnership would be for industry to handle the marketing and sales activity at the NBTF, utilizing their existing infrastructure. Third, the NBTF can serve as a backup and supplementary supplier of accelerator-produced radionuclides for the commercial vendors. Finally, commercial ventures could be spawned as a result of the new radiopharmaceuticals utilizing radionuclides produced at the NBTF. The latter two scenarios have the potential to generate royalty payments as described in the IOM report.

In summary, our findings are that the NBTF must be located at a University integrated into the campus. This university should have a medical school and hospitals as well as activities in the basic sciences in order to integrate the NBTF into a well-rounded program. The economic, operational and programmatic advantages of a university over siting at a national laboratory are substantial.

B. Introduction

Background

Our study began with a review of existing information on a dedicated accelerator for the production of radioisotopes. This review included: The Role of a High-Current Accelerator in the Future of Nuclear Medicine, Proceedings of a DOE-LANL Workshop, 1989 (1); Review of the Office of Health and Environmental Research Program in Nuclear Medicine, 1989 (2); National Biomedical Tracer Facility Planning and Feasibility Study, 1991(3); and Proceedings of the Purdue National Biomedical Tracer Facility Workshop, 1992 (4). The concern regarding this issue was prompted by the reduction in operating time at the two parasitic facilities in the US at Los Alamos and at Brookhaven National Laboratories. These documents were remarkably similar in their recommendations for the physical parameters of the facility.

There was some disagreement on the mission of the facility. Initially, there was a strong focus on production including commercial applications. The Purdue workshop recommended that commercial production be a low priority for the NBTF. The results of that workshop were adopted by the SNM/ACNP Task force in a revised mission statement. Subsequently, the requirement for the NBTF to pay for itself as part of full cost recovery were changed by Congress, giving the Secretary of Energy leeway in determining isotope pricing.

The Institute of Medicine Panel's Report on Isotopes for Medicine and the Life Sciences (5) took the results of the prior workshop further in developing recommendations for the mission of the NBTF. They included a clear focus on Research and Development for isotope production including target design, separation chemistry and generator development. They recommended that any radiopharmaceutical chemistry research should be conducted with funds resulting from peer review rather than the NBTF operating funds. The formation of a public-private partnership resembling the TRIUMF-Nordion model was encouraged. An advisory panel should assist with the NBTF operations and prioritization.

The IOM panel recommends that the NBTF accelerator have the capacity to accelerate protons to 80 MeV and a minimum of 750 microamperes of current. The panel declined making a recommendation on whether this should be a cyclotron or a linac. These parameters for the accelerator are in line with prior recommendations.

DOE provided us with instructions in the Request for Proposals, additional Guidelines for the Study, and other written and oral communications.

Specific Aims and Guidelines

The RFP for the Project Definition Study outlined four specific aims for the Study.

1. Further refine the design, construction schedule, and cost estimates for the NBTF.

2. Examine the radioactive waste management, disposal, and other environmental issues associated with the NBTF.

3. Develop a business plan for commercial operation of the NBTF over its expected lifetime (including reimbursement to the Government for its construction)

4. Assist DOE in deciding whether or not construction and operation of the NBTF would satisfy current and future radioisotope needs for medical and industrial applications and whether or not such a facility could be operated by the private sector.

The guidelines for the study ask that the report include: a narrative and sketch for a large proton accelerator to produce radioisotopes; narrative and sketch for the radioisotope production facility; preliminary cost estimate for the design and construction of the NBTF; a description of the Federal State and local permitting process; a detailed plan for waste handling; a business plan; a detailed plan of operation; an annual isotope production schedule; and the ability to provide an education and training program in radiochemistry and related topics.

Methodology

The UAB Project Definition Study was performed by a team. The team included members of the UAB faculty and staff, contractors, two advisory committees, and members of the staff at ORNL. Such a large, diverse group provided a lot of information. While we didn't always reach a consensus, all sides were given an opportunity to voice their thoughts and opinions. The contractors as a group met three times with staff from UAB and twice with the advisory committees.

Despite the fact that the bulk of our work was completed before the IOM Panel Report was published, the study's findings were remarkably consistent with their recommendations. Of course, the remarkable consistency of prior studies and workshops likely contributed to the agreement between the UAB Study and the IOM Panel's report.

Individual contractors were responsible for specific parts of the study. In most cases, their final submission is included as an appendix to this study. Abridged versions of their submissions appear here, in part for the sake of brevity and in part because some of their work was necessarily site specific and thus proprietary.

Members of the UAB team made visits to Mallinckrodt Medical in St. Louis, MO, Dupont Merck in Billerica, MA, and TRIUMF in Vancouver, BC. Scheduling problems prevented a visit to Amersham/Medi+Physics in Arlington Heights, IL. These visits gave us the opportunity to tour operating production facilities and to get information from the operations staff about specific issues. Among these issues were cyclotron operation and maintenance, facility layout, material handling in the production process, waste handling, remote target handling, ALARA concerns, and other ESH issues pertinent to the accelerator operations and target processing. We also had the advantage of visiting Mallinckrodt during the installation of their newest cyclotron which gave us the opportunity to discuss detailed issues in cyclotron installation. We scheduled our trip to Vancouver to coincide with a scheduled maintenance shutdown of one of the Nordion cyclotrons. We were able to inspect the cyclotron and to discuss maintenance issues in detail with the staff there.

In generating a business plan, we relied heavily on two previous studies of isotope production. One was an audit of the Isotope Production and Distribution Program performed by Arthur Andersen for the DOE (6). The other was a market survey for the radionuclide market by Hospital Finance Corporation (7). For the sake of economy, we elected to use data which was developed in these reports. We polled members of our advisory panel to determine if any of the historical data or market projections in either of these documents was misleading. In addition, where we could find the data, we would attempt to make some market projections for isotopes that are not routinely produced. In an exercise such as this, it was extremely difficult to make any substantive market projections. With a projected startup in the year 2000, many customers were unable to give us hard market data. In view of the uncertainty of domestic supply in the interim, these customers indicated that alternate suppliers would likely be identified for many of the commercial isotopes on our list. We elected, therefore, to make the most conservative projections on most of these in our income analysis.

C. Equipment Selection

C.1. BASIC APPROACH

The lack of high availability accelerator sources that stand ready to meet the needs of the nuclear medicine research community has given a sense of urgency to proceeding with a National Biomedical Tracer Facility (NBTF). The contribution made by this document to an NBTF Project Definition Study (PDS) is to describe the nature of the equipment needed to meet the NBTF mission.

The major cost driver for all accelerator approaches of practical import for NBTF (refer to Section 3) is the required beam energy. All other factors being equal, the beam energy and thus the accelerator cost is minimized when the charge-to-mass ratio of the accelerated particle is maximized. This occurs for protons, which leads to the selection of a proton accelerator as the method of choice for most neutron-poor isotopes. However, we will identify a subset of the isotopes of interest for NBTF that require an alternative type of accelerator for optimum production.

To a large extent, top-level specifications are driven by the list of isotopes to be produced, the required production rate of such isotopes, and the specifics of the nuclear reactions selected to produce those isotopes. In this section, we identify the isotopes that determine the characteristics of the NBTF.

The Addendum is a compilation of the complete set of (neutron-poor) isotopes used as the starting point for specifying NBTF equipment. For most isotopes, a single candidate target and the associated reaction is listed; in a few cases, more than one target/reaction is included. In all cases, only proton beams have been considered because accelerator economics dictate that the workhorse NBTF accelerator will be a proton machine. In cases in which the candidate reaction listed is known to the authors to have been referred to in published literature as the basis for making the isotope in question, the target and the reaction are shown in ordinary typeface; if not, this data appears in italics. The column "On DOE NBTF List?" refers to the specific list of isotopes in the DOE solicitation for grant requests; that list was actually generated at the NBTF Workshop held in April 1992 at Purdue University. The final column in the table that comprises the Addendum lists the field of medicine and/or research for which the isotope is deemed to hold the most promise.

The column "NBTF Mission Responsiveness" in the table constituting the Addendum describes which of the aspects of the NBTF mission are met by the production of each isotope. Each isotope has been categorized as falling into one of the following five aspects of the NBTF mission:

- **Commercially Viable Now**: isotopes that can be sold through commercial channels and for which demand exceeds supply.
- **Education and Training**: isotopes and/or production processes that are regarded as especially useful in the training of future researchers in nuclear and radiochemistry.
- **Has Been Used in Research**: published literature exists that is indicative of research interest in this isotope.

- **Has Been Used as Tracer**: published literature exists which is indicative of interest in this isotope for use as a tracer.

- **Future Potential**: isotopes about which there is little or no published data but which nevertheless are regarded as having promise for future use in research.

To summarize the role of the various categories of isotopes in the NBTF business plan as presently conceived, revenues from the sale of Commercially Viable Now isotopes are expected to exceed the cost of production, while revenues from the sale of Have Been Used for Research and Have Been Used as Tracers isotopes are expected to cover at least a portion of the cost of production. No revenues will be generated from producing Education and Training isotopes and the conservative assumption is made that the same holds for Future Potential isotopes.

The decision to supply selected Commercially Viable Now isotopes dictates the standards to which the facility must adhere and has important implications for process flow. It is to be emphasized in this regard that the role of NBTF is not to compete with existing isotope suppliers but rather to close specific, sometimes transient, gaps between supply and demand, thus improving the availability of key isotopes to the nuclear medicine community. In particular, the existence of NBTF will provide backup capability to ensure continuity of supply in the event of loss of production capability elsewhere.

The siting, staffing and institutional linkages of the NBTF are driven in large measure by the Education and Training aspects of the mission, as emphasized in the recently issued Institute of Medicine report. The decision to use the NBTF for this purpose has far-reaching consequences for equipment layout and system safety.

Given their particular importance for NBTF facility definition, the Commercially Viable Now and Education and Training isotopes are used as the primary drivers of accelerator requirements. The nuclear data needed to derive the accelerator requirements for these isotopes are listed in Tables 1-1 and 1-2, respectively.

A word is in order regarding the manner in which the nuclear data are presented. The conventional measure of isotope production rate is the activity of the desired product produced per unit beam current on target per unit beam time on target, the standard unit being mCi/μA-hr. This is appropriate for specifying an operational schedule to produce a given number of doses of an approved agent and this will be the way information on the production schedule of the NBTF will be tabulated. However, NBTF is expected to devote a large fraction of beam time to research isotopes, for which dosages and production requirements are not yet defined. Because of the objective of this document is to derive the equipment specifications for the complete set of isotopes, we have chosen to characterize production rate in a form that is directly coupled to those requirements: the current in μA required to produce 1 Ci of the isotope in a time equal to 10% of the half life. If the accelerator current exceeds this value, it will be possible to produce high saturation yields of that isotope. The Institute of Medicine panel went through an equivalent exercise for the more limited list of isotopes for which the desired production can be quantified and reached virtually identical conclusions to those reached in this report.

TABLE 1-1. ACCELERATOR RADIOISOTOPE PRODUCTION REQUIREMENTS: ISOTOPES THAT ARE COMMERCIALLY VIABLE NOW

Iso-tope	Target Nuclide[1]	Proton Reaction[1]	Half Life τ	σ at Given Energy (MeV)	Range[2] in Target	μA to Make 1 Ci in τ/10	Additional Comments
^{22}Na	^{27}Al	p,3p3n	2.6 a	40 mb @ 40	0.8 g/cm^2	130	Now produced by spallation
^{54}Mn	^{56}Fe	p,2pn	312 d	140 mb @ 40	1.1 g/cm^2	50	Need isotopically enriched target;
^{57}Co	^{58}Ni	p,2p	272 d	680 mb @ 28	0.7 g/cm^2	20	Need isotopically enriched target; <0.25% c and ^{58}Co; ^{56}Fe (p,γ) has σ = 4 b @ 3 MeV
	^{60}Ni	p,α		100 mb @ 55	1.5 g/cm^2	40	
	^{57}Fe	p,n		640 mb @ 10	0.1 g/cm^2	150	
^{58}Co	^{60}Ni	p,2pn	70.9 d	170 mb @ 41	1.1 g/cm^2	25	Need isotopically enriched target; possible γ interference for PET
	^{58}Fe	p,n		870 mb @ 11	0.1 g/cm^2	100	
^{67}Ga	^{68}Zn	p,2n	78.3 h	580 mb @ 22	0.4 g/cm^2	50	Need isotopically enriched target
^{68}Ge	^{69}Ga	p,2n	271 d	560 mb @ 20	0.3 g/cm^2	60	Demand > LANL + BNL capacity; major revenue source (125/mCi)
^{81}Rb via ^{81}Sr	^{85}Rb	p,5n + β-decay	4.58 h	20 mb @ 62	2.0 g/cm^2	300	Need isotopically enriched target; also made by ^{79}Br(α,2n) and by Kr (gas target)
^{83}Rb via ^{81}Sr	^{85}Rb	p,3n + β-decay	86.2 d	400 mb @ 38	1.2 g/cm^2	30	Also made by ^{83}Kr(p.n) (gas target)

TABLE 1-1. ACCELERATOR RADIOISOTOPE PRODUCTION REQUIREMENTS: ISOTOPES THAT ARE COMMERCIALLY VIABLE NOW (continued)

Iso-tope	Target Nuclide[1]	Proton Reaction[1]	Half Life τ	σ at Given Energy (MeV)	Range[2] in Target	μA to Make 1 Ci in τ/10	Additional Comments
^{82}Sr	^{85}Rb	p, 4n	25.6 d	240 mb @ 50	1.6 g/cm^2	40	Need isotopically enriched target; ; demand > LANL + BNL capacity; major revenue source ($82/mCi)
^{85}Sr	^{85}Rb	p,n	64.8 d	260 mb @ 10	0.1 g/cm^2	500	Also made by ^{85}Rb(d,2n)
^{103}Pd	^{103}Rh	p,n	17.0 d	700 mb @ 10	0.1 g/cm^2	200	Method used by Theragenics
^{109}Cd	^{109}*Ag*	*p,n*	462 d	320 mb @ 10	0.1 g/cm^2	400	Now produced by spallation
^{111}In	^{112}Cd	p,2n	2.81 d	900 mb @ 25	0.6 g/cm^2	30	Need isotopically enriched target
	^{111}Cd	p,n		500 mb @ 10	0.1 g/cm^2	300	
^{123}I via Xe	^{124}Xe	p,2n + β-decays	13.1 h	700 mb @ 28	NA (gas target)	30	Gas target. Need isotopically enriched target. No ^{124}I
	^{127}I	p,2n + β-decay		280 mb @ 62	2.4 g/cm^2	40	No ^{124}I
^{125}I	^{126}Te	p,2n	59.9 d	est. 1000 mb @ 20	0.4 g/cm^2	est. 50	Need isotopically enriched target; no data < 300 MeV
^{127}Xe	^{133}Cs	p,2p5n	36.4 d	TBD	TBD	TBD	Demand > LANL + BNL capacity
	^{127}Xe	p,n		170 mb @ 12	0.2 g/cm^2	60	

TABLE 1-1. ACCELERATOR RADIOISOTOPE PRODUCTION REQUIREMENTS: ISOTOPES THAT ARE COMMERCIALLY VIABLE NOW (continued)

Iso-tope	Target Nuclide[1]	Proton Reaction[1]	Half Life τ	σ at Given Energy (MeV)	Range[2] in Target	μA to Make 1 Ci in τ/10	Additional comments
^{178}W	^{181}Ta	p,4n	21.5 d	740 mb @ 38	1.8 g/cm^2	25	
^{195}Au	^{195}*Pt*	*p,n*	186 d	TBD	TBD	TBD	Need isotopically enriched target
^{201}Tl via ^{201}Pb	^{203}Tl	p,3n + β-decay	28.1 h	1100 mb @ 30	1.2 g/cm^2	25	Need isotopically enriched target

1 Reactions shown in normal type have are referred to in open literature; those in italics are hypothesized reactions.

2 Target density times the target thickness needed to attenuate beam by 8 MeV or 20% of the energy, whichever is smaller.

TABLE 1-2. ACCELERATOR RADIOISOTOPE PRODUCTION REQUIREMENTS: ISOTOPES USEFUL FOR EDUCATION AND TRAINING

Iso-tope	Target Nuclide[1]	Proton Reaction[1]	Half Life τ	σ at Given Energy (MeV)	Range[2] in Target	μA to Make 1 Ci in τ/10	Additional Comments
^{11}C	^{14}N	p,α	20.3 m	100 mb @ 15	<0.1 g/cm^2	250	Gas target
^{13}N	^{16}O	p,α	9.97 m	30 mb @ 12	<0.1 g/cm^2	1200	Gas target
^{15}O	^{19}F	p,αn	122 s	TBD	<0.1 g/cm^2	TBD	Gas target
^{18}F	^{18}O	p,n	110 m	40 mb @ 14	<0.1 g/cm^2	700	Need isotopically enriched target; also $^{16}O(\alpha,2n)$, $^{20}Ne(d,\alpha)$
^{77}Br	^{78}Se	p,2n	57.0 h	840 mb @ 21	0.4 g/cm^2	40	Need isotopically enriched target; also made by Kr (gas target) and by d an α beams
^{124}I	^{124}Te	p,n	4.17 d	520 mb @ 12	0.2 g/cm^2	200	Need isotopically enriched target; possible γ interference for PET
^{125}I	*^{126}Te*	*p,2n*	59.9 d	est. 1000 mb @ 21	0.4 g/cm^2	est. 40	Need isotopically enriched target; no data < 300 MeV

1 Reactions shown in normal type have are referred to in open literature; those in italics are hypothesized reactions.

2 Target density times the target thickness needed to attenuate beam by 8 MeV or 20% of the energy, whichever is smaller.

TABLE 2-1
PRODUCTION RATES OF ISOTOPES THAT
ARE COMMERCIALLY VIABLE NOW

Iso-tope	Proton Reaction[1]	Half Life τ	Production rate in mCi/μA–h @ E(MeV)	Additional Comments
^{22}Na	^{27}Al(p,3p3n)	2.6 a	0.003 @ 40	Now produced by spallation
^{54}Mn	^{56}Fe(p,2pn)	312 d	0.03 @ 40	Isotopically enriched target; also made by reactor (n,γ)
^{57}Co	^{58}Ni(p,2p)	272 d	0.08 @ 28	Isotopically enriched targets
	^{60}Ni(p,α)		0.04 @ 55	
	^{57}Fe(p,n)		0.01 @ 10	
^{58}Co	^{60}Ni(p,2pn)	70.9 d	0.1 @ 41	Isotopically enriched targets
	^{58}Fe(p,n)		0.06 @ 11	
^{67}Ga	^{68}Zn(p,2n)	78.3 h	3 @ 22	Isotopically enriched target
^{68}Ge	^{69}Ga(p,2n)	271 d	0.03 @ 20	Major potential revenue source
^{81}Rb via ^{81}Sr	^{85}Rb(p,5n) + β-decay	4.58 h	7 @ 62	Isotopically enriched target; also made by ^{79}Br(α,2n) and by Kr (gas target)
^{83}Rb via ^{83}Sr	^{85}Rb(p,3n) + β-decay	86.2 d	0.2 @ 38	Also made by ^{83}Kr(p,n) (gas target)
^{82}Sr	^{85}Rb(p,4n)	25.6 d	0.04 @ 50	Isotopically enriched target; major potential revenue source
^{85}Sr	^{85}Rb(p,n)	64.8 d	0.01 @ 10	Also made by ^{85}Rb(d,2n)
^{103}Pd	^{103}Rh(p,n)	17.0 d	0.01 @ 10	Method used by Theragenics
^{109}Cd	^{115}In(p,2p5n)	462 d	TBD[2]	Now produced by spallation and by ^{109}Ag(d,2n)
^{111}In	^{112}Cd(p,2n)	2.81 d	5 @ 25	Isotopically enriched targets
	^{111}Cd(p,n)		0.5 @ 10	

TABLE 2-1
PRODUCTION RATES OF ISOTOPES THAT ARE COMMERCIALLY VIABLE NOW (continued)

Isotope	Proton Reaction[1]	Half Life τ	Production Rate in mCi/μA-h @ E(MeV)	Additional Comments
^{123}I via ^{123}Xe	^{124}Xe(p,2n) + two β-decays	13.1 h	30 @ 28	Isotopically enriched (gas) target
	^{127}I(p,5n) + β-decay		20 @ 62	
^{125}I	*^{126}Te(p,2n)*	59.9 d	TBD	Isotopically enriched target
^{127}Xe	^{133}Cs(p,2p5n)	36.4 d	TBD[2]	Demand > LANL + BNL capacity
	^{127}I(p,n)		0.02 @ 12	
^{178}W	^{181}Ta(p,4n)	21.5 d	0.8 @ 38	
^{195}Au	*^{195}Pt(p,n)*	186 d	TBD	Isotopically enriched target
^{201}TI via ^{201}Pb	^{203}TI(p,3n) + β-decay	73 h	5 @ 30	Isotopically enriched target

[1] Reactions shown in normal type have been referred to in the literature; those in italics are hypothesized reactions.

[2] Data not found at proton energies on target of interest for NBTF.

The result of the accelerator requirements analysis, the subject of Section C.2, is that an accelerator which can produce the Commercially Viable Now and the Education and Training isotopes is adequate for virtually all isotopes listed in the Addendum. Thus a facility designed in this fashion will satisfy the research aspects of the NBTF mission as well. The only isotope of interest that we have identified which cannot be produced in this manner is ^{211}At (and its parent ^{211}Rn). There are no practical proton-based reactions for this isotope and an alternative accelerator must be considered; this issue is dealt with in Section C.2.4.

A specific subset of the list of isotopes must be identified to define the types of targets required and to optimize the disposition of target caves about the accelerator. The isotopes that we have used a guidance to this process fall into three categories:

- **The conventional PET isotopes:** ^{11}C, ^{13}N, ^{15}O, and ^{18}F, which are viewed as essential to the Education and Training mission

- **Important commercial isotopes for which demand presently exceeds supply:** ^{22}Na, ^{57}Co, ^{82}Sr, ^{123}Xe, (^{123}I)and ^{201}Tl.

- **High potential research isotopes with low current availability:** ^{77}Br, ^{122}Xe and ^{211}At.

The reactions involved in producing these isotopes span a large range of threshold energies and cross sections, as well as encompassing a variety of target types and production isotopes half lives. In this sense they provide a thorough test of NBTF capabilities. The implications of these particular processes for facility layout are discussed in Section C.4.3.

C.2. ACCELERATOR OPERATING PARAMETERS

The key accelerator operating parameters of interest are the peak energy, the range and precision of energy control, and the maximum time-averaged current. These are discussed in Sections C.2.1, C.2.2 and C.2.3, respectively, in the context of the proton-induced reactions tabulated in the Addendum. Section C.2.4 summarizes the findings and points out how a lower energy, lower current alpha particle accelerator complements the higher energy, higher current proton accelerator.

C.2.1. PEAK ENERGY

At a minimum, the accelerator energy must exceed the energy threshold for all the reactions of interest. A good estimate of the energy required for a particular nuclear reaction can be derived from quite general considerations. The type of reactions most useful for isotope production via proton bombardment are those which produce only neutrons in addition to the reaction product. A reaction in which x neutrons is produced (x = 1, 2, ...) is referred to by the expression (p,xn). Such a reaction may be represented by

$$p + {}^{A}_{Z}T \rightarrow {}^{A-x+1}_{Z+1}R + xn,$$

where T is the target nucleus, R is the reaction product, the superscripts refer to the atomic weight and the subscripts refer to the atomic number. In the following, we adhere to the standard convention and describe such a reaction by the shorthand form

$$^{A}T(\,p,xn)^{A-x+1}R.$$

In this expression, the subscripts have been dropped because the target (T) and reaction product (R) designators uniquely define the atomic number.

The threshold energy for any nuclear reaction can be written as

$$E_{min} = -Q^{\circ} F_{KE},$$

where Q is the difference between the rest energy of the target nucleus and the total rest energy of all the particles produced in the reaction and F_{KE} is a kinematic factor. For all reactions of interest ($m_T \gg m_p$) a satisfactory estimate of the threshold for the reaction can be obtained by setting F_{KE} = 1, in which case the threshold energy is simply equal to -Q.

From the definition of Q, the threshold energy can be expressed in terms of the proton-neutron mass difference and the difference in binding energy between the target and reaction nuclei. Because the target and reaction nuclei have similar atomic weight and atomic number, they have comparable binding energy per nucleon, implying that the following is a reasonable approximation:

$$Q.xm_n - m_p - (x-1)\text{amu} = x \cong 1.008982\text{amu} - 1.007593\text{amu} - (x-1)\text{amu}$$

$$= 0.0014\text{amu} + (x-1) \cong 0.00892\text{amu} = 1.3\text{MeV} + (x-1) \cong 8.4\text{MeV}.$$

Thus the threshold energy for a (p,xn) reaction is approximately equal to the sum of the p-n mass difference and (x-1) times the average binding energy per nucleon. The (p,xn) reactions with the highest threshold energy are the ones with the largest x, such as ^{133}Cs(p,6n)^{126}Ba. The arithmetic above leads to an expectation of a threshold energy of approximately 50 MeV for such a process. The actual value is several MeV less than this because nucleons are somewhat less tightly bound in a highly neutron deficient isotope such as ^{126}Ba.

The threshold energy for each of the reactions tabulated in the Addendum has been estimated and experimental data has been sought out for those reactions with the highest predicted threshold energies. Among all the isotopes listed, the highest threshold energy is 48 MeV, which occurs for two reactions:

$^{127}I(p,6n)\,^{122}Xe$ and $^{133}Cs(p,2p,5n)\,^{127}Xe$

In general, the cross section increases rapidly with energy above threshold (phase space factor) but depends less sensitively on energy for energies more than about 10 MeV above threshold. Figure 2-1, which displays theoretical estimates of the cross sections of the $^{127}I(p,xn)$ reactions, is illustrative of the typical case. Successive peaks arise for x = 1, 2, 3, ... as the energy increases. To a first approximation, the curves are all the same, except that they are shifted in energy by an amount of order the average binding energy per nucleon. It is often desirable to keep the energy below the value for a significant reaction rate for the reaction in which one additional neutron is produced, because the production of an additional isotope may degrade the isotopic purity of the desired end product. If that reaction presents a contamination problem, the maximum yield at high purity will be achieved by choosing the energy near this threshold and choosing a target thickness that degrades the energy by an amount that approximates the 8-10 MeV gap between the two thresholds.

Adding margin of 8-10 MeV for both the phase space factor and the energy degradation in the target to the 48 MeV maximum threshold energy yields the conclusion that a 65-70 MeV beam can produce all the isotopes listed. Degradation of beam energy by passage through well-designed windows and through a beam transport system with an adequate vacuum adds typically 1-5 MeV, with the smaller values being applicable to higher energies. It is concluded that 70 MeV is an appropriate choice for the maximum accelerator energy.

This choice of 70 MeV is to be compared with the 80 MeV figure called out in the Institute of Medicine report. Of all the reactions identified in the Addendum, only two would benefit from operation above 70 MeV: $^{133}Cs(p,2p5n)^{127}Xe$ and $^{133}Cs(p,6n)^{128}Ba$. In both cases, the advantage is merely a modest gain in the specific activity achievable. Because we judge this gain not to be worth the extra cost involved in the accelerator and shielding, we choose to limit the energy to 70 MeV.

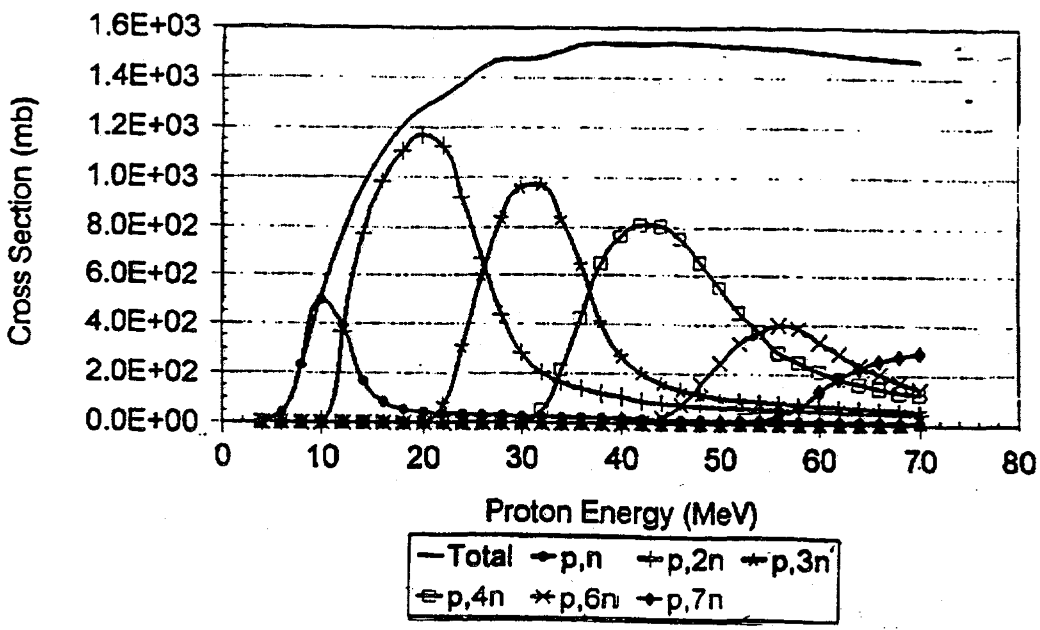


Fig. 2-1 Cross sections for (p,xn) reactions on ^{127}I

C.2.2. ENERGY CONTROL RANGE

The total yield has much stronger dependence on energy than does the cross section because of the relatively narrow operating range for acceptable radionuclidic purity. This places a premium on the control of accelerator energy. To demonstrate this consider the reaction $^{127}I(p,5n)^{123}Xe$, for which the cross section data are shown in Figure 2-1. Together with the positron decay of ^{123}Xe, this reaction is one method to produce ^{123}I, a very promising isotope for imaging. However, the isotope is of practical use only if contamination by other iodine isotopes is limited. The practical window in beam energy on target for producing high purity ^{123}I is approximately 50 to 60 MeV. Below 50 MeV, the cross section drops rapidly while above 60 MeV, the (p,7n) reaction and subsequent decay of ^{121}Xe produces ^{121}I, which inhibits the medical utility of ^{123}I. It follows that the highest yield at acceptable purity occurs for an incoming beam of about 60 MeV. There will inevitably be a penalty in yield or purity if the accelerator energy cannot be tuned to the optimal energy. Operation at 58 Mev, for example, entails a sacrifice of more that 25% in yield, a figure that is obtained by comparing the integral of the (p,5n) cross section curve from 58 to 50 MeV to that from 60 to 50 MeV. Such a penalty can be directly translated into figures of merit for facility productivity.

Because of this sensitivity, we specify an energy selectivity (reproducible energy control setting) as tight as allowed with straightforward accelerator technology: ±1.5 MeV. Because the optimal choices of energy for reactions of interest span essentially the complete range from 10 to 70 MeV, it is necessary to be able to extract beam with precision of 1.5 MeV or better over that entire energy range. For the same reason, we also specify that the energy spread in the beam emerging from the accelerator does not exceed 1.5 MeV. We also recommend that the reproducibility will be within 1 % or less.

For a substantial number of the Future Potential isotopes, the existing nuclear data base is inadequate to support an informed production plan. Hence the need will arise to make cross section measurements of potentially useful reactions about which little is known. Fine control over the energy is essential for this purpose. The 1.5 MeV or better precision specified above is acceptable to obtain the type of nuclear data needed to render informed judgements regarding potential isotope production scenarios.

C.2.3. CURRENT

Increased beam current yields more product per unit time, thus improving the overall economics of the facility. In addition, increased beam current permits obtaining higher specific activity, which adds to the utility of the product. On the other hand, higher beam current makes target design increasingly complex.

Typical PET facilities operate with tens of microamperes of beam current. Isotope production accelerators at radiopharmaceutical manufacturers operate in the 200-500 μA range and usually support production of only one isotope at any given time. The currents achievable in NBTF should be higher because of the desire to split the beam to irradiate more than one target at a time and because of the requirement to make use of some reactions with comparatively low cross sections. There is no single reaction that drives the choice of current so one must examine a range of isotope production requirements in order to make an informed estimate. The nuclear data in Tables 1-1 and 1-2 have been tabulated in a form that is tailored to this need. In particular, data are provided on the number of microamperes of current on target required to produce one Curie of each isotope in one-tenth of the product isotope half life, a criterion that is used to ensure that high specific activity can be achieved. All of the Commercially Viable Now isotopes (refer to Table 1-1) meet this criterion if the current is 1 mA. Specific activity is less of an issue in the Education and Training isotopes (refer to Table 1-2) but all except ^{13}N also have this property. Hence we select

1 mA as a tentative value for the NBTF current. It is worth noting that none of the high energy reactions require more than 500 μA, in part because the increased range improves the production rate. One important implication for NBTF is that no target need be designed for the full power of the beam.

Specifying a current significantly above 1 mA is inadvisable because target heating becomes a major engineering issue. For example, stopping a 40 MeV, 1 mA proton beam in a copper target corresponds to a power density of order 100 kW/cm^3 unless the beam is expanded to greater than 1 cm in diameter. It is possible to cool such a target but higher power would lead to major engineering challenges in the target cooling and/or the beam transport equipment. It is worth noting in this regard that one commercial facility (Theragenics) operates 24 hours per day using internal targets with power densities and currents comparable to those required in NBTF. Many years of isotope production using the ORNL 86" cyclotron have provided additional confidence in operation in the 1 mA range.

C.2.4. SUMMARY RECOMMENDATION

Based upon the analyses described in Sections C.2.1 through C.2.3, the recommended accelerator parameters are as listed below:

Extracted particle:	proton
Energy range:	10 - 70 MeV
Energy selectivity:	Reproducible steps of ≤1.5 MeV steps over full range
Current:	1mA

These recommendations were reviewed and approved by the NBTF Advisory Committee. Exception was taken by a small minority of this group regarding limiting the energy to 70 MeV but it was generally felt that little was to be gained by an increase to the 100 MeV level.

One important caveat must be mentioned with regard to this selection: the inability of such an accelerator to make ^{211}At or its parent ^{211}Rn. This is a major shortcoming because of the promise exhibited by ^{211}At for radiotherapy. The absence of appropriate stable targets makes it impractical to produce isotopes of astatine by any of the normal proton reactions such as (p,xn), (p,αxn) or (p,xnyp). Proton accelerators of several hundred MeV energy have succeeded in producing ^{211}At via $^{232}Th(p,3\alpha 10n)$, but only with poor radionuclidic purity.

This shortcoming of an NBTF based upon a 70 MeV proton accelerator can be overcome by adding a moderate energy alpha particle accelerator. The reaction $^{209}Bi(\alpha,2n)^{211}At$ has a 900 mb cross section at 30 MeV, allowing a production rate of approximately 8 mCi/μA-hr. Table 2-1 lists a number of (α,n) and (α, 2n) reactions with cross sections in the 10-30 MeV range approaching 1 barn that provide sensible alternatives to the proton reactions baselined. A 30 Mev alpha particle (^4He) accelerator will be adequate for this purpose.

An alternative approach to ^{211}At production is to use a lithium beam on a bismuth target. The helium beam involves more straightforward accelerator technology and also gives rise to the other promising reactions called out in Table 3-1. In addition, a ^4He machine can be configured to operate with deuteron or ^3He beams, providing further flexibility to the facility. For these reasons, we advocate the addition of a second accelerator: a 30 MeV ^4He machine. The current is tentatively specified at 100 μA, recognizing the difficulty of obtaining a high current He^{++} ion source.

In addition to complementing the weaknesses of the proton accelerator for commercial and research isotope production, the ^{4}He accelerator will improve the Education and Training aspects of the NBTF. For example, it will allow working with internal and external targets with fluxes typical of PET centers and industrial isotope production sites. It also allows working with ^{18}F, a common PET isotope, without the added expense entailed with the use of the ^{18}O-enriched targets needed in a proton accelerator (refer to Table 3-1).

TABLE 3-1
REPRESENTATIVE REACTIONS
ACHIEVABLE WITH A LOWER ENERGY ^{4}He ACCELERATOR

Isotope Desired	Reaction with p Beam	Alternative with α Beam	Potential Impact of Changing from p to α Beam	
			Reaction Rate[1]	Target
^{18}F	$^{18}O(\alpha, pn)$	$^{16}O(\alpha,pn)$		No isotopic tailoring
^{22}Na	$^{27}Al(p,3p3n)$	$^{19}F(\alpha,n)$	Higher σ, lower energy	
^{54}Mn	$^{54}Cr(p,n)$	$^{51}V(\alpha,n)$		No isotopic tailoring
^{58}Co	$^{60}Ni(p,2pn)$	$^{55}Mn(\alpha,n)$	Higher σ	No isotopic tailoring
	$^{57}Fe(p,n)$			
^{81}Rb	$^{85}Rb(p,5n)$ + β-decay	$^{79}Br(a,2n)$	Much higher σ, lower energy	
^{211}At	no practical reaction	$^{209}Bi(\alpha,2n)$	p beam not practical, α beam practical	

C.3. SELECTION OF ACCELERATOR TYPE

Among proton accelerators, the highest energies have been achieved in synchrotrons, but such machines are limited in average current to much less than 1 mA. Currents of many amperes have been achieved in electrostatic accelerators, but these devices are limited to much less than 70 MeV. Just two types of proton accelerators have been shown to be capable of meeting both the energy and current requirements of the NBTF: the cyclotron and the radio frequency linear accelerator (linac).

The selection of accelerator type thus reduces to a comparison of the advantages and disadvantages of these two options. Table 4-1 summarizes seven major points of comparison; the subsections that follow deal with these points one at a time.

C.3.1. RISK OF SHORTFALL IN TOP LEVEL OPERATING PARAMETERS

Figure 3-1 illustrates the operating regimes achieved in cyclotrons around the world; industry has supplied the cyclotrons for those entries in boldface type. With the exception of the 235 MeV proton therapy facility now under construction at Massachusetts General Hospital, all the high energy cyclotrons have been national laboratory or university built machines. There are multiple industrial suppliers of cyclotrons for both position emission tomography (PET) and isotope production applications (refer to Section C.5). The PET machines range in energy up to 18 MeV and in current up to about 80 μA. Isotope production facilities have been built for energies up to 70 MeV but most are in the 15-30 MeV range. Many of the older facilities are limited to operation at 100 μA or less, but the more modern H^--based machines operate with external beams at currents of several hundred microamperes. Such H^- cyclotrons dominate the market for radioisotope production equipment today. On trips taken to the leading suppliers of neutron-poor radioisotopes in the United States and Canada, we observed operation at specification of 30 MeV H^- cyclotron made by two different manufacturers.

The issues involved in extending industrial cyclotron technology to the energy needed in NBTF largely decouple from the issues associated with increasing the current. None of the issues are viewed as high risk. One major cyclotron manufacturer is now building a 235 MeV, low current machine and has built two H+ cyclotrons used for isotope production continuously at currents above 1 mA. Two cyclotron manufacturers have demonstrated 1 mA H^- operation in factory tests; both are considering offering this capability in their next generation product lines. Industry is thus clearly in a position to supply a 70 MeV, 1 mA H^- cyclotron engineered to allow convenient integration into an isotope production environment.

Ion linac technology has advanced in recent years through initiatives to use high brightness accelerator beams for strategic defense. This has led to more compact, reliable and energy efficient low energy machines. Of particular interest in this regard is Radio Frequency Quadruple (RFQ) technology, which greatly simplifies the first few MeV of a high current linac. These defense initiatives have also led to transitioning from national laboratories to industry some of the know-how required to produce the type of high performance accelerating structures and RF systems that dominate linac costs.

Both the NBTF energy and current requirements are well within the linac state-of-the-art and at least two firm fixed price bids can be expected in response to a 70 MeV, 1 mA linac solicitation. There is, however, considerably less operational experience with proton linacs than with cyclotrons in an industrial/production capacity. This conclusion is supported by Figure 3-2, which displays the range of proton (and deuteron) linac operating parameters achieved to date.

TABLE 4-1
CYCLOTRON/LINAC COMPARISON SUMMARY

Basis of Comparison	Synchronous Cyclotron	Radio Frequency Linear Accelerator	Preferred Option
Risk of shortfall in top-level operating parameters	• Energy and current achievable • Considerable representative operating experience in industry	• Energy and current achievable • Representative operational experience, but only in national labs	Small edge to Cyclotron
Versatility to support diverse production objectives	• Continuous energy variability • Simultaneous extraction at virtually any combination of energies	• Rapidly switched extraction at several preset (discrete) energies • Gaps in energy filled by degrader	Major edge to Cyclotron
Availability/reliability to support aggressive production schedule	• Simple structure with low part count • Good experience in industry for process applications	• More complex; higher part count • Target heating a bigger issue • Promising, but data is limited	Cyclotron
Environmental, safety and health issues	• H^- machines a major improvement • Target area dominates	• Negligible activation • Target area dominates	No clear preference
Capital cost of accelerator and related support equipment	• Dominated by accelerator structure • Costs traceable to existing industrially supplied machines	• Accelerator structure and rf equipment comparable cost • Traceable to existing equipment	No clear preference
O&M costs of accelerator and related support equipment	• Proven control system used in comparable applications • Strong component supplier base	• Technology compatible with high efficiency, automated operation • RF system a concern	Cyclotron
Facility costs correlated to accelerator choice	• Considerable flexibility in layout options • Compact footprint but high ceiling	• Minimal remote maintenance • Large (long) accelerator building • Building height can be less	No clear preference

With the exception of the Los Alamos Meson Production Facility (LAMPF), the machines listed in Fig. 3-2 with energy above 25 MeV are injectors for high energy accelerators. Industrial experience does not extend to either the energy or the current required for NBTF. In fact, it is clear by inspection of Figs. 3-1 and 3-2 that industrial experience is far greater for cyclotrons.

Neutron-rich isotopes are also very important to the nuclear medicine community. In most cases, neutron-rich isotopes are more cost-effectively produced by fission reactors. In our judgement, the additional licensing and ES&H issues accompanying the use of a reactor make inclusion of a reactor in the NBTF facility unwise. However, because accelerators can also produce neutron-rich isotopes, some consideration was given to the three techniques listed below, which are regarded as the most promising such methods.

- Fragmentation of target nuclei (usually of high Z targets such as ^{232}Th) via proton bombardment.

- Spallation neutron sources arising from bombardment of (generally high Z) targets by high energy protons, used either for (n,γ) reactions or to produce fission isotopes in a subcritical assembly.

- Stripping neutron sources resulting from proton bombardment of stable light nuclei (such as ^{7}Li or ^{9}Be) having more neutrons than protons; such sources may be appropriate for isotope production via (n,γ) reactions,

Any or all of these techniques could be implemented within the NBTF, but there are strong arguments against doing so. The fragmentation reactions are characterized by such poor isotopic purity that they are not a good standard for use in research. Both the fragmentation and spallation approaches require proton energies considerably higher than that needed for any of the neutron-poor isotopes of interest. As evidence of this, consider the fact that spallation reactions produce less than one neutron per incoming proton for all energies below 150 MeV, establishing this as a practical lower limit for the accelerator energy, and contrast this with the observation that virtually all accelerator-based isotope production facilities operate at 30 MeV or less.

The additional costs and facility complications caused by building in such capability is not balanced by a corresponding increase in productivity, given the availability of reactors to accomplish these tasks. With regard to the third option listed above, there is considerable interest in the development of proton accelerator-based secondary neutron sources for neutron capture therapy. Pushing the accelerator and target technology to the present state-of-the-art yields neutron fluxes which are still a factor of 1000 less than those achievable in existing test reactors. Hence, this approach is not justifiable in the context of the NBTF. The recently issued Institute of Medicine report "Isotopes for Medicine and the Life Sciences" also reaches the conclusion that such techniques, which have not been proven to be competitive with reactor sources, should not be funded in an NBTF.

Summary The risks of performance shortfalls are small with either type of accelerator. The extensive experience with cyclotrons for comparable applications provides further risk reduction for the cyclotron approach.

Energy	< 10 μA	10 - 100 μA	100 - 1000 μA	> 1000 μA
> 100 MeV	Indiana; **MGH (planned)**; CIBA		TRIUMF	PSI
50 - 100 MeV	UC Davis		Michigan State; **Medi-Physics**	PSI
25 - 50 MeV	Neutron therapy facilities	**Many isotope production facilities**	**Many isotope production facilities**	
12 - 25 MeV		**Many PET and isotope production facilities**	**Many isotope production facilities**	ORNL; **Thera-genics**
< 12 MeV		**Many PET facilities**		

Time averaged current

Fig. 3-1. Operating parameters of existing or previously operated proton or deuteron cyclotrons. Boldface entries correspond to industry-supplied machines.

C.3.2. VERSATILITY TO SUPPORT DIVERSE PRODUCTION OBJECTIVES

To support the large diversity of NBTF production requirements, it is important to be able to irradiate more than one target at a time. This can be accomplished in some instances by stacking targets, but this approach entails additional target cooling problems and increased energy spread in the beam delivered to the targets lower in the stack. The preferred approach is to deliver beam at a range of energies and currents to multiple target vaults simultaneously. Multiple beam operation is accomplished in quite different ways in cyclotrons and linacs. The current can be varied continuously in a linac and beam splitters can be designed to deliver prescribed fractions of the total current to the target caves desired. Energy variation is less flexible in a linac because the fundamental quantity is the energy gain per linac accelerating section, which is typically in the 10 to 20 MeV range. Unless complex and expensive RF control techniques are implemented, the only energy variability comes from deactivating individual sections, so the steps available are only 10-20 MeV. One way of supporting target stations at multiple energies is by activating switching magnets situated between linac accelerating sections.

	< 10 μA	10 - 100 μA	100 - 1000 μA	> 1000 μA
> 100 MeV		BLIP; IPNS	Fermilab; BLIP (1995)	LAMPF
50 - 100 MeV	Serpukov; CERN; Rutherford; Fermilab			
25 - 50 MeV		Argonne		
12 - 25 MeV	Neutron therapy facilities			
< 12 MeV			**Industry RFQs**	National lab RFQs

Time averaged current

Fig. 3-2. Operating parameters of existing or previously operated proton or deuteron RF linacs. Boldface entries correspond to industry-supplied machines.

For example, a proposal made by the Superconducting SuperCollider group for a proposed isotope production application involves extraction at 30 MeV, 50 MeV and 70 MeV. Although not strictly speaking simultaneous, sufficiently frequent switching (e.g., 1 kHz or higher) will have the same effect as continuous target bombardment.

Extraction in a negative ion cyclotron is normally accomplished by passing the beam through a thin carbon foil that changes the beam from H^- to H^+, whereupon the magnetic field bends the beam outward through openings in the magnet yoke to the beam transport system. With a well-designed extraction system, more than 99% of the circulating beam can be captured by the transport system. This can be accomplished at any energy up to full energy. Extraction at multiple energies is accomplished by the use of a wire grid instead of a foil. Such a device will function identically to a foil but will ~~only~~ kick out those beam particles that strike the grid; particles not intersecting the grid will continue to be accelerated to higher energy. This procedure allows the extraction of several beams of various energies. No beam splitters are required to meet the requirements of supporting a range of energies and currents in the various caves. Stable, repeatable operation with two beamlines at two different energies is routinely achieved in 30 MeV H^- machines now in operation. Extension to as many as four independently controllable extracted beams is possible but achieving stable repeatable operation is a major challenge.

Perhaps the strongest discriminator between linacs and cyclotrons for NBTF is the nearly continuously variable nature of the energy available in a cyclotron compared to the discrete set of energies available from a linac. As discussed in Section C.2.2, yield optimization sets a ≤1.5 MeV specification on the energy steps and the large number of reactions in effect makes this a requirement over the full range of energies. The limit on energy variability in a cyclotron is the energy gain per turn, which is typically several hundred keV. In practice, there is some overlap in particle orbits in H^- cyclotrons, so the typical energy spread in an extracted beam is about 1 MeV. In contrast, conventional linacs can meet this requirement only with the use of degraders, which are absorbing media placed in the beam path. Degraders can be integral to a target design but the resultant "thick" targets are more difficult to process and the additional heat (and activation) brought about by the energy deposited in the high energy end of the target adds engineering complexity. The use of degraders also introduces a non-negligible energy spread. For example, obtaining a 50 MeV beam on target by degrading a 70 MeV beam adds approximately 2 MeV to the energy spread in the beam. An alternative approach is to use an energy analyzer (a bend in the transport system that selects a narrow energy spectrum). Unfortunately, the combination of degraders and energy analyzers adds considerable cost to the beam transport system, adds complexity to the operating system, increases the amount of local shielding required and, most importantly for an isotope production facility, reduces the flux on the target by a large factor.

Summary The continuous energy variability makes cyclotrons the clear preference over linacs for supporting a broad experimental agenda.

C.3.3. AVAILABILITY/RELIABILITY TO SUPPORT AGGRESSIVE PRODUCTION SCHEDULES

Cyclotrons have demonstrated high reliability in commercial isotope production facilities. A few such units operate in an entirely unmanned fashion. In other installations, such as the Dupont-Merck facility in Billerica, MA, skeleton crews (4 people) operate as many as six cyclotrons simultaneously. Construction of a cyclotron entails complex manufacturing tasks but the net result is hardware with few highly stressed components and essentially no moving parts. Historically, the downside of cyclotron maintenance has been the need to wait for a cooldown period of perhaps 24 hours prior to undertaking any lengthy hands-on tasks. This situation has changed for the better with the switch to negative ion acceleration. Routine maintenance on H^- cyclotrons can be undertaken with a minimal cooldown period. The supporting equipment is all available from multiple suppliers and exhibits long life. The RF power equipment, a prime source of down time in accelerators, is less of a problem in cyclotrons because the units required can take advantage of the commercial developments in radio transmitter equipment.

There is comparatively little experience in industrial proton linac operation. However, lower energy electron linacs, which exhibit a number of the same engineering features as proton linacs, are in use in more than 1000 medical facilities in the United States. The greatest concern about reliability in an NBTF proton linac is the need for multiple (perhaps as many as 50) tube-based RF power sources. The loss of any one unit will lead to down time. Fortunately, the RF equipment in question will be located in an area with a negligible radiation field.

The ion sources for both types of accelerators contain components (filaments) of comparatively short operational life (typically hundreds of hours). Replacement is simpler in a linac but can be accomplished in both types of accelerators as a part of routine preventative maintenance. Some facilities, such as the TR30 installation at TRIUMF, maintain complete spare ion sources, allowing filament replacement to be performed off-line. In general, the linac will require more preventative maintenance because of the larger part count associated with the large number of accelerating cavities.

Stripper foils used to remove the electrons from the H^- particles are a special problem for cyclotrons. Their operational life is usually less than that of an ion source so mechanisms have been devised to change foils automatically. However, these mechanisms have not demonstrated good reliability. Fortunately, a changeout can be accomplished manually in a few minutes if sufficiently reliable automated techniques cannot be implemented. Indeed, the current generation of H^- cyclotrons utilize stripper support structures that permit complete changeout of a stripper without breaking vacuum.

Because of the high level of activation and the associated difficulty in performing maintenance, the target areas are expected to be a greater source of facility productivity loss than problems with the accelerator. The use of largely redundant, multiple target caves will ameliorate this problem. Linacs can be expected to experience more frequent target-related problems because of the added energy dissipation associated with the use of degraders.

Summary Acceptable availability and reliability will be achievable in either a cyclotron-based NBTF or a linac-based NBTF. Because of their simpler operational nature and the greater industrial experience, it will be easier to achieve this objective with a cyclotron.

C.3.4. ENVIRONMENTAL, SAFETY AND HEALTH ISSUES

Until the late 1980s, isotope production was dominated by H^+ cyclotrons. Such machines have had difficulty complying with increasingly stringent worker dose limits. The primary problem is activation of the machine owing to inefficiencies inherent in extraction. The only practical means of achieving high productivity with an H^+ machine is to use internal targets, and this procedure results in high levels of activation and contamination of the cyclotron. This in turn leads to extensive cooldown periods and inefficient maintenance with higher than necessary personnel doses.

The advent of H^- cyclotron technology reduced the losses associated with extraction in compact cyclotrons from 10% or more to well under 1%, permitting the use of external targets. This reduces the activation to the extent that adequate accelerator cooldown occurs in some facilities in the time required to open the shield door. In addition, shifting the source of the radiation dose from the cyclotron vault to the target caves has the advantage that redundancy can be incorporated in target caves, thus minimizing the impact on production owing to hardware problems in an activated area.

In a properly engineered linac, the beam can pass the entire length of the accelerator with only a very small fraction ($\ll$1%) of the beam being scraped-off on the surfaces of the beamline. As a consequence, very little radiation will be generated. Because extraction from a linac is cleaner than even an H^- cyclotron, hands-on maintenance should be possible with essentially zero cooldown time. In this respect, a linac has an advantage over a cyclotron.

A generic advantage of accelerators as tools for isotope production is the small total radioactivity inventory needed on-site at any one time. With careful attention to scheduling, materials handling, waste handling and shipping, the total inventory should stay at a level several orders of magnitude lower than would be possible in a reactor-based facility. Additional attractive safety-related features of an accelerator-based NBTF are the ability to cease production on an essentially instantaneous ($\ll$ 1 ms) basis and the small amount of stored energy in the target. These features imply acceptable consequences of the various credible fault conditions.

The accelerating structures will gradually acquire some activation from scattering on residual gas. With careful vacuum techniques and attention to choice of materials, this residual activation will be reduced to a level compatible with reuse of the structures comprising the accelerator as scrap metal after an acceptable period of time.

The transfer lines that transport the beam from the accelerator to the targets are very similar in the two accelerators. Proper design and instrumentation will permit the losses to be minimal. However, the accumulated effect of collimation losses and infrequent beam spills will make the beamlines an activation concern.

The environmental, safety and health issues associated with the accelerator and beam transport systems are minor compared to those associated with the target caves, target handling and post-irradiation processing steps. Careful attention to choice of materials and to local shielding renders these problems manageable; however, target cave maintenance will present many challenges, even for such "routine" equipment as wiring, lighting and pneumatic tubes. The use of degraders with a linac makes this a bigger concern for a linac than for a cyclotron.

Summary A linac is less vulnerable to activation than a cyclotron but the more serious problem with the additional activation in linac target vaults offsets this advantage. We judge the environmental, safety and health issues to be equivalent for cyclotron-based and linac-based NBTF designs.

C.3.5. CAPITAL COST OF ACCELERATOR AND RELATED SUPPORT EQUIPMENT

With the advent of RFQ technology, low energy (up to about 3 MeV) proton linacs can be made less expensively than proton cyclotrons. Cyclotrons control the present PET market (energies in the 10-20 MeV range) but linac approaches based upon developmental, higher energy RFQs are under serious investigation. Proton cyclotrons have a stranglehold on the market for isotope production (typically using 30 MeV devices). This might lead one to conclude that linacs are cost-competitive in the energy ranges achievable with RFQ accelerating structures while the higher energy linear accelerating structures are more expensive per unit energy than cyclotrons. However, the costs projected for the linac for the Superconducting SuperCollider (canceled prior to completion of the linac) suggest than linacs made outside the national laboratories may indeed be cost-competitive at energies of interest for NBTF. We have obtained three rough cost estimates for 70 MeV, 1 mA accelerators. The linac estimate was between the two cyclotron estimates and the three span a range of only 20%, which is within the uncertainty of the estimates. For the purposes of this assessment, we assume that the two approaches are essentially the same in cost.

Because of the circulating nature of the beam in a cyclotron, extraction can occur at any angle. This facilitates a compact layout of the various targets/caves, leading to a relatively inexpensive beam transport system. Sending beams to multiple caves with a linac requires a somewhat more complex and therefore higher cost beam transport system.

Summary The cost of a cyclotron with its supporting equipment is very similar to the cost of a linac and its supporting equipment.

C.3.6 OPERATION AND MAINTENANCE COST OF ACCELERATOR AND RELATED SUPPORT EQUIPMENT

With modern control system techniques, the operation of the accelerator, whether cyclotron or linac, can be a highly reliable and automated procedure. This fact has been demonstrated more convincingly in cyclotrons because of the greater prevalence of proton cyclotrons in process applications. We observed operation of several modern H^- cyclotrons using industrial-standard control equipment and commercially available software packages. There is every reason to believe that proton linacs will eventually achieve the same status, perhaps in the next product cycle. The staffing required to operate the radiochemistry facilities will be significantly greater than that required to operate the accelerator, so this is not a major issue for making the choice of accelerator type.

The cost of expendibles is a significant budgetary consideration and the most important contributor to this category is the cost of electricity. The beam emerging from the accelerator has a power of 70×10^6 V x 10^{-3} A = 70 kW. An estimate of efficiency for a cyclotron can be gleaned from the experience on the highest current cyclotron used in radioisotope production: the 18 MeV device at Theragenics. This machine operates at greater than 30% electrical efficiency (ratio of beam power to power supplied by the electric utility). Using a somewhat more conservative estimate of efficiency for NBTF, the accelerator is expected to require about 300 kW of power when the beam is on and about 50% of this when the system is in a state of ready-for-beam. (Additional power will be consumed in target cooling and beamline magnets; see Section 4.3.) Linacs operating at very high currents (many mA) exhibit higher efficiency than any conventional cyclotron has ever demonstrated. However, at beam currents relevant to NBTF, conventional linear accelerators tend to have slightly lower electrical efficiency than cyclotrons because of greater losses in the RF system.

Cooling is also important for operating costs because only a tiny fraction of the power required to run the accelerator is actually doing useful work (transmuting nuclei); the remaining energy must be removed as heat. The accelerator and supporting power equipment consume 200-250 kW of power, virtually all of which is removed by cooling water; the beam power, which can reach 70 kW, appears as target (or beam stop) heating. Cooling the targets is actually the more challenging of the engineering problems because of the small volumes over which the heating takes place. (Fortunately, no reaction presently under consideration requires both full current and full energy so it will not be necessary to engineer any single target for the full 70 kW.) The target cooling problem will be somewhat more severe with a linac because of the additional dissipation in the degrader.

The term maintenance costs encompasses both scheduled and unscheduled maintenance. Scheduled maintenance deals with components of known lifetime limits, the most common being ion source components, RF components and foil strippers (cyclotron only). Production schedules are designed to accommodate these scheduled maintenance periods. Unscheduled maintenance is needed when unforeseen operational problems surface. Such problems have been common in accelerators early in their operational life, especially for units that entail pushing technology beyond the previously demonstrated state-of-the-art. The NBTF accelerator can be expected to have the normal complement of start-up problems common to first-of-a-kind units, but the comparatively conservative parameters and designs foreseen give every reason to expect that accelerator maintenance will be a comparatively small fraction of operating costs.

Summary Accelerator operation and maintenance costs will not dominate the NBTF operating budget. Two reasons lead to the conclusion that a cyclotron will be more cost-effective in operation than a linac. The first is the greater complexity and higher part count of the linac, especially the reliance on an RF system that has many comparatively delicate components placed in series. The second is the greater experience in process applications with proton cyclotrons, which translates into a strong supplier base that gives the user additional options to deal with problems as they arise.

C.3.7. FACILITY COSTS CORRELATED TO CHOICE OF ACCELERATOR

The facility costs driven by the accelerator are predominately those associated with the footprint of the accelerator and related support equipment, the shielding required to meet the applicable standards for the radiation dose outside the accelerator and target areas, and the need for specialized manipulators and related hardware to deal with tasks for which the radiation dose mandates remote handling.

The cyclotron vault has basically a radial build, comprising a circular accelerator of diameter approximately 4 m, a clearance of a few meters between the cyclotron and the shield to provide room for beam transport equipment, and a concrete shield wall approximately 3 m thick surrounding each target area that is subjected to impingement by a 70 MeV beam, with thinner shield walls for lower energy target areas. Target areas can be positioned in all directions around the machine; this attribute has led to a number of clever arrangements of support equipment. More information on the facility layout is found in Section C.4. The cyclotron incurs a building cost penalty from the high ceiling required to accommodate the size of the accelerator (3-4 m in height), the clearance required to open the accelerator for maintenance (somewhat less than 1 m) and an estimated 2 m of shielding. Installation has been accomplished successfully both from the top (with plug-style shielding above the cyclotron) and from the side; the preferred approach is very much site-dependent.

The linac is a long slender structure, on the order of 1 meter in length for every 1 MeV of beam energy. This is a significant constraint on site selection. If structural shielding were required, the much greater surface area of the linac compared to the cyclotron would translate into a significant cost penalty. In practice, however, the convenience of trenching for a linac means that earth can be used for most of the shielding, in which case shielding costs are typically less for a linac than for a comparable performance cyclotron. The long footprint of a linac leads to a need to distribute much of the support equipment in modular form along the length of the accelerator, with a resulting penalty in building costs. Target layouts are more constrained than in a cyclotron because the beam emerges only in one direction.

The dominant contribution to the radiation dose to workers is expected to come from target-related equipment because virtually all of the interaction between the beam and matter occurs in the targets and because the automated mechanisms used in target handling are subject to failure. Because the target-related systems are the same for the cyclotron and linac approaches, the costs associated with remote handling are expected to be comparable.

Summary The arguments presented here suggest that the facility costs driven by the choice of accelerator can be expected to be very similar for a cyclotron-based NBTF and a linac-based NBTF.

C.3.8. RECOMMENDATION

Review of Table 4-1 makes it clear that the cyclotron is the clear preference for a 70 MeV, 1 mA proton accelerator. It is worth noting that the cyclotron is the tool of choice for all facilities dedicated to accelerator-based isotope production. All the linacs used for isotope production were originally built for another purpose and later became involved in isotope production as an ancillary activity that took advantage of existing facility capabilities.

One argument that favors the linac is the comparative cost of upgrading the energy and/or the current. Because this is not a significant factor in the design of the NBTF it was not used as one of the bases of comparison. However, it is conceivable that a multi-mA linac would be the best choice for a single purpose, high volume production facility. Indeed, the United States is presently leaning toward a facility of this type for tritium production.

A cyclotron is also recommended for the 30 MeV, 100 μA alpha particle accelerator, but for quite different reasons. The 70 MeV, 1 mA machine will dominate the NBTF facility design in terms of targetry, shielding, ES&H considerations, power requirements, and cooling requirements, so the smaller machine should not be evaluated primarily on those issues. The more pertinent matter is overall facility operation. It is far more convenient and cost effective to operate with two similar machines in terms of controls, maintenance, spare parts inventory, required technician skills, etc. Hence, the preference for a 30 MeV alpha particle cyclotron stems largely from having selected a cyclotron for the larger machine.

C.4. EQUIPMENT LAYOUT CONSIDERATIONS

The arrangement of the primary NBTF equipment is described in three forms in the three subsections that follow. Section C.4.1 describes the functional relationships of the key hardware components. Section C.4.2 presents the baseline layout of the accelerators, target caves, and the beamlines that link them. Section C.4.3 indicates the approach being taken to interface control. Information is being compiled in a form that will be issued during the design phase as an Interface Control Document, which summarizes the equipment data in the form needed to define the interfaces with facility utilities and structural members.

In developing this information, we have utilized a design philosophy with a number of clearly defined tenets, listed below in two categories. The first category is keyed to achieving the high availability essential to the success of the NBTF.

- Rely upon proven techniques; in particular, minimize the need for development for any of the basic hardware.
- Restrict the hardware in the cyclotron vault to the minimum required in order to limit the need for manpower in the vault.
- The number of caves should significantly exceed the number of beams to permit preparing for future operations without interrupting present operations.
- Minimize hardware within the caves because of the need to perform many tasks remotely.

The second category of design tenets is keyed to the need for NBTF to perform a diverse set of tasks with the highest standards of quality and safety.

- For the high energy, high intensity cyclotron, use only targets located in caves shielded from the cyclotron in order to limit personnel dose associated with cyclotron maintenance.
- Incorporate as much experimental flexibility as practical, in order to more easily adapt to needs that are presently unforeseen.
- Arrange the process flow for any production isotope in such a manner that the possibility of cross contamination is eliminated.
- Provide an extra degree of isolation for the Education and Training isotope area, to accommodate use by less experienced personnel.
- Integrate into a facility in a manner that minimizes foot traffic through any areas that handle radioactive material.

C.4.1. OPERATIONAL FLOW AND INTERCONNECTS

As part of a process that results in a pharmaceutical product, material flow must be planned and tracked with great precision in NBTF. The first stage in establishing such a material flow path is illustrated in Figure 4-1, which is a highly stylized representation of the operational linkages and the primary interconnects between the principal items of NBTF equipment.

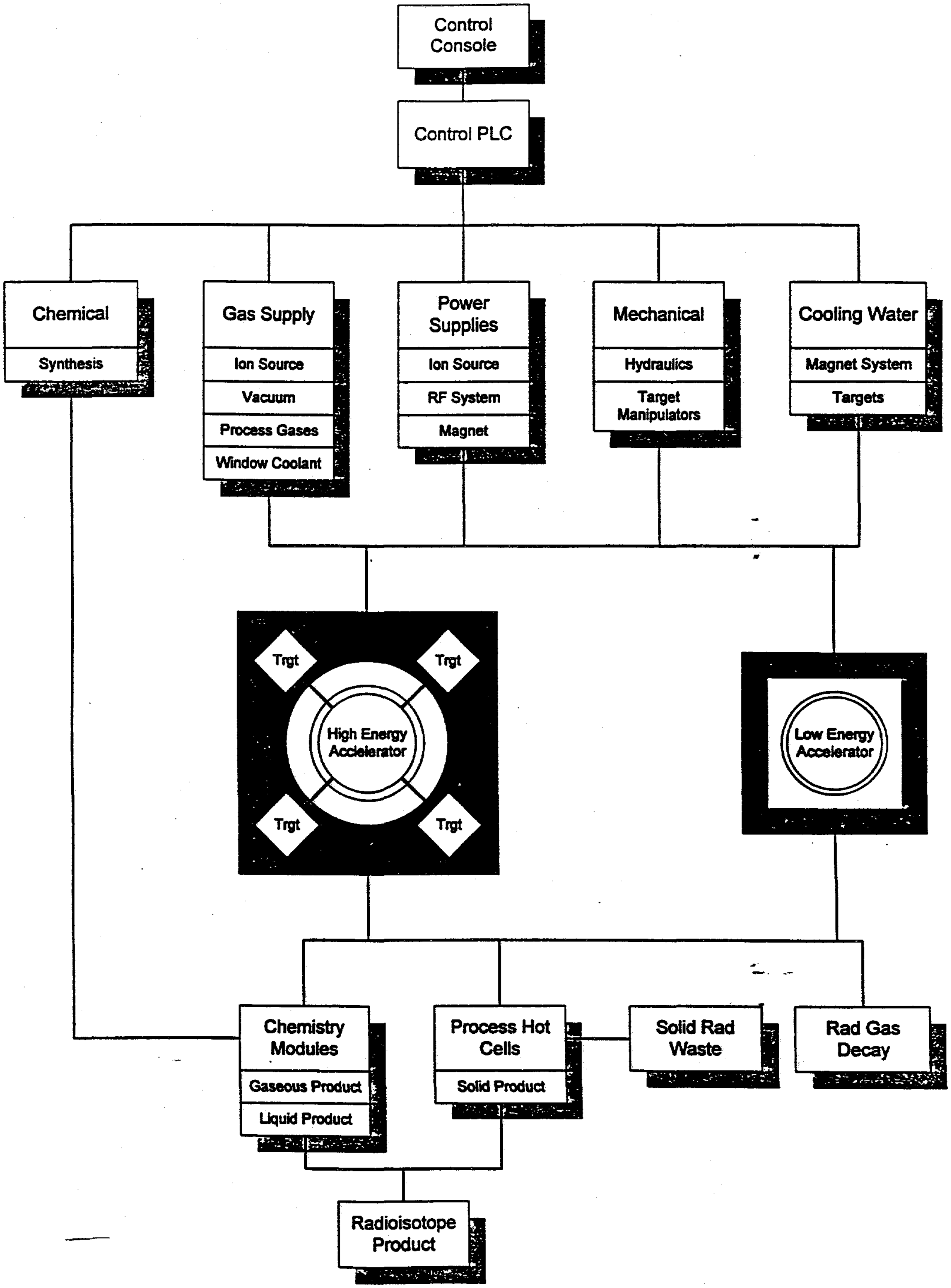


Fig. 4-1. NBTF operational flow and interconnects.

The complete process is controlled through one or more consoles in the control room. Operator instructions are entered through a modem graphical user interface and are executed via programmable logic controllers (PLCs). Because the approach is identical for all functions (electrical, mechanical, chemical, ...), the system can easily accommodate expansion to include new classes of targets and/or processing stages.

The system is designed so that all functions during normal operation can be carried out from the control room. This includes target installation and removal; accelerator pumpdown, startup/shutdown, and checkout; flow of all materials requiring accountability; and monitoring of all facility environmental and safety-related figures of merit. Ideally, the most frequent accelerator maintenance procedures, such as stripper replacement or ion source filament replacement, can also be accomplished directly from the control room. However, this is not essential, and the tendency of such automated mechanisms to have reliability problems of their own suggests that this may not always be the wisest course of action.

C.4.2. BASELINE LAYOUT

The baseline equipment layout must adhere to the general guidelines for facility design spelled out in the beginning of this section. In addition, it must be adequate to support the list of isotopes identified in section 1 as the focus of initial NBTF operation. This list, which was generated to allow the design to move from the general to the specific, is repeated here for convenience.

- **The conventional PET isotopes:** ^{11}C, ^{13}N, ^{15}O and ^{18}F, which are viewed as essential to the Education and Training mission.
- **Important commercial isotopes for which demand presently exceeds supply:** ^{22}Na, ^{57}Co, ^{82}Sr, ^{123}Xe,(^{123}I) and ^{201}Tl.
- **High potential research isotopes with low current availability:** ^{77}Br, ^{122}Xe and ^{211}At

Among the equipment layouts we observed in our visits to various isotope production sites, we were most impressed with the approach used in installing the sixth and most recent cyclotron at the N. Billerica, MA Dupont-Merck radiopharmaceutical production facility. This entailed installing the bulky cyclotron support equipment (such as that used to provide power, water and air) above the shielding over the accelerator and target vaults. This minimizes the footprint of the equipment and reduces the distances between the individual pieces of support equipment and the equipment they serve. In addition, the vertical feedthroughs minimize interference with maintenance procedures and reduce clutter on the floor of the vaults. In such a configuration, installation (as well as major repair, if needed) is best accommodated by side access to the accelerator vault. We have adopted this approach in our baseline layout.

Of course, the layout of the accelerator and target-related NBTF equipment must be in accord with the attributes of the hardware. Particularly important in this regard are:

1. **The physical size of the high energy accelerator and the access required for installation and maintenance.** Based on discussions with potential suppliers, we assume an accelerator in the shape of a cylinder with diameter 4.5 m and height (the direction of the axis of the cylinder) of 4 m. An extra meter of vertical clearance is included to allow opening the cyclotron for maintenance.

2. **Practical engineering limitations on the beam transport hardware.** This hardware is used to capture the beam emerging from the accelerator, steer it to the proper target vault and focus it on the target with the appropriate spot size. Each beamline is conceptualized as a collection (dipole) magnet near the accelerator, followed by a quadruple triplet to achieve independent control of the horizontal and vertical spot on target, and a final dipole to steer the beam onto the target. For conservatism, we have located all of this hardware in the accelerator vault. A more space-effective layout is possible if magnets can be placed in the shield walls; this can be achieved using bench aligned equipment that can be retracted into the accelerator vault for maintenance.

3. **The number of extracted beams and the parameters of these beams.** We assume three extraction ports at 90° spacings. One port is restricted to low current, low energy beams appropriate for Education and Training, while the other two ports can extract the higher current, higher energy beams called for in the production of isotopes for research or commercial sale.

4. **The number of target vaults and the maximum beam energy delivered to each vault.** These parameters are the primary determinant of shielding requirements. In the configuration we have laid out, the high energy accelerator can irradiate targets in eight caves, three to the full 70 MeV, four limited to 40 MeV and one limited to 20 MeV.

Figure 4-2 shows the baseline NBTF equipment layout, which implements the approach described above. This version of the layout is intended to convey the relationships between the major pieces of hardware and the primary activities carried out in the facility.

However, it becomes progressively more schematic as one moves outward from the accelerator to the supporting laboratories. For accurate dimensions of the latter facilities, refer to the facility layouts generated by RUST International.

The primary accelerator vault, referred to as vault #1, is approximately 11 m x 14 m, as dictated by considerations 1 and 2 above. This vault is surrounded on three sides by nine other vaults, eight (vaults #2-9) for targets and one (vault #10) for the lower energy alpha particle accelerator. The fourth side of vault #1 does not abut other vaults, facilitating comparatively unimpeded access for installation and maintenance. Similar access is provided for the 30 MeV device. The vaults on each of the three sides of vault #1 themselves abut one of the three isotope production laboratory complexes, shown in Figure 4-2 as the medium level labs (supporting the education and training activities), the high level labs supporting commercial production, and a group of high level labs supporting the research and development activities. The support services for both accelerators, not shown in this ground floor plan view, are above the vault area.

Table 5-1 lists the isotopes to be made in the various vaults in the nominal operational scenario, which addresses primarily the isotopes identified as the focus for initial operation. Table 5-1 also defines the range of beam parameters and target types planned in each vault. Vaults #2 and #3 are dedicated to the Education and Training mission, with vault #2 focusing on the conventional PET isotopes and vault #3 incorporating the kind of instrumentation necessary to carry out accurate cross section and dosimetric measurements. Vaults #4-7 are dedicated to isotopes in the Commercially Viable Now category; vaults #4 and #5 are designed to tolerate the

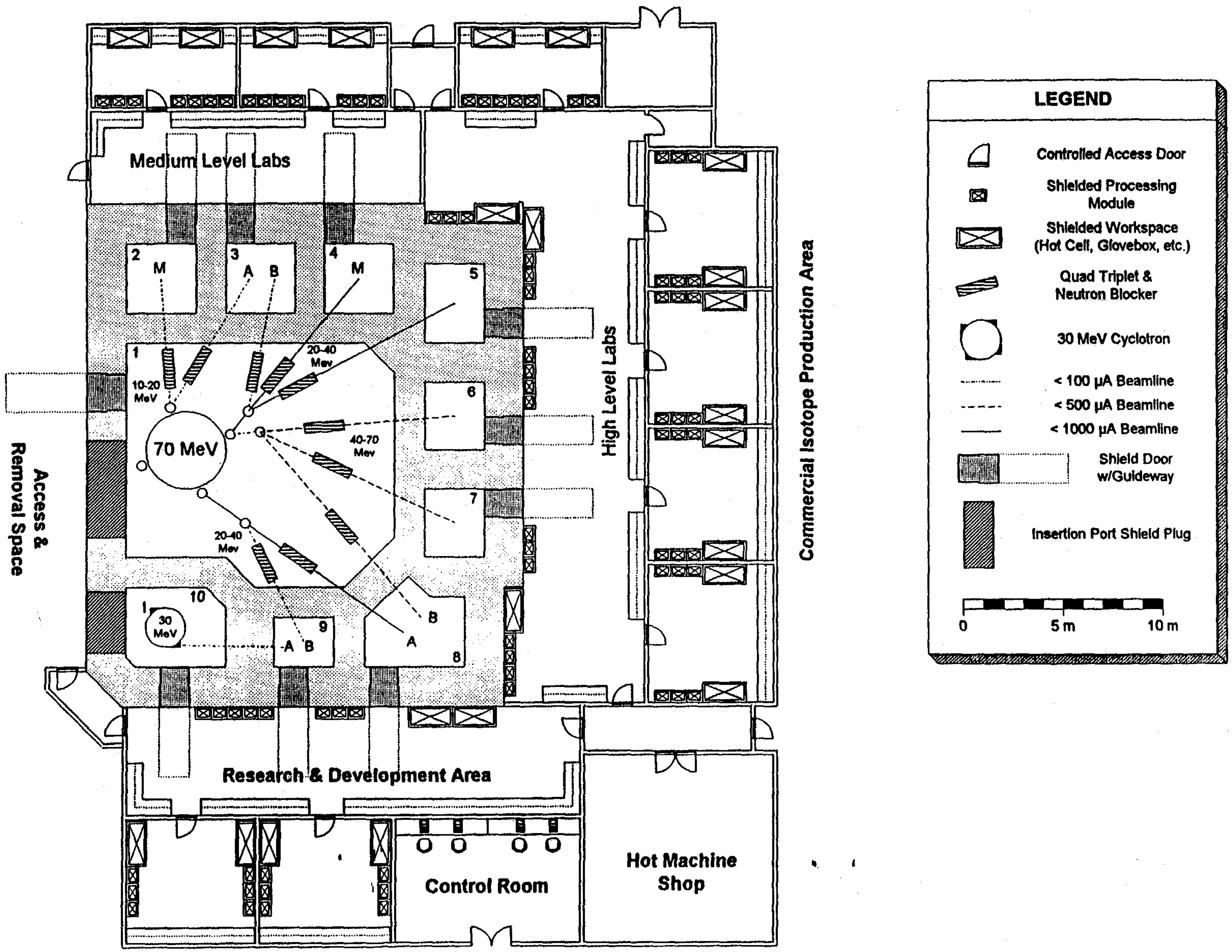


Fig. 4-2. Baseline NBTF equipment layout.

full beam current at beam energies of 20-40 MeV and vaults #6 and #7 are designed for full energy beams up to 500 µA. Vaults #8-10 support the Research Laboratory exclusively. Note that the alpha particle accelerator irradiates both an internal target (in vault #10) and an external target (in vault #9), both of which support the Research Laboratory, in accordance with the specific isotopes to be made in those vaults. Vault #8 is especially equipped for target development, and has target stations for both 20-40 MeV and 40-70 MeV beams.

The types of targets planned for the various vaults are indicated in Table 5-1. As indicated in Figure 4-2 and in the first column of Table 5-1, vaults #3, #8 and #9 contain two target stations (fed by two beamlines), vault #1 has no targets, and all other vaults have a single target station. Only vault #10 has an internal target. The target stations in vaults #2 and #4 contain multiple individual targets (thus the designator M at these target stations), with the beam being guided to the individual targets by steering magnets in the vaults. In such multiple target assemblies, the complete unit, comprising several individual targets, is cooled as an integral assembly.

All target vaults are sized to permit maintenance personnel to access the target hardware from all sides without having to make contact with the (activated) vault walls. The vaults that support the education and training activities are larger, in recognition of the less experienced personnel involved in those operations.

The beamlines that direct the beams to these vaults emerge from one of three ports of the cyclotron. The specific layout of beamlines is a matter requiring considerable further study and the arrangement shown in figure 4-2 should be regarded as indicative only. This matter will be addressed using the TRANSPORT code in the next (site-specific) phase of the program.

During day shift operation, it is anticipated that two beams will be in essentially continuous use, one supporting the educations and training activities in the medium level labs and one supporting the Research and Development Laboratory. These beams emerge 180° apart around the cyclotron and can be independently controlled in a straightforward manner by a technician-level operator. During off-shift operation, it is anticipated that only one beamline will be in use at any one time and, in most cases, this will involve irradiation of a commercial production target for long periods of time at or near full beam current into one of vaults #4-7, the four areas equipped for this condition. This type of off-shift operation is compatible with use of a skeleton crew.

The shielding thicknesses shown in Figure 4-2 represent rather conservative estimates for the beam conditions pertinent to each vault. The thickest shielding is required for vaults #6-8, which receive the full 70 MeV beam. Two options for reducing the shielding volume will be examined in the design phase: (1) the enclosure of the highly activated target stations in pneumatically-driven local shielding of the clamshell variety, and (2) the use of special materials on the inside surfaces of the high energy target vaults. In both cases, the idea is to use local shielding to moderate the high energy neutron spectrum that is the major driver of shield thickness. High density concrete (usually with steel admixture) is another way of reducing shield thickness but the additional costs associated with this approach make it preferable only when space is at a premium.

Table 5-1
VAULT CHARACTERISTICS

Vault Number and Target Designation	Beam Parameters			Target Type	Representative Isotopes	Technical Emphasis
	Parti-cle	Energy (MeV)	Max. Current			
1-none	p	10-70	1 mA	NA	NA	NA
2-M	p	10-20	100 μA	Multiple - 2 gas, 1 liquid, 1 solid	^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{124}I	Education and Training, mainly PET
3-A	p	10-20	10 μA	Variable	Various	Nuclear physics for Education and Training
3-B	p	20-40	5 μA			
4-M	p	20-40	1 mA	Multiple - 2 solid, 1 hockey puck	^{57}Co, ^{77}Br, ^{125}I	Education and Training, high power target research
5	p	20-40	1 mA	Solid	^{22}Na, ^{201}Tl	Commercial production
6	p	40-70	500 μA	Hockey puck	^{122}Xe, ^{123}Xe	Commercial production
7	p	40-70	500 μA	Solid	^{82}Sr	Commercial production
8-A	p	20-40	1 mA	Variable	Various	Research; target development
8-B	p	40-70	500 μA			
9-A	α	20-30	100 μA	Solid	^{211}At	Research
9-B	p	20-40	100 μA	Solid	Various	Research
10-I	α	10-30	100 μA	Internal - solid	^{54}Mn, ^{58}Co	Research

C.4.3. INTERFACES

An Interface Control Document has been started, listing the approximate physical dimensions, weights and utility requirements of all accelerator-related hardware components. Because of the substantial effort required to compile all the requisite information, this goes beyond the scope of the Project Definition Study; the document will be issued early in the design phase of the project. A sample sheet from the document is provided as figure 4-3.

Virtually all of the parameters provided are preliminary, because the hardware concepts have not been subjected to thorough design and analysis. Even though the data will change, it is important to begin working the interface problem now in order to have a consistent design concept at each stage of the design evolution.

The specific interface data for the 70 MeV, 1mA cyclotron has been provided by one potential supplier, Ion Beam Applications; this is why some of the entries in the table are referred to by IBA product name, such as CYCLONE 70. The cyclotron design is at the concept stage so one can expect the data to change as the design effort becomes more intense. Linking the facility design to one potential supplier's equipment can be fraught with peril. Fortunately, the second strong candidate cyclotron supplier, Ebco, utilizes a design with all pertinent parameters and functional characteristics close to those of the IBA design. We have held substantive discussions with both firms and regard the interface control data presented here to be a sound basis for proceeding with facility design.

Note:	Item:	Cyclone 70 Target Cells
	Physical:	
	Primary Equipment:	Cyclone 70 Gaseous, Liquid and Solid Targets
	Auxiliary Equipment:	Beam Lines, Target Coolant Manifold, Target Transport Systems
	Dimensions:	
	Area:	TBD
	Height:	TBD
	Opening:	TBD
	Access:	TBD
	Shielding:	
	Walls:	3.5 m ordinary concrete(2.3 t/cu. m)
	Ceiling:	3 m ordinary concrete (or equivalent?)
	Floor:	TBD
	Feedthroughs:	Req'd(TBD)
	Floor Loading:	TBD
	Pit:	TBD
	Other:	TBD
	HVAC:	
	Temperature:	17-28 deg. C (62-83 deg. F)
	Humidity:	35-65%
	Power Dissipated in Air:	TBD
	Lighting:	
	Standard Lighting:	250 Lux
	Emergency Lighting:	recommended
	General Electrical:	
	Ground:	TBD
	Single Phase Outlets:	3 m intervals
	Power:	TBD
	Plumbing:	
	Floor Drains:	recommended (local codes)
	Fire Protection:	
	Hazard Types:	electrical; flammable/explosive gas release
	Operational Interconnects:	
	Power Supply Area:	(?)
	Controller:	Process Valve control lines
	Water Coolant Area:	Target coolant lines
	Gas Supply Area:	compressed air, process gas, target window coolant lines
	Laboratory Process Modules:	gaseous, liquid, solid product transport
	Safety Interlocks:	
	TBD	

Fig. 4-3. Excerpt from preliminary Interface Control Document (not yet ready for release).

Table 5-2 indicates the physical dimensions of all vaults and the shielding thicknesses needed for essentially unrestricted access outside the shield. Shielding thicknesses can be reduced between two unoccupied areas, such as the shield between two target vaults.

Table 5-2
VAULT SIZES AND SHIELD THICKNESSES

Vault Number	Width x Depth (m)	Ceiling Height (m)	Shielding Thickness (m)
1	14 x 11	5.0	2.0*
2	3.5 x 3.5	2.5	2.0*
3	3.5 x 3.5	2.5	2.0*
4	3.5 x 3.5	2.5	2.0*
5	5.0 x 3.0	2.5	2.5*
6	3.5 x 3.0	2.5	3.0*
7	3.5 x 3.0	2.5	3.0*
8	3.5 x 2.5	2.5	2.5*
9	3.5 x 2.5	2.5	2.0*
10	5.0 x 4.0	4.0	2.0*

*The shielding thickness <u>between</u> vaults can be lower.

The subject of hardware interlocks is central to the operational safety of the facility. This issue will be the subject of considerable attention in the next phase of the program but we mention here one such interlock that is implicit in the layout shown in Figure 4-2. Beam shutters (sometimes called beam blockers) have been implemented on all beamlines. These are beam stops, usually made of graphite or steel, that are mounted within the vacuum region of a beamline. When beam is called for in that beamline, the beam shutters are held above the path of the beam by pneumatic values; if the pneumatic valves are deactivated, the beam shutters drop into the path of the beam and prevent beam from being transmitted. Interlocking the pneumatic valves with the shield doors to the target cave for that beamline provides a failsafe mechanism that permits (limited) access to vaults when beam is being directed to other vaults. (Gate valves that break vacuum when beam is inadvertently delivered down a beamline is an alternative approach.) This approach is representative of an operational philosophy that we endorse: for safety-related matters, insist upon hard-wired interlocks. Software-based solutions are too easy to inadvertently circumvent. A second level of safety protection will be implemented in the form of closed circuit video coverage of each vault. Thus visual inspection of each vault will be available to the operator at all times.

Table 5-3 presents summary-level information that serves to guide facility planning at the Project Definition Study stage of the NBTF program. In particular, it summarizes the overall support service requirements for the major items of equipment, as well as the assumptions made in deducing these requirements. Note that the estimate for the beamlines assumes that only two beamlines are energized at any one time. The direct electrical power requirement is about 500 kW, which corresponds to an electrical load of approximately 600 kVA. Other substantial electrical loads include the pumps and heat exchangers in the coolant loop, which must be capable of dissipating about 500 kW of heat.

Table 5-3
TOP-LEVEL POWER AND COOLING FOR NBTF EQUIPMENT

Item of Equipment	**Electrical Power**	**Dissipated Power[1]**	**Other Support Serious Required**
70 MeV p cyclotron	300 kW[2]	230 kW[2]	Hydraulics to open cyclotron
30 MeV α cyclotron	100 kW[3]	100 kW[3]	Hydraulics to open cyclotron; He gas to cool target window
Beam transport lines	90 kW[4]	90 kW[4]	None
Target stations	<10 kW	75 kW[5]	Pneumatic target delivery; He gas for target windows; target gases and liquids

NOTES :

1 All power to be removed by deionized water.
2 Estimate based on 50 kW for main magnet, 200 kW for RF (70 kW of which accelerates the beam, the remainder being dissipated) and 50 kW of miscellaneous.
3 Estimated based on 30 kW for main magnet, 50 kW for RF and 20 kW of miscellaneous (includes a contingency). The 3 kW of beam power can be ignored.
4 Based on 2 collection magnets requiring 10 kW each, 2 quadruple triplets requiring 15 kW each and 2 switching magnets requiring 20 kW each.
5 Based on 70 kW p beam and 3 kW α beam.

C.5. CAPABILITY OF INDUSTRY TO SUPPLY EQUIPMENT

Meeting the isotope demands of the U.S. nuclear medicine research community has historically been the province of the national laboratories. In view of the quite different nature of the proposed arrangement for the NBTF, it is one task of the Project Definition Study to assess the ability to accomplish the NBTF mission outside the framework of the national laboratories. This section deals with the ability of industry to supply the NBTF equipment.

The majority of the isotope production facilities constructed in the past 20 years have been installed at industrial sites, primarily at pharmaceutical firms. These facilities have been designed and operated by staff members of these firms. The facilities comprise a relatively small proportion of equipment that is designed and built in-house (this applies to target-related hardware and, in some cases, to control system development) and a relatively large proportion of equipment supplied on a fixed price basis by companies in various aspects of the accelerator, hot cell, remote handling and instrumentation business areas.

The UAB approach to NBTF follows this same pattern. The UAB team is interacting intensively with staff at operating isotope production facilities and with prospective equipment suppliers to develop a workable system concept. The UAB team member taking the lead in this part of the Project Definition Study is General Atomics (GA), a company that has extensive experience in accelerator applications in general and isotope production facilities in particular. The key steps GA is taking in facility design are:

- Working with the UAB scientific and medical staff to clarify the requirements of a successful NBTF.
- Factoring in the comments of the UAB NBTF Advisory Committee on the general approach taken to meet these requirements.
- Interacting with key individuals at operating isotope production facilities to gain insight into existing equipment and the capabilities of candidate suppliers.
- Soliciting input from prospective suppliers in the development of specifications that industry can respond to in a cost effective manner.
- Collaborating with the building contractor, RUST Engineering, to establish sensible building interfaces.

This process has developed the data base necessary to support the conclusion that industry can build a facility that is fully responsive to the NBTF mission. This conclusion is supported in Section C.5.1 by evidence of adequate capability at the component and subsystem level and in Section C.5.2 by evidence of adequate experience in the integration of systems comparable to NBTF.

C.5.1. COMPONENT AND SUBSYSTEM EXPERIENCE

The high energy, high intensity proton cyclotron is the centerpiece of the NBTF. Two companies, Ion Beam Applications (IBA) and Ebco, have the technical expertise to provide a cyclotron that meets the needs of the facility. Given the unique programmatic nature of NBTF, it is not surprising that neither firm includes a 70 MeV, 1 mA machine among its standard offerings. However, both firms offer a 30 MeV, several hundred microamp, H^- cyclotron geared to the needs of the isotope production community. In both cases, the technology employed in the existing machines scales in a straightforward manner to NBTF requirements. IBA and Ebco machines are depicted in Figures 5-1 and 5-2, respectively.

As mentioned previously, IBA has now delivered lower energy machines in which the current is specified to be in excess of 1 mA. In a recent visit to Ebco laboratories at TRIUMF, we have witnessed the achievement of 1 mA at low energy. Both of these cyclotron designs allow extrapolation of the energy to 70 MeV or higher energy at these current levels by use of a larger magnet with the same geometry as the existing units.

The cyclotron manufacturers offer standard target designs as well. However, the needs of individual users and isotope production programs vary considerably, the result being that sophisticated users generally supply their own targets. Indeed, target designs are often treated as proprietary in nature. Given the unprecedented breadth of the range of isotopes to be produced, NBTF will need to have an in-house target design competence. Hence, we specify the external targets as designed and built-in-house. Solid targets dominate the reactions listed in the Addendum and constitute the majority of the reactions baselined in Table 5-1. The overriding technical issue in NBTF solid target design is heat dissipation. The target design specifics will be based upon the following established design practices:

- Thin specimens mounted on a high thermal capacity, high thermal conductivity backing plate such as copper or silver.
- Cooling by high flow velocity water through channels in the backing plate.
- Canting the target specimen/backing plate assembly at a severe angle to the incoming beam, reducing the peak heat flux on target and leading to thinner targets, thus making heat transfer less sensitive to target material properties.
- Sizing target specimen cross-sectional area to the beam aperture produced in the beam transport system.
- Sizing the thickness of the target specimen to correspond to maximize yield at acceptable purity, taking into account the narrow angle of incidence between the beam and the target.

Despite these general principles, there is a great deal of art involved in solid target design and fabrication. In addition, gas targets, liquid targets, pressed powder targets and targets that undergo a change of state all have their special design features not dealt with here. The participation of Oak Ridge National Laboratory (ORNL) as a team member will be extremely valuable in this regard; ORNL arguably has more experience in target design than any other institution in the world. Working with ORNL adds efficiency to the process in another respect: they are the primary supplier of stable, enriched isotopes in the United States and such materials are required for a significant fraction of the targets foreseen in NBTF.

Table 6-1 presents a summary of the present NBTF equipment procurement plan. The accelerators, hot cell shielded enclosures, beamlines magnets, and some remote handling equipment will be purchased via competitive procurements based upon specifications generated by the design team. The laboratory equipment, the radiation safety hardware (detectors, badges, alarms), the tools used in target fabrication, and the remainder of the remote handling equipment will be purchased as catalog items.

It is concluded that the capability exists in industry to provide the equipment necessary for a successful NBTF.

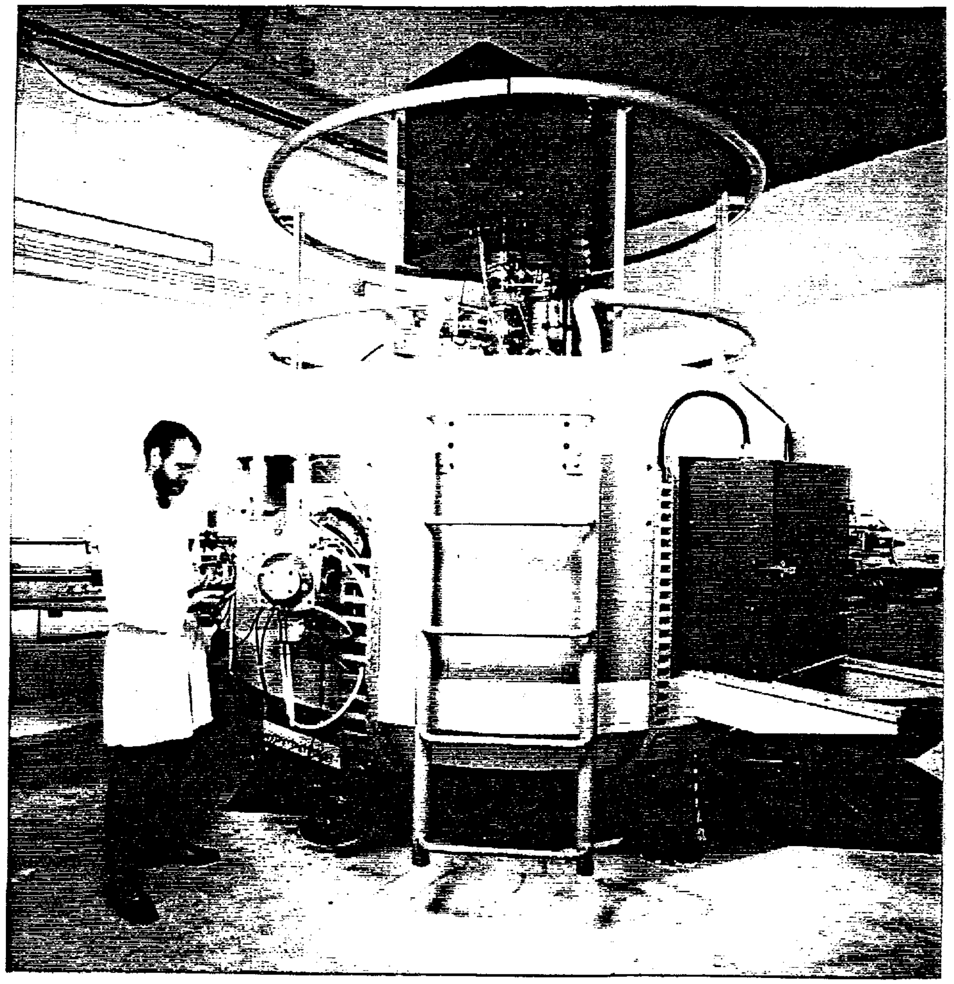


Fig. 5-1. Installation of an IBA 30 MeV H^- cyclotron, now in use at 17 facilities.

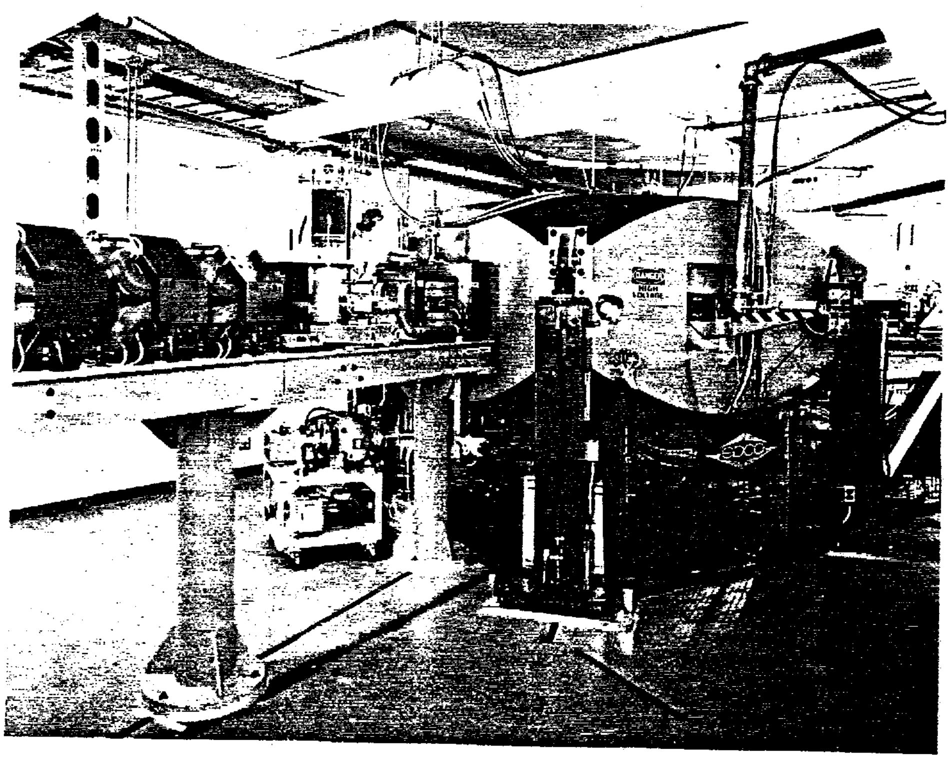


Fig. 5-2. Ebco 30 MeV H^- cyclotron, now in use in Taiwan.

C.5.2. SYSTEM-LEVEL EXPERIENCE

Clearly defined responsibilities have been established for the team members. GA will execute the make/buy plan summarized in Table 6-1. In addition, the remaining beam transport equipment, the external targets, the safety-related software, and all equipment integration tasks will be a GA responsibility. Facility shielding will be specified by GA, but procured and installed by RUST Engineering, the building contractor. RUST will also supply all the power, water and gases specified in the Interface Control Document at agreed-upon hand-off points. RUST will also control the overall project schedule, and take responsibility for obtaining the various licenses and permits needed. UAB will provide all NBTF permanent staff. This staff will have design review and approval responsibility, and will serve as the point of contact with the DOE. The NBTF staff will participate fully in facility commissioning and will assume full responsibility for operation and maintenance upon project completion.

Work previously completed successfully by the firms involved in NBTF provides a good measure of the capability to take hardware responsibility for NBTF. Work presently underway by these firms supplements this information by verifying whether the current staff at these firms is will matched to the needs of NBTF.

Perhaps the best example of industry-supplied equipment for the process-related aspects of NBTF is the radioisotope-radiopharmaceutical facility commissioned by the National Atomic Energy Agency of Indonesia (BATAN) at a nuclear research and development center near Jakarta. This facility produces 3 types of fission product and 21 types of activation-product isotopes. Among these products is 12,000 ^{99m}Tc generators (1-4 Ci each) annually. BATAN contracted with GA to design and equip this facility, which is sketched in Figure 5-3.

The Northeast Proton Therapy Center (NPTC), now under construction in Boston, provides a good example of the ability of industry to supply the equipment for a complex, high performance cyclotron-based facility. Figure 5-4 shows the layout of the first phase of the NPTC equipment. The cyclotron, being supplied by IBA, is rated at 235 MeV but at a current of much less that 1 μA. The low current rating does not signify a technological limitation; rather, it corresponds to the desired dose rate for cancer treatment. The energy of the beam delivered to the patient, controllable over the range of 70-235 MeV, is determined by an energy selection system comprising a degrader and a momentum selector. The beam energy determines the distribution of radiation dose as a function of depth in the patient. The beam is transported to a patient in one of several treatment rooms. A rotating gantry, together with a multiple-degree-of freedom patient support system, allows irradiation of any point within the patient from any direction. The beam transport system, gantry and patient positioner are all being supplied by GA.

RUST International has served as facility contractor for many high technology facilities, including the Advanced Photon Light Source at Argonne National Laboratory and a number of complexes at Oak Ridge National Laboratory that deal with similar technical problems.

Based upon this information, it is concluded that the UAB industrial team members possess the knowhow to competently

- Conceptualize an NBTF commensurate with the mission that DOE has defined;
- Design, specify, procure, install and commission that hardware; and

- Integrate the various components and subsystems into a technically succheesful and productive facility.

TABLE 6-1
EQUIPMENT PROCUREMENT STRATEGY

Item Description	Make/Buy Plan	Examples of Candidate Suppliers
70 MeV proton cyclotron	Compete to specification	Ion Beam Applications, Ebço
30 MeV ^{4}He cyclotron with external targets	Compete to specification	Ion Beam Applications, Ebco, CTI
Beam transport equipment	Make, magnets built for facility	Not applicable
External targets and supporting equipment	Make with help from ORNL	Not applicable
Hot cells and shielded enclosures	Compete to specifications	Von Gahlen, Capintec, Wälischmiller, ANSTO
System safety related software	Modify cyclotron supplier software	Not applicable
System safety related hardware	Catalog purchase	Victorean, Ludlum, Eberline, Capintec
Quality assurance related equipment	Catalog purchase	Hewlett Packard, many others
Remote handling equipment	Compete to spec/ some catalog items	Central Research Lab, PAR, Wiesener, Wälischmiller
Process hoods	Catalog purchase	Kewaunee, Labconco
Target fabrication equipment	Catalog purchase	Brown & Sharpe, Cincinnati Machine Tools

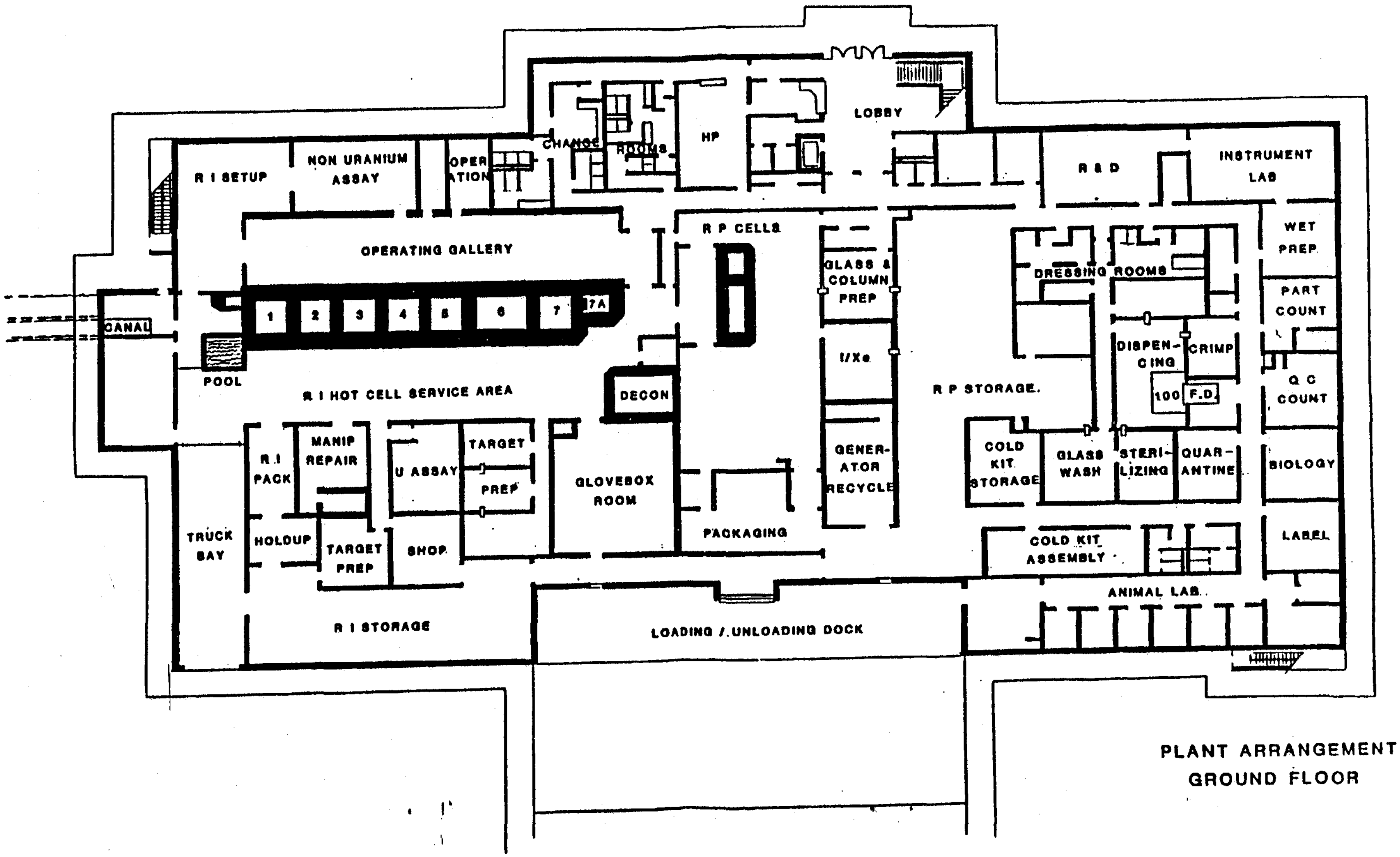


Fig. 5-3. GA designed and equipped this radioisotope/radiopharmaceutical facility in Indonesia.

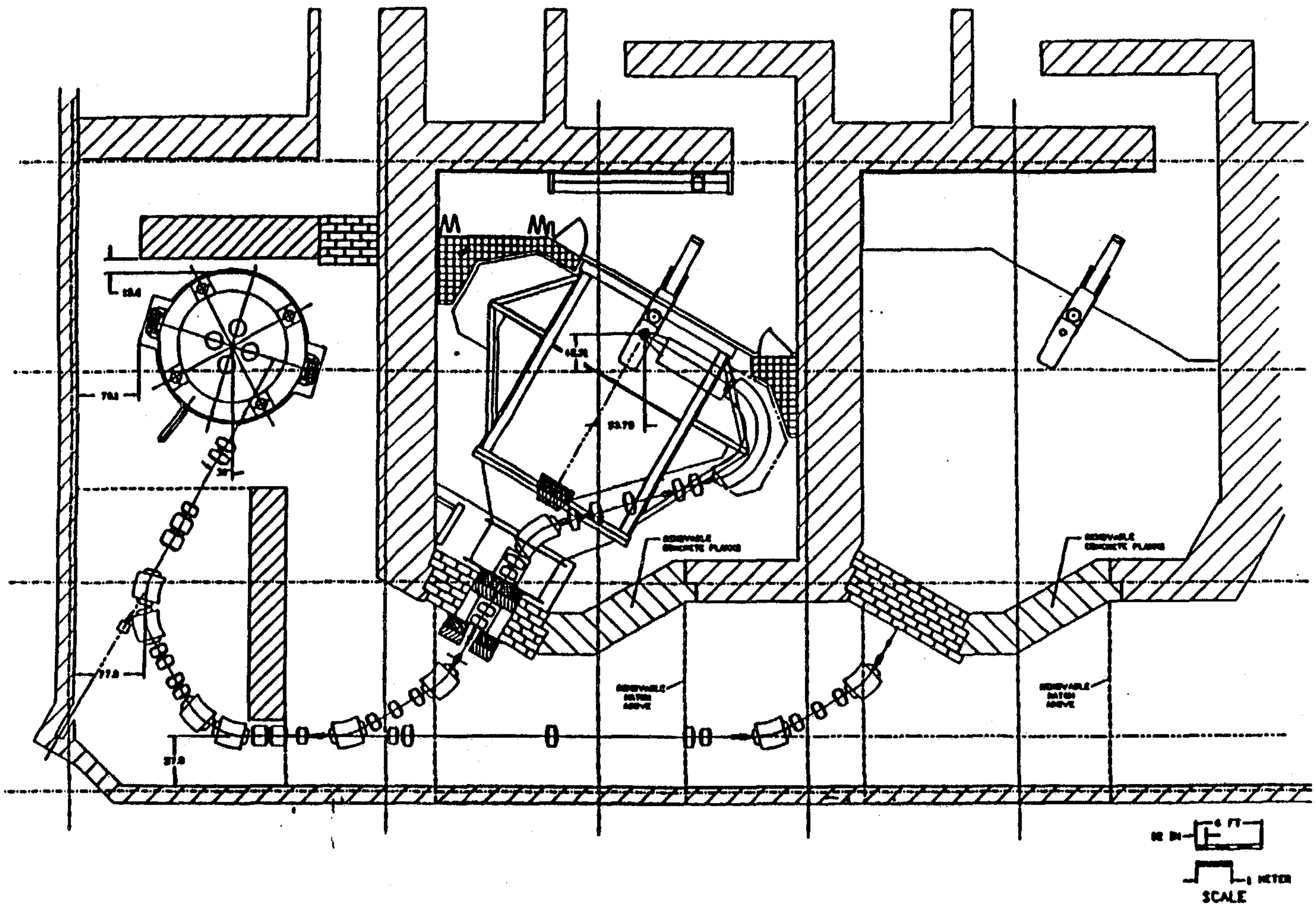


Fig. 5-4. Equipment layout for the Northeast Proton Therapy Center, now under construction.

ADDENDUM: ACCELERATOR RADIOISOTOPE PRODUCTION PROCESSES OF INTEREST FOR NBTF

Radio-isotope	Target Nuclide[1]	Proton Reaction[1]	On DOE NBTF List?	NBTF Mission Responsiveness	Medical and/or Research Utility
^{7}Be	^{7}Li	p,n	yes	Has been used as tracer	Be tracer
^{11}C	^{14}N	p,α	no	Education and training	PET
^{13}N	^{16}O	p,α	no	Education and training	PET
^{15}O	^{19}F	p,αn	no	Education and training	PET
^{18}F	^{18}O	p,n	no	Education and training	PET
^{22}Na	^{27}Al	p,3p3n	no	Commercially viable now	Source radioisotope
^{28}Mg	*^{31}P*	*p,4p*	yes	Future potential	Mg tracer
^{38}K	^{38}Ar	p,n	no	Future potential	K tracer; PET
^{47}Sc	^{48}Ti	*p,2n*	yes	Future potential	Antibody radiotherapy
^{44}Ti	^{45}Sc	*p,2n*	no	Future potential	Parent of ^{44}Sc, which has no current use
^{48}V	^{48}Ti	*p,n*	no	Future potential	Environmental monitoring
^{49}V	^{52}Cr	p,α	yes	Future potential	?
^{51}Cr	^{51}V	*p,n*	no	Has been used in research	Cell labeling
^{54}Mn	^{56}Fe	p,2pn	no	Commercially viable now	Counter calibration
^{52}Fe	^{55}Mn	p,4n	no	Has been used in research	Parent of ^{52m}Mn, which is used for PET imaging

ADDENDUM:
ACCELERATOR RADIOISOTOPE PRODUCTION
PROCESSES OF INTEREST FOR NBTF (continued)

Radio-isotope	Target Nuclide[1]	Proton Reaction[1]	On DOE NBTF List?	NBTF Mission Responsiveness	Medical and/or Research Utility
^{55}Co	^{56}Fe	*p,2n*	no	Has been used in research	PET imaging; antibodies
^{56}Co	^{56}Fe	*p,n*	no	Has been used in research	γ-ray standard; source isotope
^{57}Co	^{58}Ni	p,2p	yes	Commercially viable now	X-ray fluorescence spectroscopy; gamma camera quality assurance
	^{60}Ni	p,α			
	^{57}Fe	p,n			
^{58}Co	^{60}Ni	p,2pn	no	Commercially viable now	Source radioisotope
	^{58}Fe	p,n			
^{64}Cu	^{64}Ni	p,n	yes	Has been used in research	PET blood flow imaging
^{67}Cu	^{68}Zn	p,2p	yes	Has been used in research	Monoclonal antibody labelling (cancer); antibody radiotherapy
^{62}Zn	^{63}Cu	p,2n	yes	Has been used in research	Parent of ^{62}Cu, which is used for blood flow imaging (PET)
^{66}Ga	^{68}Zn	*p,3n*	no	Has been used in research	PET
^{67}Ga	^{68}Zn	p,2n	no	Commercially viable now	Soft tissue tumor localization
^{68}Ge	^{69}Ga	p,2n	yes	Commercially viable now	Parent of ^{68}Ga, which is used for transmission images for PET

ADDENDUM:
ACCELERATOR RADIOISOTOPE PRODUCTION PROCESSES OF INTEREST FOR NBTF (continued)

Radio-isotope	Target Nuclide[1]	Proton Reaction[1]	On DOE NBTF List?	NBTF Mission Responsiveness	Medical and/or Research Utility
^{71}As	^{72}GE	*p,2n*	no	Future potential	SPECT; tracer for ^{72}As
^{73}As	^{74}Ge	p,2n	yes	Future potential	Tracer for ^{72}As?
^{72}Se	^{75}As	p,4n	no	Has been used in research	Parent of ^{72}As, which is used for PET imaging
^{75}Br	^{76}Se	p,2n	no	Has been used in research	PET imaging
^{76}Br	*^{78}Se*	*p,3n*	yes	Has been used in research	PET
^{77}Br	^{78}Se	p,2n	yes	Has been used in research; education and training	Radiotherapy via bromine-labeled estrogens; monoclonal antibody imaging
^{80m}Br	*^{80}Se*	*p,n*	yes	Has been used in research	Radiotherapy via bromine-labeled estrogens
^{81}Rb via ^{83}Sr	^{85}Rb	p,5n + β–decay	no	Commercially viable now	^{81}Kr parent
^{83}Rb via ^{83}Sr	^{85}Rb	p,3n + β–decay	no	Commercially viable now	Rb tracer
^{82}Sr	^{85}Rb	p,4n	yes	Commercially viable now	Parent of ^{82}Rb, which is used for PET myocardial perfusion imaging
^{85}Sr	^{85}Rb	p,n	no	Commercially viable now	Source radioisotope
^{87}Y	*^{87}Sr*	*p,n*	no	Has been used in research	Imaging/dosimetry studies for ^{90}Y
^{88}Y	^{88}Sr	p,n	yes	Has been used in research	Measure biodistribution of Y to model ^{90}Y

ADDENDUM: ACCELERATOR RADIOISOTOPE PRODUCTION PROCESSES OF INTEREST FOR NBTF (Continued)

Radio-isotope	Target Nuclide[1]	Proton Reaction[1]	On DOE NBTF List?	NBTF Mission Responsiveness	Medical and/or Research Utility
^{88}Zr	*^{89}Y*	*p,2n*	no	Has been used in research	^{88}Y parent
^{89}Zr	*^{89}Y*	*p,n*	no	Has been used in research	PET; antibody labeling
^{94}Tc	^{94}Mo	p,n	no	Has been used in research	PET
^{95m}Tc	^{95}Mo	p,n	yes	Has been used as tracer	Long-lived biodistribution studies for ^{99m}Tc; environmental research
^{96}Tc	^{96}Mo	p,n	yes	Has been used as tracer	Long-lived biodistribution studies for ^{99m}Tc; environmental research
^{97}Ru	^{103}Rh	p,α3n	yes	Has been used in research	SPECT imaging for radioimmunodiagnosis
^{101m}Rh	*^{101}Ru*	*p,n*	no	Future potential	No current use
^{103}Pd	*^{103}Rh*	*p.n*	no	Commercially viable now	Auger emitter
^{107}Cd	*^{107}Ag*	*p.n*	no	Has been used in research	Auger emitter
^{109}Cd	*^{109}Ag*	*p,n*	yes	Commercially viable now	Parent of ^{109m}AG, which is used to study heart blood flow and as a source radioisotope
^{111}In	^{112}Cd	p,2n	no	Commercially viable now	Planar imaging; SPECT
	^{111}Cd	p,n			
^{114m}In	*^{114}Cd*	*p,n*	yes	Has been used in research	In biodistribution; possibly therapy

ADDENDUM:
ACCELERATOR RADIOISOTPE PRODUCTION PROCESSES OF INTEREST FOR NBTF (continued)

Radio-isotope	Target Nuclide[1]	Proton Reaction[1]	On DOE NBTF List?	NBTF Mission Responsiveness	Medical and/or Research Utility
^{118}Te	*^{121}Sb*	*p,4n*	no	Has been used in research	^{118}Sb parent
^{119}Te	*^{121}Sb*	*p,3n*	no	Future potential	SPECT?
^{123}I via ^{123}Xe	^{124}Xe	p,2n + β-decay	yes	Commercially viable now	SPECT brain imaging; planar imaging
	^{127}I	p,5n + β-decay			
^{124}I	^{124}Te	p,n	yes	Education and training; Has been used in research	PET
^{125}I	*^{126}Te*	*p,2n*	no	Commercially viable now; Education and training	I tracer; Auger emitter
^{122}Xe	*^{127}I*	*p,6n*	yes	Has been used in research	^{122}I parent
^{127}Xe	^{133}Cs	p,2p5n	yes	Commercially viable now	Ventilation imaging
	^{127}I	p,n			
^{128}Ba	*^{133}Cs*	*p,6n*	yes	Future potential	^{128}Cs parent
^{135}La	*^{136}Ba*	*p,2n*	no	Future potential	Actinide tracer
^{134}Ce	*^{139}La*	*p,6n*	no	Future potential	^{134}La parent
^{139}Ce	^{139}La	p,n	no	Commercially viable now	Source isotope

ADDENDUM:
ACCELERATOR RADIOISOTOPE PRODUCTION PROCESSES OF INTEREST FOR NBTF (continued)

Radio-isotope	Target Nuclide[1]	Proton Reaction[1]	On DOE NBTF List?	NBTF Mission Responsiveness	Medical and/or Research Utility
^{140}Nd	^{141}Pr	*p,2n*	no	Future potential	Auger emitter ?
^{146}Gd	^{151}Eu	*p,6n*	no	Future potential	^{146}Eu parent
^{151}Gd	^{151}Eu	*p,n*	no	Has been used in research	Monitor biodistribution of Gd to model Gd-based MRI
^{155}Tb	^{155}Gd	*p,n*	no	Future potential	SPECT; Auger emitter
^{166}Yb	^{169}Tm	*p,4n*	no	Future potential	90 keV γ for imaging ?
^{173}Hf	^{175}Lu	*p,3n*	no	Future potential	SPECT ?
^{178}W	^{181}Ta	p,4n	no	Commercially viable now	Parent of ^{178}Ta, which is used for myocardial imaging
^{183}Re	^{184}W	*p,2n*	no	Has been used in research	Long-lived Re tracer
^{184}Re	^{184}W	*p,n*	no	Future potential	Long-lived Re tracer
^{191}Os	^{193}Ir	*p,2pn*	no	Has been used in research	Parent of ^{191m}Ir, which has potential for pediatric perfusion imaging
^{193m}Pt	^{193}Ir	*p,n*	no	Has been used in research	Auger emitter; Pt tracer
^{195m}Pt	^{197}Au	*p,2pn*	no	Future potential	Auger emitter; Pt tracer
^{195}Au	^{195}Pt	*p,n*	yes	Commercially viable now	Source isotope for ^{201}TI, which is used for quality assurance

ADDENDUM:
ACCELERATOR RADIOISOTOPE PRODUCTION
PROCESSES OF INTEREST FOR NBTF (continued)

Radio-isotope	Target Nuclide[1]	Proton Reaction[1]	On DOE NBTF List?	NBTF Mission Responsiveness	Medical and/or Research Utility
^{195m}Hg	*^{197}Au*	*p,3n*	no	Has been used in research	Parent of ^{195}Au, which has potential for perfusion imaging
^{201}Ti via ^{201}Pb	^{203}Ti	p,3n + β-decay	no	Commercially viable now	Myocardial imaging
^{203}Pb	^{203}Ti	p,n	yes	Has been used in research	SPECT imaging for radioimmunodiagnosis
^{205}Bi	*^{206}Pb*	*p,2n*	yes	Has been used as tracer	Bi tracer
^{206}Bi	^{207}Pb	p,2n	yes	Has been used as tracer	Bi tracer
^{207}Bi	^{207}Pb	p,n	yes	Future potential	Bi tracer
^{211}At	none	no (p,X) reactions	no	Has been used in research	Radiotherapy
^{211}Rn	none	no (p,X) reactions	no	Has been used in research	^{211}At parent
^{235}Np	*^{238}U*	*p,4n*	yes	Has been used as tracer	Source radioisotope; calibration standard
^{236}Np	*^{238}U*	*p,3n*	yes	Has been used as tracer	Source radioisotope; mass spectroscopy quality assurance
^{237}Pu	*^{237}Np*	*p,n*	yes	Has been used as tracer	Monitor Pu movement in geosphere

[1]Reactions shown in normal type are referred to in open literature; those in italics are hypothesized reactions.

D. Facility Design

It was evident shortly after we started to examine issues surrounding the construction of the NBTF that this phase could not be done generically. There are issues of substance that need to be addressed in the cost of construction that are site-dependent. These issues had an impact on the Business Plan as well since the issue of reimbursement of the government is directly related to total cost of construction. As it developed, the cost of construction was lowest in Birmingham when compared to the other four sites or the two national laboratories expressing interest in the facility.

Given our desire to site the facility at UAB, we elected to base our construction costs on building the facility in Birmingham. This also helped focus the cost of utilities as well as other operating costs. The combination of firmer cost of construction at this phase of the development process as well as better figures for the cost of operation will ensure that further decision making on the project is based upon realistic assumptions.

D.1 LOCATION

THE NATIONAL BIOMEDICAL TRACER FACILITY to be located in Birmingham, Alabama is conceived as a two-story facility located on the University of Alabama at-Birmingham (UAB) campus in close proximity to the medical school, University of Alabama hospitals and the schools of engineering and sciences. The NBTF has been designed to serve the three missions of isotope production, research and development, and training and education as outlined in the Institute of Medicine report "*Isotopes for Medicine and the Life Sciences*" in a facility of approximately 81,000 net square feet.

Immediately to the east of the proposed site is University owned property of approximately the same size allowing for potential expansion of the NBTF and other spin-off type activities. The site was selected due to its physical location on the UAB campus. This site is also presently owned by the University and adds no cost to the NBTF program. Campus wide systems such as computer networks, building management systems and telephone systems may be easily extended to this facility. The site has the added advantage of being sloped enabling most of the radioactive work and storage to be conducted underground taking advantage of this natural shielding.

D.2 CONSTRUCTION ADVANTAGES

There are many advantages to constructing the NBTF in the Birmingham area. Birmingham has a very low earthquake potential being in a very stable seismic zone, thus eliminating concerns about earthquake problems and reducing the cost of design and construction. Earthquake design information was taken from design guides published by the Federal Emergency Management Agency National Earthquake Hazards Reduction Program (NEHRP).

The Means Building Construction Cost Data set is used to compare the cost of construction around the country. Cost estimates that are developed for one region of the country can be adjusted to reflect the cost of construction in other areas of the country. This database is useful in determining the cost of constructing the NBTF in different regions According to MEANS Building Construction Cost Data set, construction in Birmingham has a cost advantage over the other potential sites, as much as 60% over the New York area or 40% when compared to Los Angeles or the Sacramento, California area. This does not factor in additional costs to satisfy seismic design requirements in these other geographical areas. Table D.1 below provides a comparison of construction costs and seismic data.

TABLE D.1 CONSTRUCTION COST COMPARISON AND SEISMIC DATA

LOCATION	COST INDEX	% CHANGE INC.	SEISMIC ZONE
BIRMINGHAM, AL.	82.5	0.0	2
SACRAMENTO, CA.	112.1	35.9	6
LOS ANGELES, CA.	115.2	39.6	7
DALLAS, TX.	87.6	6.2	2
W. LAFAYETTE, IN.	93.8	13.7	2
LOS ALAMOS NAT'L LAB	89.9	9.0	3
BROOKHAVEN NAT'L LAB	132.6	60.7	3

Design acceleration criteria Zone 2=0.05g, Zone 3=0.10g, Zone 6=0.3g, Zone 7=0.4g

Careful consideration went into the selection of the proposed site and design of the NBTF. Two committees representing industry and academia have been formed and have provided invaluable, real world guidance into the needs and requirements of the NBTF. The NBTF team visited three operating facilities and much has been learned from Mallinckrodt Medical of St. Louis, MO., DuPont/Merck of N. Billerica, MA. and Nordion/TRIUMF of Vancouver, BC. about design aspects of an NBTF. The NBTF design team wishes to thank Messrs. Roy Brown and Lawrence Tuberty of Mallinckrodt, Messrs. Carl Seidel, Sterling Kline and Dr. Peter Holton of DuPont and Dr. Tom Ruth and Dr. Karl Erdman of Nordion for their interest and willingness to share their expertise in this field. Some of the top researchers and educators from regional universities, medical centers, and the Oak Ridge National Laboratory guided us to provide the best facility design to meet the needs of future researchers and educators in this field. Among these individuals there is a strong consensus that the NBTF should be collocated on a medical school, hospital and academic campus, and that a major emphasis should be placed on teaching and training as well as on research into new materials for target design and uses of radioisotopes.

The proposed site is located within 15 minutes of the airport and conveniently located within two blocks of four hotels with some offering airport shuttle service. There is easy access to restaurants, shopping and entertainment providing for a more pleasant stay for the visiting researcher.

D.3 ISOTOPE PRODUCTION--FIRST FLOOR

The first floor contains the production activities. It has been developed to be both safe and user friendly. It contains the two cyclotrons and supporting areas. The target vault area is segregated into three distinct zones for the production of radioisotopes as either low level, medium level or high level zones depending on the energy and current of the beam lines serving the zone. The vaults and beam control system have been designed to allow maximum flexibility of usage. Each vault can be utilized independently of activities in adjacent vaults through the careful design of shielding and beam controls. The cyclotrons, shield doors, beam stops and other safety systems will all be integrated into a single control system for maximum protection. The RUST automated systems division has designed numerous systems with this philosophy from the fully automated production of thermoplastics and pharmaceuticals to the remote controlled continuous propellant mix process for the space shuttle solid rocket boosters.

NATIONAL BIOMI
PROJECT I

THE U.S. DEPA

DEVELOPMENT OF THIS PROJECT WAS JOINTI
U.S. DEPARTMENT OF ENERGY AND THE STA

EDICAL TRACER FACILITY

DEFINITION STUDY

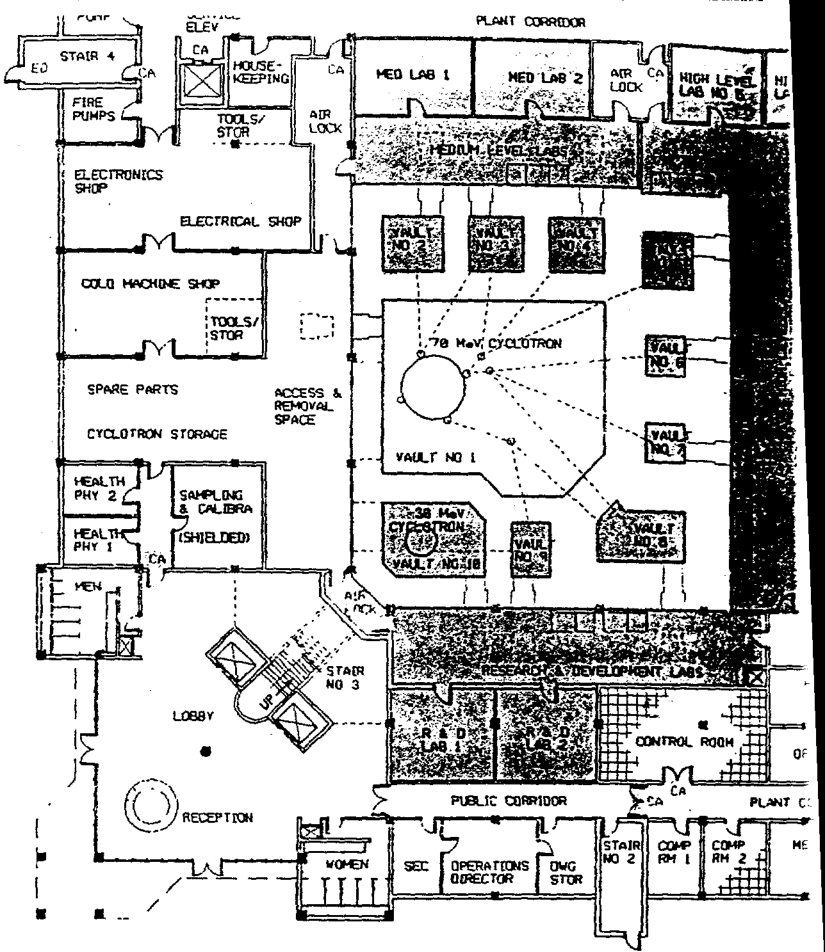
FOR

ARTMENT OF ENERGY

OINTLY FUNDED BY THE
E STATE OF ALABAMA

RUST
Contract 21-6196

Rust
International
Corporation
Birmingham, Alabama



FIRST FLOOR PLA

CA = CONTROLLED ACCESS DOOR
ED = EXIT ONLY DOOR

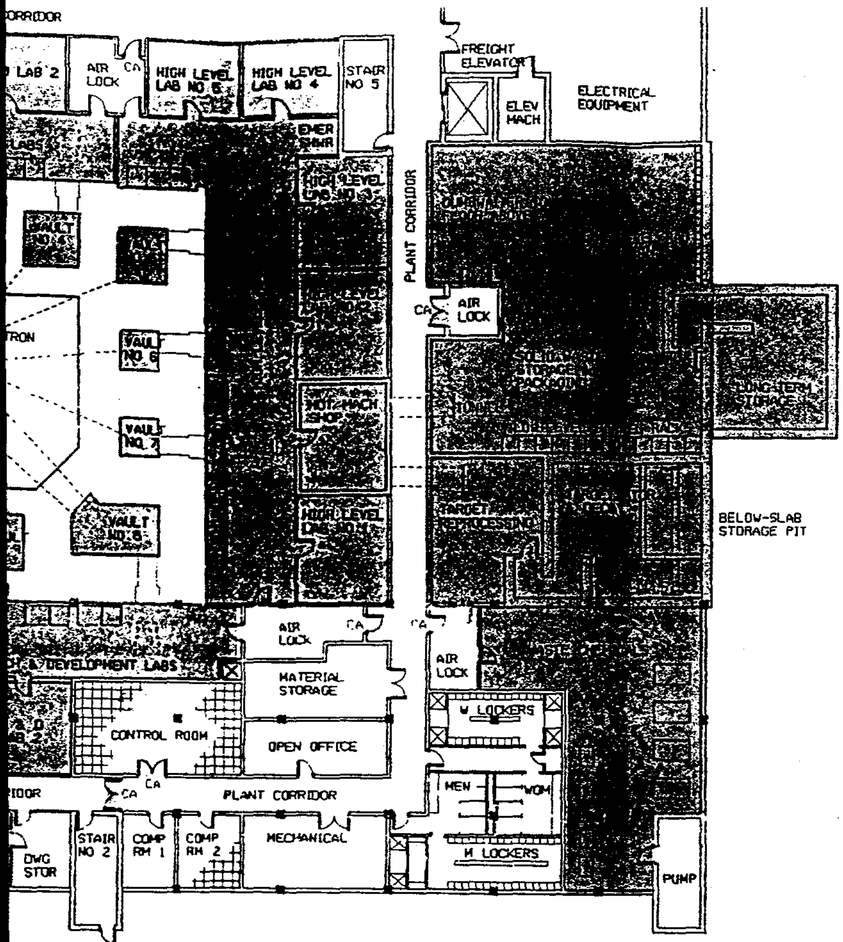
REVISIONS	MADE	CKD.	DATE	NO.	REVISIONS	MADE	CKD.	DATE	DRAWING NO.
RELEASED FOR D O E REVIEW	WDT		12/5/95						

GRAPHIC SCALE

STEP-DOWN

ACCESS CONTROL

CONTROLLED AREA



FIRST FLOOR PLAN

CA = CONTROLLED ACCESS DOOR
EO = EXIT ONLY DOOR

0 8' 32' 48'
GRAPHIC SCALE

PRELIMINARY
FOR PROJECT DEFINITION STUDY

W.D. TOUCHSTONE 8/24/95
W.D. TOUCHSTONE 8/24/95

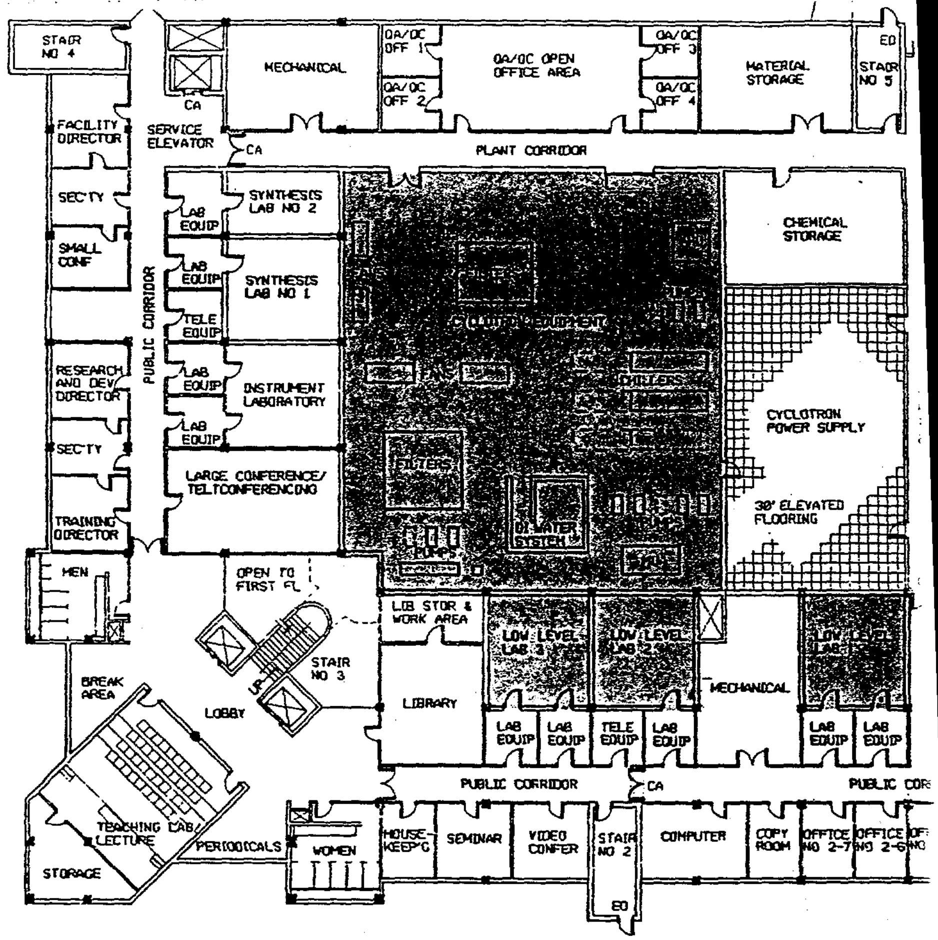
NATIONAL BIOMEDICAL TRACER FACILITY
FOR THE U.S. DEPARTMENT OF ENERGY

RUST International Corporation Birmingham, Alabama
Contract 21-8198

FIRST FLOOR PLAN

DRAWING NUMBER 24-0011A

REV. NO. A



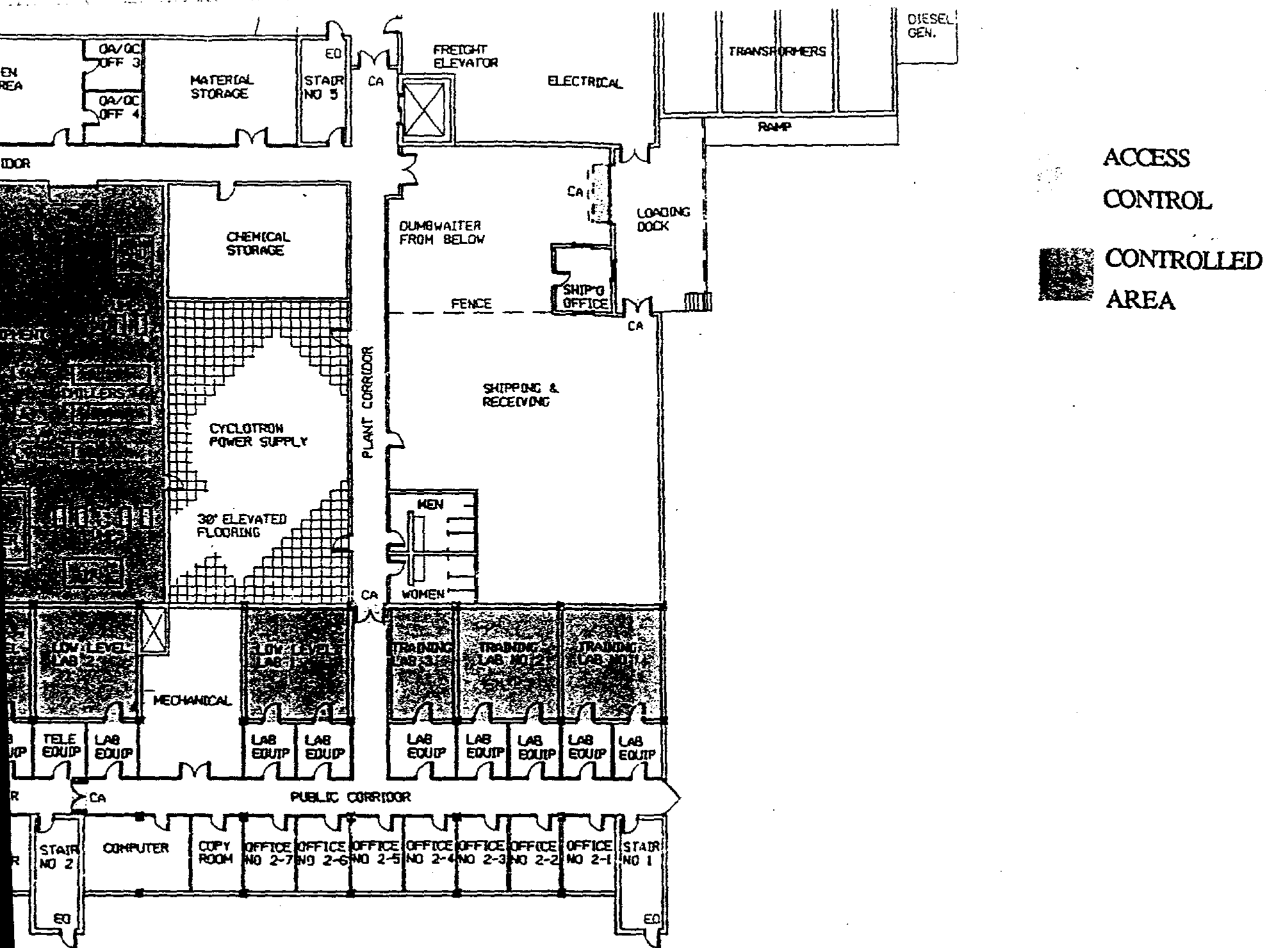
SECOND FLOOR PLA

CA = CONTROLLED ACCESS DOOR

EO = EXIT ONLY DOOR

ED FOR D O E REVIEW	WDT		12/15/95							
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

GRAPHIC SCALE



SECOND FLOOR PLAN

CA = CONTROLLED ACCESS DOOR
EO = EXIT ONLY DOOR

0 8' 32' 48'
GRAPHIC SCALE

PRELIMINARY
FOR PROJECT DEFINITION STUDY

DESIGNED BY V.D. TOUCHSTONE	6/26/95
DRAWN BY V.D. TOUCHSTONE	6/26/95

NATIONAL BIOMEDICAL TRACER FACILITY FOR THE U.S. DEPARTMENT OF ENERGY

SECOND FLOOR PLAN

RUST International Corporation Birmingham, Alabama
Contract 21-6198

DRAWING NUMBER 24-0012A
REV. NO. A

SPACE ALLOCATION LIST

FIRST FLOOR	45,550 Sq Ft Gross Area (Footprint)
Room Name	Net Area (SF)
Lobby (including stair and elevators)	3154
Public Rest Rooms (2 at 295 SF each)	590
Air Lock	109
70 MeV Cyclotron (Vault 1)	1742
Vault No. 2	144
Vault No. 3	132
Vault No. 4	132
Vault No. 5	121
Vault No. 6	68
Vault No. 7	68
Vault No. 8	283
Vault No. 9	95
30 MeV Cyclotron Vault 10	321
Research and Development Labs (common space)	1217
R and D Lab No. 1	428
R and D Lab No. 2	425
Control Room	683
Secretary	156
Operational Director	309
Drawing Storage	192
Public Corridor	382
Stair No. 2	207
Computer Room 1	172
Computer Room 2	206
Corridor (Stair 2 to lockers)	454
Mechanical	452
Men	189
Men's Lockers	396
Women	308
Corridor and Storage Room (at Women's Lockers)	138
Groundwater Pump Room	207
Waste Chemicals	1833
Air Lock (at waste chemicals)	172
Target Reprocessing	629
Target Storage and Decay	925
Corridor (Lockers to Freight Elevator Lobby)	926
Hot Machine Shop	425
Air Lock (R& D to High Level Labs)	237
Material Storage	389
Open Office	331

FIRST FLOOR (Continued) 45,550 Sq Ft Gross Area (Footprint)

Room Name	Net Area (SF)
High Level Labs (common space)	2391
High Level Lab No. 1	423
High Level Lab No. 2	423
High Level Lab No. 3	423
High Level Lab No. 4	303
High Level Lab No. 5	299
Stair No. 5	207
Solid Waste Storage and Packaging	3338
Long Term Storage	727
Air Lock (at solid waste storage and packaging)	103
Electrical Equipment	1267
Elevator Machine Room	131
Freight Elevator	131
Freight Elevator Lobby	403
Corridor (Freight Elevator Lobby to Stair No. 4)	1412
Air Lock (Medium Level Labs to High Level Labs)	218
Medium Level Labs (Common Space)	826
Medium Level Lab No. 1	379
Medium Level Lab No. 2	380
Air Lock (Medium Level Lab to Access and Removal Space)	369
Electronics & Electrical Shop (includes Tools/Storage)	1268
Groundwater Pump Room	107
Stair No. 4	207
Service Elevator	90
Cold Machine Shop (includes Tools/Storage)	880
Spare Parts and Cyclotron Storage	890
Access and Removal Space	1161
Sampling and Calibration	397
Corridor (at Health Physicists' offices)	141
Health Physicist No. 1	150
Health Physicist No. 2	161

SECOND FLOOR	53,431 SF Gross Area (Footprint)
Room Name	Net Area (SF)
Lobby (includes Break Area, Periodicals, stair and elevators; does not include open space)	1942
Teaching Lab/Lecture Storage	275
Teaching Lab/Lecture	889
Public Rest Rooms (2 @295 SF each)	590
Library Storage and Work Area	216
Library	540
Public Corridor	96
Housekeeping	169
Seminar	244
Video - Conference	247
Stair No. 2	207
Computer	349
Copy Room	166
Office No. 2-1	177
Office No. 2-2 through 2-7 (6 @166 SF each)	996
Stair No. 1	207
Corridor (Stair #1 to Stair #2)	878
Lab Equipment (near Stair #1)	117
Lab Equipment (3 @ 120 SF each)	360
Lab Equipment (@Training Lab No. 3)	157
Lab Equipment (3 @123 SF each)	369
Telephone Equipment	123
Lab Equipment (2 @120 SF each)	240
Low Level Lab No. 1 through No. 3 (3 @485 SF each)	1455
Mechanical	692
Air Shaft (@ Mechanical)	50
Training Lab No. 1 and No. 2 (2@ 483 SF each)	966
Training Lab No. 3	295
Men	210
Women	175
Shipping and Receiving (both sides of fence)	4444
Shipping Office	160
Corridor (Freight Elevator Lobby to Corridor @ West Wing)	639
Chemical Storage	867
Cyclotron Power Supply	2348
Cyclotron Equipment	6794
Large Conference Room	767
Training Director	245
Secretary	176
Research and Development Director	244
Vestibule	170
Small Conference	197

SECOND FLOOR Continued 53,431 SF GROSS AREA (Footprint)

Room Name	Net Area (SF)
Service Elevator	80
Secretary	181
Facility Director	302
Corridor (Lobby to Stair No. 4; includes Serv. El. Lobby	877
Instrumentation Laboratory	499
Lab Equipment (2 @124 SF each)	248
Telephone Equipment	121
Lab Equipment	121
Lab Equipment	150
Synthesis Lab No. 1	487
Synthesis Lab No. 2	295
Stair No. 4	207
Mechanical	665
Air Shaft (@ Mechanical)	59
Corridor (Facility Director to Freight Elevator Lobby)	1080
QA/QC Office No. 1 through No. 4 (4@ 126 ea.)	504
QA/QC Open Office	892
Material Storage	685
Stair No. 5	189
Freight Elevator Lobby	267
Freight Elevator	131
Electrical	1424
Transformer Vaults (4 @257 SF each)	1028
Diesel Generator	143
Loading Dock (Outside; enclosed 3 sides)	665

ıt)

The laboratory area for the processing of the irradiated targets covers in excess of 8100 square feet and is subdivided into 9 individual labs for the segregation of experiments, developmental projects or production. The labs will be designed to be somewhat modular and highly adaptable to accommodate resident researchers or those visiting from industry or academia. This layout can support all of the goals mentioned previously as well as provide secure space for use by industry on proprietary projects. Each laboratory will be furnished appropriately with hot cells, glove boxes etc. to fulfill its mission of production, research or training.

This level has been designed to concentrate all high radioactivity processes to the rear of the building away from the general public and where the most natural shielding exists. Activities in this area such as target processing/reprocessing, waste handling, packaging, and radioactive waste hold up, decay and storage are all segregated from the general population and accessible to selected individuals with proper cardkey clearances.

Production support functions located on this level eliminate long transit distances of radioactive materials. Each area was evaluated against an exposure criteria with extra shielding added where required to prevent any restricted use of space. As an added convenience locker room facilities have been provided for all personnel at this level. The Director of Operations and his staff are located on the first floor in order to maintain hands-on contact with the day to day operations of the cyclotrons. Access to any portion of this floor is gained via a circumferential corridor which precludes entering any space through another area. Entry to the laboratories is via multiple airlocks from the corridor. This arrangement has the advantage of facilitating group tours, a necessity for a national facility of this type. The visitor groups must be escorted by authorized personnel as all sensitive areas are accessible only by cardkey entry doors. The proposed system will limit access to certain areas depending on a person's clearance level prohibiting unauthorized entry into sensitive areas. Inside the plant corridors glass windows have been used, where appropriate, to aid in viewing and instruction.

D.4 RESEARCH and EDUCATION--SECOND FLOOR

The needs of the research and education community are served by the second floor of the NBTF. This area contains four conference/seminar rooms for both formal and informal meetings, a 40 seat teaching/lecture auditorium, multiple laboratory spaces for training and synthesis of new products, office space for research and academic staff and three directors offices. The NBTF Director, the Research and Development Director and the Training Director are all located on this level. A library and periodical area will service the needs of the staff. To facilitate the research and instruction functions of the NBTF, the second floor is equipped with both teleconferencing and videoconferencing capabilities. Computers in the facility can be either networked to the campus system or independent, depending on the user's requirements.

D.5 MECHANICAL and ELECTRICAL SYSTEMS--SECOND FLOOR

The mechanical the electrical systems for the facility have been designed to provide high reliability and stability of operation. Redundancy has been designed into the facility through duplication of critical components, shared load from multiple equipment components and connection to a redundant power grid. Also, an uninterruptable power supply and emergency diesel generator connected to critical loads such as exhaust systems and control systems is proposed. This will allow the facility to operate under any single point failure and provide for operation of all safety related systems without interruption. As part of this safety consciousness, the facility has been designed as a "zero" radioactivity release facility. All effluents will be closely monitored prior to discharge. All gaseous emissions will undergo two stages of HEPA filtration and single stage carbon filtration to eliminate discharge of any gaseous or particulate radioactivity. All liquid wastes will be contained locally, checked for radioactivity and/or toxic waste and either discharged directly or diverted to waste hold up tanks for decay or other disposal route. For long lived radioactivity provisions have been made for transportation and long term storage or destruction at either the Barnwell, SC. or Wake County, NC. disposal sites or in Kingston, Tennessee. Chem- Nuclear, a RUST affiliated company, in collaboration with Coleman Research Corp. will handle the waste disposal aspects for this facility.

D.6 ENERGY CONSERVATION

Energy conservation is an important consideration for any facility but especially so for a DOE installation. Careful selection of architectural materials coupled with high efficiency mechanical and electrical systems assures a low BTU per sq. ft. per year consumption rate. To meet Model Energy Code and 10 CFR 435/436 requirements items such as high efficiency chillers, variable speed primary/secondary loop pumping systems, variable speed fans where applicable, high efficiency lighting, energy management systems, exhaust air heat recovery and more will contribute to energy conversation while providing a pleasant operating environment and meeting all process specific needs.

The NBTF is contiguous to the UAB Campus chilled water loop. During Phase II design studies, life-cycle cost analyses will be performed to determine the best system for chilled water supply in the building. For much of the higher temperature chilled water requirements of the NBTF, chilled water return flow from the Bevill Biomedical Research Building will be analyzed for this use, thus avoiding new chilled water demand capacity while better utilizing existing, installed loop capacity.

D.7 MATERIALS FLOW

Flow of material into and out of the facility is controlled at the second floor loading dock which is at grade at the rear of the building. All materials are bar-coded and tracked through the facility. The shipping and receiving area has been designed to segregate incoming and outgoing products and accommodate multiple shipments of materials daily. A freight elevator has been located at the shipping dock to facilitate movement of materials between the two floors. Provisions have been made in this area for personnel to handle transportation and shipping, health safety control, and QA/QC related functions.

D.8 COST AND SCHEDULE

In view of the intolerance that has been experienced lately for cost overruns, notably with the SSC, we have endeavored to make all estimates for the cost of construction as conservative as possible. In getting quotes from vendors and suppliers of equipment, we have made no attempt to get the "best" price for any item. In addition, we have made very conservative assumptions regarding shielding, building codes, regulatory hurdles, etc., in order to provide the most realistic time and cost schedule. We also included a $3 million dollar add-on in the construction estimate to provide a cushion in our estimate for unforeseen problems and costs.

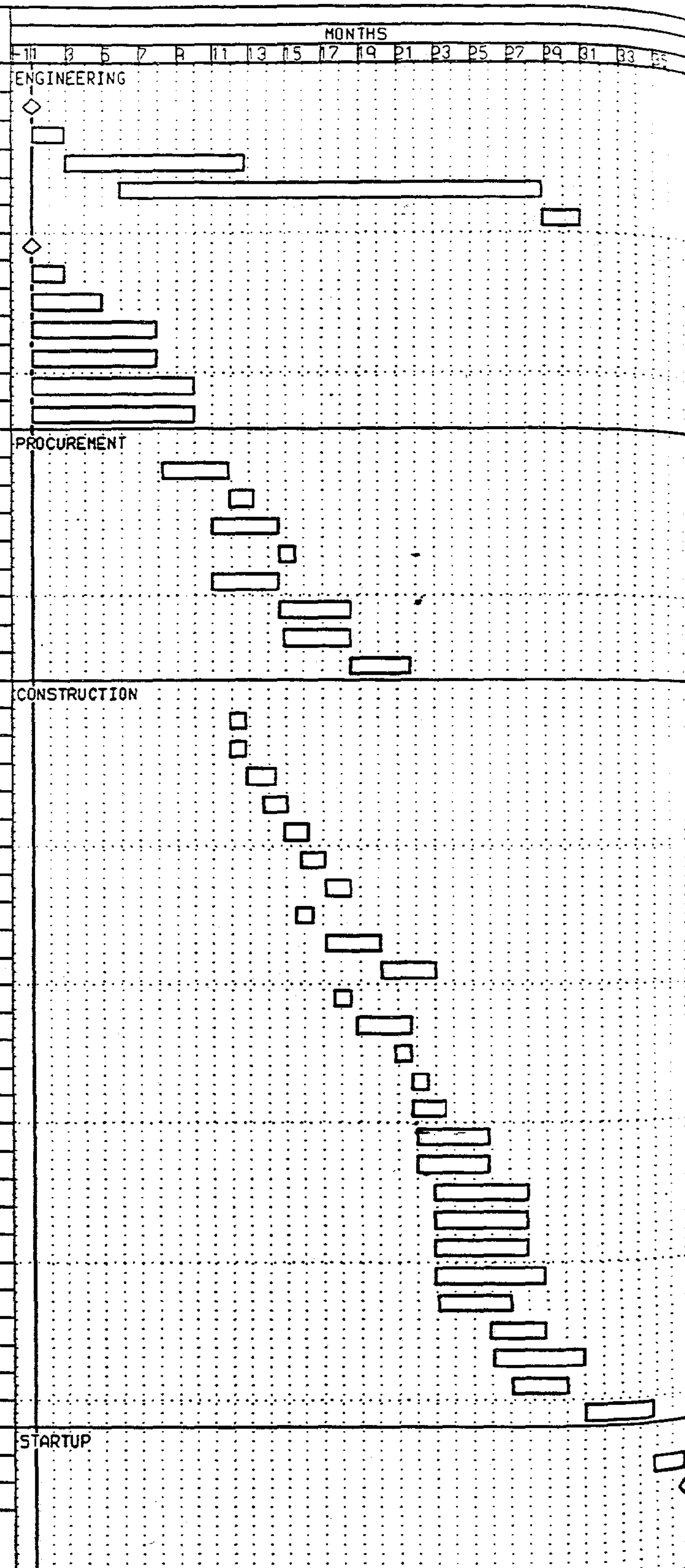
The cost estimate for this facility was developed from the preliminary plans, vendor quotations for certain equipment and systems, historical cost data for those items sufficiently detailed and/or cost estimating allowances. The overall facility cost is estimated at $82,528,416. The cost was calculated for Birmingham, Alabama in 1995 dollars, non-escalated through the construction period. This approach was used due to the uncertainty of the actual construction start date.

The 36 month construction schedule for the NBTF is driven not by physical constraints but by cyclotron delivery. The attached schedule represents construction based on cyclotron delivery approximately 29 months after project start. All design and construction activities that can be performed prior to actual cyclotron selection and delivery will be performed during this period. This procurement duration is an average of times submitted by both EBCO of Vancouver, B. C. and Ion Beam Applications, IBA, of Belgium for cyclotron delivery. Due to the long lead time for cyclotron delivery but early requirement for facility design information, the entire design/construction duration is extended. Should the manufacturers be able to compress their delivery schedule the entire construction sequence may be shortened resulting in construction and financing cost reduction.

Budget information removed - pp. 67-79

NBTF--PROPOSED CONSTRUCTION SCHEDULE

ACTIVITY ID	ACTIVITY DESCRIPTION
	ENGINEERING
100	NOTICE TO PROCEED TO CYCLOTRON VENDOR
105	REQUIREMENTS DEFINITION - CYCLOTRON VENDOR
110	SYSTEM DESIGN - CYCLOTRON VENDOR
115	CYCLOTRON MANUFACTURING & TESTING
120	CYCLOTRON SHIPPING
125	NOTICE TO PROCEED - E/P/CM CONTRACTOR
130	SPEC,BID,AWD, RECV SOILS REPORT
135	CIVIL DESIGN
140	STRUCTURAL DESIGN
145	ARCHITECTURAL DESIGN
150	ELECTRICAL/CONTROLS DESIGN
155	MECHANICAL/PIPING/HVAC DESIGN
	PROCUREMENT
160	ASSM/APPV/BID/EVAL/APPV/AWARD SITE DEV PKG
170	SITE DEV CONTRACTOR PROCURE MATERIALS
175	ASSM/APPV/BID/EVAL/APPV/AWARD CONCRETE PKG
180	CONCRETE CONTRACTOR PROCURE MATERIALS
190	ASSM/APPV/BID/EVAL/APPV/AWARD STR STEEL PKG
195	STEEL CONTRACTOR PROCURE & DELIVER STEEL
205	ASSM/APPV/BID/EVAL/APPV/AWARD GEN CONTR PKG
210	GENERAL CONTRACTOR PROCURE MATERIALS
	CONSTRUCTION
163	MOBILIZE CONSTRUCTION MANAGER
165	MOBILIZE SITE DEV CONTRACTOR
220	DEMOLITION OF PARKING LOTS & STRUCTURES
225	INSTALL SHEET PILING
230	EXCAVATION AND DEWATERING
240	INSTALL BUILDING PILING
235	UNDERGROUND UTILITIES AND DRAINS AND TIE-INS
185	MOBILIZE CONCRETE CONTRACTOR
245	BUILDING FOUNDATIONS & CONCRETE WALLS
255	BUILDING ELEVATED FLOORS AND FOUNDATIONS
200	MOBILIZE STEEL CONTRACTOR
250	ERECT BUILDING STEEL
215	MOBILIZE GENERAL CONTRACTOR
270	INSTALL ELEVATORS
260	BUILDING ROOFING
275	SET & INSTALL MAJOR EQUIPMENT
280	INTERIOR ROUGH-IN AND FRAMING
285	INSTALL PLUMBING & PIPING
290	INSTALL HVAC SYSTEMS
295	INSTALL FIRE PROTECTION & SUPPRESSION
300	INSTALL ELECTRICAL,LIGHTING, & COMMUNICATIONS
265	EXTERIOR ARCHITECTURAL
305	INSTALL INSTRUMENTS & CONTROLS
310	INTERIOR ARCHITECTURAL & FINISHES
315	FINAL GRADING, PAVING, & LANDSCAPING
320	CYCLOTRON INSTALLATION
	STARTUP
325	ACCEPTANCE & COMMISSIONING
330	PROJECT COMPLETE



Plot Date 9JAN95
Data Date 2JAN95
Project Start 2JAN95
Project Finish 4JAN98

Activity Bar/Early Dates
Critical Activity
Progress Bar
Milestone/Flag Activity

NBTF — Sheet 1 of 1

NATIONAL BIOMEDICAL TRACER FACILITY
PROPOSED PROJECT SCHEDULE

Date	Revision	Checked	Approved

D.9 RUST INTERNATIONAL

RUST International possesses expertise in all disciplines required for the successful completion of this project from Project Definition Study through facility decontamination and decommissioning. Careful attention to detail during the development of the basis of design, with the client, industry and academia, and use of an integrated approach to facility design will assure meeting program requirements. As part of RUST's ISO 9001* compliance procedures constructability reviews will help assure construction problems and delays are minimized and prevent cost overruns. As Engineer/Construction Manager, RUST will ensure facility construction will meet not only the plans and specifications but also the intent of the client. RUST consistently ranks in the top 20 design/construct firms in this country. The latest available ranking by *Engineering News Record* of the top 500 design firms places RUST No. 12 overall.

RUST has a long history of serving the needs of industrial, institutional and governmental clients including the U.S. Department of Energy. For 24 years through 1990 RUST performed construction management, construction activities, remediation and miscellaneous engineering design services for the three plants at Oak Ridge National Laboratory. Peak employment during that period reached 2100 people involved in Title I and Title II services for projects covering design and construction for both existing and new facilities. Examples of the work are design and construction of radioactive and chemically contaminated areas, sophisticated piping and instrumentation work, large concrete pours, clean rooms, security and monitoring systems, and remediation and waste prevention of both high level and low level areas. This work was performed under FAR, DEAR, and EPA regulations as well as the DOE approved Cost Schedule Control System (CS^2) reporting system. RUST implemented an ANSI/ASME NQA-1 program for the site. Work on the Oak Ridge Facility was recognized by the DOE with six consecutive Awards of Excellence for Environmental Safety and Health and received the "Superior" rating in Quality Assurance. RUST also received six National Safety Awards, five Awards of Honor and one Award of Merit, six consecutive DOE Small Business Awards, four Disadvantaged Business Awards and numerous other citations during this period. Over 5 million employee workhours were completed without a lost time case.

RUST works hard to maintain its outreach to the local small business and small disadvantaged business community having received both the Corporate Award and Award of Appreciation from the U.S. Small Business Administration for work in this area. RUST was selected as the Southeastern Regional winner of the Majority Private Sector Firm of the Year Award in 1991. RUST is dedicated to exceeding small business and small disadvantaged business goals.

Other DOE projects in which RUST has been involved include the Paducah, KY. Gaseous Diffusion Plant, the Portsmouth, OH. Gaseous Diffusion Plant, and the Feed Material Production Center at Fernald, OH. As construction manager for these projects RUST was involved with all aspects from conventional construction to specification, design, and installation of highly sophisticated systems and equipment. RUST possesses the necessary expertise to provide the integrated design for the NBTF. RUST is presently the construction manager for the Advanced Photon Source Facility at the Department of Energy's Argonne National Laboratory. As construction manager, RUST is managing the construction contracts, the installation of the technical components, machinery and support utilities, value engineering studies, cost estimates and analysis of contractor's pricing proposals, as well as development and implementation of the Quality Assurance Program, and development of a comprehensive Environmental, Safety and Health Assurance Program (ES&H). The project is on schedule and within budget for a 1995 completion. This long, successful association between RUST and the Department of Energy will serve the NBTF Project well.

---

* Validation Audit concluded Jan. 20, 1995

E. Environmental, Safety, and Health Considerations

We developed our recommendations on ES&H matters after extensive discussions with our contractors, members of our advisory committee from National Laboratories, and the commercial vendors.

Waste Disposal - We have studied the waste disposal issue in depth and have made several recommendations on the proper facility design to minimize the waste handling and disposal issue. Waste minimization has to be built in to the design, including supercompaction. Storage has to be adequate to enable the NBTF to operate on a decay and discard principle, rather than disposing of all radioactive trash as low level radioactive waste. In this regard, we discovered that the Southeast Compact is the only radioactive waste compact in the U.S. that has a functioning disposal site. We believe that the new site for the waste depository, slated for opening in 1996 or 1997, is farthest along in development and we understand that no substantial objection has been raised to this facility. If the NBTF were to begin construction today, the only sites that could be considered are in the Southeast region, based upon that region's ability to dispose of low level radioactive waste.

ES&H Construction Regulatory Issues - We have outlined the regulations that would apply to the NBTF. In spite of the fact that accelerators are regulated at the state level, we have determined that the use of federal funds to construct the facility expanded the scope of regulatory review. This includes regulations concerning air and water releases. This will obviously have an impact on the timelines and cost of this phase of the construction. At the state level, the cost and time are not significant. At the federal level, we have determined that an Environmental Impact Statement is required. This will result in a substantial commitment of time and money.

ES&H Operational Regulatory Issues - This facility would be operated under the supervision of the state regulatory authority unless it was constructed at a national laboratory. We have determined that there are significant resources within the national laboratory system that could be drawn upon to construct an effective and efficient ES&H "culture" at the NBTF. The experience of the labs in coming into compliance with all applicable Federal, State and Local regulations has also provided us with a model for training of the workforce at the NBTF. Our advisory committee strongly recommended that the NBTF not be located at a National Laboratory, in part due to excessive and redundant ES&H factors.

The following Environmental, Safety and Health (ES&H) considerations were evaluated during the course of the NBTF Project Definition Study. They include a review of the relevant federal, state and local regulations; a recommendation for minimum standards of training for workers at the NBTF; and an analysis of waste generated and waste disposal with a focus on radioactive waste.

E.1 Environmental, Safety and Health Regulations and Training.

E.1.1. Identify and describe the primary ES&H issues for the NBTF

The main ES&H issues for the NBTF include:

- limiting releases of radioactive and hazardous materials to the environment including air emissions and sewer releases;
- minimization, management, and proper disposal of radioactive, mixed (radioactive/chemical), toxic and hazardous wastes;
- proper transportation of radioactive materials, both product and waste;
- training of all personnel involved with the NBTF mission;

- maintaining internal and external radiation doses As Low As Reasonably Achievable (ALARA);

- maintaining inventory and control of radioactive materials, including sealed sources and waste; and

- proper radiological control supervision.

These issues must be reviewed in association with environmental statutes pertinent to proposed operations. The following are environmental statutes that we will consider in the review of the NBTF and its operation:

STATUTE:	REFERENCE:
Medical Waste Tracking Act of 1988	40 CFR 259
Clean Water Act	40 CFR 100 - 140
Toxic Substances Control Act (TSCA)	40 CFR 701 - 720
TSCA - PCBs	40 CFR 761
TSCA - Asbestos	40 CFR 763
DOT Regulations	40 CFR 170- 173
Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)	40 CFR 150-189
Safe Drinking Water Act (SDWA)	40 CFR 141-143
Spill Prevention, Containment and Control Act (SPCC) Plan	40 CFR 112
Superfund Amendments and Reauthorization Act (SARA) Title III	40 CFR 355-372
Clean Air Act (CAA)	40 CFR 1-99
Resource Conservation and Recovery Act (RCRA)	40 CFR 240-280
Comprehensive Environmental Response, Compensation and Liability Act (CERCLA)	40 CFR 300-302
Occupational Health and Safety Administration (OSHA)	29 CFR 1910.1200
Hazardous Waste and Emergency Response Operations (HAZWOPER)	29 CFR 1910.120
Chemical Hazard Plan	29 CFR 1910.1450

The following DOE orders outline other recommended environmental, safety, and health requirements:

- DOE Order 5480.1B, Environmental, Safety, and Health Program for the Department of Energy Operations.

- DOE Order 5480.4B, Environmental Protection, Safety, and Health Protection Standards.

- DOE Order 5485.1, Environmental Protection, Safety, and Health Protection Information Reporting Requirements.

- DOE Order 5400.1, General Environmental Protection Plan.

E.1.2. Identify, describe and address the primary ES&H issues for the operations of an NBTF.

The main ES&H issues for the NBTF include:

- the regulations in Section 1.;
- issues specific to an accelerator facility including radioactive activation of materials and components;
- handling, packaging and shipment of short-lived, intensely radioactive materials produced in the accelerator; and
- other hazardous material, chemical, or life-safety considerations.

The following are additional topics that we will review relative to environmental compliance. Generally, these issues are indicative of a proactive contractor.

- 1990 Clean Air Act Amendments
- Hazardous Waste Generation/Waste Minimization/Pollution Prevention (P^2)
- Self Assessment Program
- NEPA Document and Review -Required for the NBTF
- Management Systems for environment compliance (e.g., Communications, Regulation Tracking, Training, Emergency Response, Site Management, Lessons Learned, Conduct of Operations, Resource Allocation, Records Retention, Audits, Etc.)

E.1.3. Radioactive gases (e.g. $^{15}0$) may be produced in the vault and hot cells. What are the new Air Emission Standards re. radioactive gas emissions? What needs to be included in the facility for containing these gases?

Air Emission Standards for radioactive emissions include the following:

- DOE radioactive air effluent guidelines (10 CFR 834) - These concentrations correspond to a dose for 100 mrem/yr and are not necessarily meant to be used as "limits";
- EPA radioactive air effluent limits - NESHAPs (40 CFR 61, Subpart H) - These regulations are based upon limiting the dose to the public to a total of 10 mrem/yr and a sub-limit of 3 mrem/yr from radioiodines;

During our study, we did not find any requirements or mandate for an air emission stack, but it may be desirable to have one to meet the effluent dose limits. This determination will be dependent upon the isotopes and their respective activity levels expected to be released, and the location of the facility with respect to neighboring buildings. Due to the short half-lives of many of the expected radioactive effluents, it may be very helpful to have a temporary holding tank, charcoal filters, or some other delayed release system. This decision will require further information and analysis and may need to be addressed in Phase II.

The following rules and regulations also will be reviewed relative to the construction and operation of the NBTF:

- 1990 CAA Amendment Section 112 (q) (2-3), Radioactive Isotopes.
- SARA Title III Section 313.
- Applicable DOE orders, in particular 5480.11 & 5482.2

E.1.4. What specific regulations need to be examined relative to the construction and operation of the NBTF.

Federal Rules

A) EPA Regulations:

- National Air Emissions Standards for Hazardous Air Pollutants (NESHAPs) for radioactive emissions from DOE facilities (40 CFR
- RCRA regulations applicable to hazardous and mixed waste.

B) DOE Regulations

- Nuclear Safety Management (10 CFR 830);
- Radiation Protection of the Public and Environment (10 CFR 834);
- Occupational Radiation Protection (10 CFR 835)

C) Department of Transportation (DOT) Regulations

- Hazardous Materials Regulations (49 CFR parts 100-177).

D) Food and Drug Administration (FDA)

- Radiopharmaceutical manufacture

  Radiolabeling - 21 CFR 201.57, 21 CFR 310.503

  GMP - 21 CFR 211.170, 21 CFR 312.23

State Regulations

- Radioactive Material Generation and Disposal, Dept. of Public Health, State of Alabama
- Registration of Accelerator, Dept. of Public Health, State of Alabama
- Application for Air Contaminant Source, Dept. of Environmental Management, State of Alabama.

DOE is making a transition between its older DOE Orders and regulations published as part of the Federal Register and codified in the Code of Federal Regulations (CFR). The following changes are being made:

DOE Order		------------------> CFR
5700.6C	Quality Assurance	10 CFR 830 Nuclear Safety Management
5400.5	Radiation Protection of the Public and the Environment	10 CFR 834 Radiation Protection of Public and the Environment
5480.11	Radiation Protection for Occupational Workers	10 CFR 835 Occupational Radiation Protection

10 CFR 830 and 10 CFR 835 have been published as Final Rules in the Federal Register and 10 CFR 834 has been published as a Proposed Rule in the Federal Register. The current status of Part 834 is unclear to us at this time.

Other similar documents which may be relevant to the design and operation of the NBTF include:

DOE Radiological Control Manual (DOE / EH-0256T) - This manual provides a base document for programmatic guidance for radiological control programs in the DOE system. The guidance is mostly general in nature but some important specific requirements are included. There is a requirement that each facility develop their own site-specific "RadCon Manual" based upon the DOE document.

DOE Guide to Good Practice - SLAC-327 Health Physics Manual of Good Practices for Accelerator Facilities (Stanford Linear Accelerator Center)

DOE Orders

1540.1 Materials Transportation and Traffic Management

1540.2 Hazardous Material Packaging for Transport

5480.3 Safety Requirements for the Packaging and Transportation of Hazardous Materials, Hazardous Substances, and Hazardous Wastes

5480.19 Conduct of Operation Requirements of DOE Facilities

5480.2 Personnel Selection, Qualification, Training and Staffing Requirements at DOE Reactor and Non-Reactor Facilities

5820-2A Radioactive Waste Management

DOE Implementation Guides (in various final and draft forms) for use with 10 CFR 835 - cover topics including external and internal dosimetry, occupational ALARA programs, record keeping, training, radiation-generating devices, sealed sources, and posting.

National Council on Radiation Protection and Measurements (NCRP) - NCRP Report No. 51 Radiation Protection Design Guidelines for 0.1 - 100 MeV Particle Accelerator Facilities

E.1.5 ES&H Training Requirements for an NBTF.

DOE provides guidance for training at DOE facilities. The guidelines are found in Conduct of Operations DOE 5480.19, at DOE facilities and are based on accepted industrial practices. The guidelines were written to help facilities in meeting performance and safety objectives. DOE order 5480.20A, Safety of Nuclear Facilities would also apply. Training guidelines for the NBTF facility can be found in DOE order 5480.19, and DOE order 5480.20A.

Training for hazardous waste and chemical workers is required under several different laws. Environmental managers have the responsibility for identifying and implementing the environmental and safety training required by each law and regulation.

OSHA, EPA, and US Department of Transportation (DOT) administer the following laws/regulations which describe training requirements:

- OSHA's Hazardous Waste and Emergency Response Operations (HAZWOPER) (e.g., 29 CFR 1910.120);
- OSHA's Hazard Communication Standards (HCS), or "worker right-to-know";
- OSHA's standard on Process Safety Management of Highly Hazardous Chemicals (PSM);
- EPA's Resource Conservation and Recovery Act (RCRA), which requires employee training by hazardous waste generators that accumulate hazardous waste;
- EPA's Spill Prevention Control and Countermeasure (SPCC) plan's training requirements for facilities that store certain oil quantities; and
- DOT's training requirements for hazardous materials workers.

DOE has shipping/transportation training for hazardous/radioactive materials available to the DOE "family" through the Transportation Management Division (TMD). They provide training free of charge according to an annual publishing schedule.

DOE appears to require training based upon the situations, materials, and work areas a worker will encounter. Training requirements do not appear to be based on the status of the worker (i.e., not upon the full time/part time and/or temporary/ permanent worker's status).

For General Employee Radiation Safety Training, DOE describes different categories of workers, and corresponding training requirements in the Radiological Control Manual and in the Training Implementation Guide for 10 CFR 835. The categories are Radiation Workers I & II, Radiological Technicians, and Radiological Technician Supervisors. The specific training requirements are spelled out in these documents and may include significant formalized training. Visitors will be required to receive at least some basic site-specific orientation and training dependent upon areas of the facility visited and whether or not they are escorted by trained facility personnel.

E.1.6 How would we recommend that ES&H be taught?

It is recommended that initially the NBTF utilize private sector contractors that offer training for DOE contractors. The following are some of the entities which provide training to DOE contractors:

- Oak Ridge Institute for Science and Education (ORISE)
- Training Academy,
- ACME Environmental,

- Ceri,
- UNM, and
- TVI.

It will probably be necessary to develop an in-house training capability at some later date, especially if transient researchers and workers are expected to utilize the facility on a fairly regular basis.

It is recommended that the ES&H training program and requirements for the NBTF cover, at a minimum, the following topics for staff:

- Activities Planned and Authorized
- Safety Requirement Compliance
- Radiological Requirement Compliance
- Chemical Carcinogen Program
- Hazardous Material Safety Program
- Safety Equipment Availability
- Actions to Mitigate Spills
- Eating, Drinking and Smoking
- Backup Instrumentation Usage
- Verbal Communications
- Procedure Adherence
- Plant Security
- Appropriate Knowledge for Assigned Duties
- In-House and Industry Operating Experiences
- Equipment and Instrumentation Proficiency
- Lockout/Tagout
- Shift Hand-off
- Conduct of Operations
- Reporting Unusual/Off-Normal Occurrences
- Continuous Quality Improvement

E.2 Radioactive Waste Handling

E.2.1 Introduction

In the course of our study, we spent a considerable amount of time addressing ES&H issues. Among the most critical of these was the issue of radioactive waste disposal. We confirmed that only the UAB group was located in a radwaste compact that had a functioning disposal site, operated by Chem-Nuclear Systems, Inc. In addition, the Southeast compact was closest to opening the disposal site for their long-range waste disposal. Given the constraint on radioactive waste disposal, it is not clear that the NBTF could be built outside of the Southeast Compact.

Chem-Nuclear Systems, Inc. (CNSI) was requested to prepare a scoping study for the handling and disposition of radioactive waste from a proposed NBTF. The study was prepared for the RUST International Corp., who is the designated Architect-Engineer for the UAB team for this project. The facility would be located at the University of Alabama at Birmingham and be designated as the National Biomedical Tracer Facility (UAB-NBTF). The scope of the work was to identify the technical details and best proposed solutions for the handling, storage transportation, and ultimate disposal radioactive wastes arising from the isotope production processes being performed at this facility.

The study presented herein, examines the general aspects of this process and makes recommendations relative to specific design and operational considerations for radioactive waste disposition for this proposed facility. The recommendations were based on specific questions and estimates developed by RUST relative to the facility size and the volume of waste that would be produced.

This study presents a general overview of recommendations for the radioactive waste disposition; an analysis of federal and compact regulations for storage, transport, and disposal; and a summary discussion of the current status of a key problem --- the near term availability of a disposal facility.

E.2.2 Technical discussion

i. General Considerations

The NBTF is envisioned as a joint academic research and training/production facility which will produce a wide variety of radioactive isotopes for biomedical applications. The facility will utilize a proton accelerator for production purposes and these radionuclides will be processed in radiochemistry laboratories. As with all research and industrial processes, some waste material is produced. The waste arises directly from the production process and are generally called **process waste**. There would also be waste generated from the ancillary operations and this is generally called **process trash**. Finally, a contingency for waste arising from minor accidents, spills, etc. is generally made.

Typically, processes involving production by accelerators are comparatively clean relative to reactors. With reasonable precautions and well thought out, comprehensive operating practices, the waste arising as trash from ancillary operations can also be reduced to comparatively small quantities. Also, a large percentage of medical isotopes have short half-lives. Short term storage will decay the material down to levels where disposal in a landfill is permissible. In summary, it is believed that the amount of radioactive waste requiring shipment off-site for radioactive disposal can be reduced to relatively small volumes. There will be waste generated which is contaminated with longer lived isotopes, where storage to enable decay to non-radioactive categorization will not be feasible. We have manipulated this list of isotopes to illustrate several other key parameters related to transportation and disposal. This information is presented in Table E.1.

Table E.1. Baseline Estimates of NBTF Process Waste

Isotope	No. drums/yr.	Half-life	Full Decay (4.5 half-lives)
Na - 22	4 - 20	2.602 yr.	11.7 yrs.
Co-57	10	270 days	3.3 yrs.
Ge-68	10	287 days	3.6 yrs.
Sr-85	20	64.7 days	0.8 yrs.
Cd-109	8	453 days	5.6 yrs.
Tl-204	10	3.80 yrs	17.1 yrs
Total	**62-78**		

The baseline information presented in Table E.1, was used for the remainder of the study.

ii. Waste Handling

Limiting the maximum activity level within each drum to 5 mCi or less easily permits direct contact handling and minimizes the need for any local shielding during storage or handling. The fundamental handling operations performed at the facility will be:

- **Drum handling**---movement of 55G drums between compaction area, storage area and out of the facility.

- **Drumming operations**---typically, closing, radiation measurement and smearing, marking and labeling, preparation for shipping.

- **Compaction (optional)**---compaction within the 55G drum to reduce volume.

- **Waste sorting/counting (optional)**---use of counting table to segregate non-radioactive waste to reduce disposal/storage volume.

The budgetary cost of the major supplies and components is as follows:

- **Drums (Spec 7A)**---working space---2 ft. sq. x 3 ft. high --each
  steel----~$80 each
  poly----~$250 each (only for corrosive materials and liquids)

Note: Assumed that the bulk of the waste is dry and inorganic---if there is a possibility of excessive gas generation, affected drums should be outfitted with NFT filter at a cost of ~$100/drum.

- **Labeling/Marking supplies**
  ~$500 annually

- **Trash compactor**---equipment space--allocate ft. x 8 ft. (base) x 8 ft. high
  $25,000

- **Waste sorting table**---equipment space---allocate 5 ft. x 10 ft. base x 6 ft. high
  ~$75,000

Additional information on this equipment is available from suppliers. Further detail will be developed in the next phase of the NBTF development.

iii. On-site Storage

There are a variety of ways waste drums can be stored. Storage space options include:

1. **dedicated storage room**

2. **dedicated storage building**

3. **storage trailer**--(Sea-Land or equivalent)

4. **concrete storage vaults** (prefabricated)

The selection of the optimum method will depend upon other facility constraints and considerations and economic tradeoffs. At present, the simplest option is to assume that storage is available within a dedicated portion of the process building.

The storage philosophy will be based upon segregation by radioisotope to simplify storage for decay. The level at which slightly contaminated waste can be "free-released" for disposal will be determined between the operator and the cognizant regulatory agency. As an upper limit, the U.S. DOT regulations in 49 CFR 173.403(w) define radioactive material--from a transport consideration-- as a specific activity of 0.002 microCuries/gm or less. The following estimate shows that the average drum concentration of 5 mCi/drum corresponds to a value 20-25 times higher. Hence from a shipping standpoint, about 4.5 half-lives of decay is required to reduce the activity below the DOT limit.

5 mCi/drum x 10^3 microCi/mCi x 1/ (~250 lb/drum x 454 gm/lb) = 0.045 microCi/gm;

(0.045/0.002) micro Ci/gm = 22.5 times; 2**4.5~22.5 or 4.5 half-lives

Segregation of waste would probably be in three zones or storage areas. The first would be those which decay down in 60-90 days or less. The second would be for a "decay-down" period of 1-2 years or less; and the third would be for the remainder of the contaminated waste. In some cases, waste in the third group would need to be processed and disposed of to meet RCRA regulations.

The baseline data indicate that ~62 to 78 drums will be generated annually and the intent is to ship waste off-site on a quarterly basis. Since a typical Sea-Land container holds at least 80 drums an annual shipment would probably be more economical. However, shipment of 12-20 drums quarterly, could be accomplished with a far smaller vehicle.

The key question to the definition of adequate disposal space is the availability of a Southeast low-level waste compact disposal facility. Alabama is a member of the Southeast Compact. Currently, a site has been selected and facility licensing is underway for construction of a facility in North Carolina. This facility, which is in close proximity to Raleigh, NC is scheduled to open in mid-1997. Recognizing the tremendous pressure associated with the approval and construction of these facilities requires that provision be made for considerable delay in its opening. Most large generators of Low Level Radioactive Waste (LLRW) provide for about five years of storage. However, due to the nature of the waste arising at the NBTF, there are other options available and storage of 300-400 drums is probably excessive.

A more realistic design value for storage is 150-175 drums, or about a two year inventory. A reduced storage inventory is feasible for the following reasons:

- **Decay**---approximately 20-30% of the drums will have decayed down to free release levels after two years.

- **External processing**---services are available to reduce volume by sorting, super compaction, or incineration. The latter option, which is the most costly, can reduce drywaste volumes 50-100 times. The service is available at ~$750-1000/drum ($3.70/lb) at SEG's facility in Kingston, Tenn. Similarly, liquid wastes can also be burned at DSSI in Kingston, Tenn. at a cost of ~$70-100/gal.

- **Other options**---Internal measures can be taken to reduce waste or find improved means of segregation and preparation to reduce the total quantity of waste to be stored. Also possible is "outside" storage or storage at a LLRW broker facility.

Using the previous quantity assumptions, a floor layout of a storage space was made. As always, a key tradeoff is ceiling height vs. floor space. Spec 7A, 55G drums can be stored as high as 5 levels, which requires a ceiling height of 18-20 ft. (considering palleting). A reasonable assumption is 3 tier stacking, which requires a ceiling height of nominally 12 ft. (**Note:** two level stacking is possible within a 8 ft. ceiling, but requires about 50% more floor space). The LLRW storage/handling and handling room is illustrated in the floor plan. The ceiling height of this room is sufficient to handle stacking 5 high.

E.2.3 Responses to Specific Questions

Several questions relative to the facility design and waste handling practices were developed during the study. This section addresses these questions:

Q1 What type of equipment would be specified for dry waste compaction, primarily in drums? How large an area would be required for this operation and what does the equipment cost? Can a preliminary layout be provided?

Answer Information on trash compactors used for trash compaction for dry active waste is a topic for investigation in the next phase of the NBTF development. Basically, a typical cost for a utility system would be ~$25K. The system would compact within a 55G drum and reduce the waste volume by 3-5 times. The final waste density would be about 30-35 lb/CF and the drum would weigh in the 180-250 lb. range. The spatial envelope required for the compactor is about 8 ft. square with an 8 ft. height.

Additional disposition of this DAW could include either supercompaction, which would reduce the volume by an additional 50% or incineration---which reduce the volume 10-50 times depending on the percentage of organic materials (which is normally 90-100% of the total).

Q2 What cost should we include for containers and the cost of disposal? Is the Wake county (SE disposal compact) site still on schedule?

Answer As noted in the report---disposal drums, assumed to be standard 55G drums should be qualified as Spec 7A containers to simplify DOT shipping requirements. The cost of these containers is about $80 and $250 each, respectively for steel and poly drums.

The current best estimate for disposal in the Wake County, NC LLRW Disposal site will be in the $500/CF range. This estimate has a 25% tolerance due to the uncertainty surrounding the opening date of the facility. The earliest published date for the opening of this facility is mid-late 1996. However, for a conservative planning basis, start up dates as late as the year 2000 could be projected which would be in line with the opening of the NBTF.

Q3 What kind of special equipment may be required for radwaste handling and what do they cost, (i.e. liquid waste, gaseous decay, etc.)

Answer Typical radwaste handling equipment relates to the handling of 55G drums. This would include fork lifts, small jib-cranes, possibly storage racks if multi-layer storage is envisioned, and tools for loading and capping of the drums. This would be per standard catalog pricing.

Special equipment for liquid waste would primarily be concerned with corrosion and possibly fire protection. For highly acidic wastes, poly drums should be utilized. For most wastes generated at the NBTF steel drums would be adequate. The facility design would place the drums on a steel pan or else epoxy coat the concrete floor and have a means of diverting any spills to a lined floor drain for collection and sampling. Long term storage of wet organic materials leads to a gas buildup and pressurization of the drum due to decomposition. This is solved by screwing a carbon filter/vent into the drum. This filter permits venting of the waste gas as the decomposition occurs, with no drum pressurization and no release of particulate material. These filters are supplied by NFT and cost ~$100 each.

Q4 If onsite storage is required what would be the time frame and are there any special requirements for storage of wastes, i.e. total activity, types of wastes, half-lives, etc. that may preclude differing waste storage in the same location.

Answer In the current situation, considering the amount of uncertainty in new disposal site opening, a planning basis of five years storage should be an upper limit. Provision can still be made for off-site processing such as incineration or supercompaction. Efficient and safe storage of the waste is primarily an engineering--not a regulatory decision. Due to the differences in half-lives, it would be prudent to segregate short, intermediate, and long half life wastes. These definitions are arbitrary, but would be based on the time period for transition to a "non-radioactive" status. Other considerations would relate to handling ease, general industrial safety and fire hazard, structural stability, etc.

Q5 In the area of shipping, what types of transportation are typically used, size of truck etc.? Are there restrictions on quantities per shipment or types of waste per shipment that my necessitate certain storage schemes? What are typical costs for transportation?

Answer Transportation is normally via a closed van, "Sea-Land" container size (8 ft. x 8 ft. x 40 ft. long for the van). This size typically holds a minimum of 80 55G drums. However, per DOT regulations, the key parameter is if a dedicated radioactive material shipment is required. Hence, in limiting conditions even rag top, small flat bed trucks or step vans could be used--but the shipping economics would be poor. Traditionally a fork lift could be used to move a pallet of 6-12 drums from the shipping dock to the inside of the closed van.

The route from Birmingham to either the Wake county disposal site or the Oak Ridge, TN. area for processing can all be driven on interstate highways for everything except the first and last few miles of the trip. This should simplify travel logistics. Restrictions are based on the truck capacity and the legal highway truck weight for the shipment. The 80,000 lb LWT limit for travel on the related interstate highways would never be exceeded for the quantities and types of drums envisioned for this project. Current tariffs are based on a $/cwt basis. For a loaded van, the tariff costs would probably be in the $3-3.50/mile range and $1.00-1.50/mile for the return trip--if needed. This is a small cost relative to disposal at the present time.

Q6 What special labeling requirements are needed and what special equipment and at what cost would be required?

Answer The response to this questions could be extremely lengthy. It is sufficient to note that these requirements are spelled out in considerable detail in the DOT regulations (49 CFR 172-173) and are known by cognizant HP Technicians at the facility or the services of an approved LLRW broker or broker service can be contracted to ensure compliance. CNSI and others offer training in this specific area. The annual cost for labeling supplies should not exceed $500-$1000 per year.

Q7. Do we need secondary containment around temporary holding tanks for radioactive liquids, such as produced from emergency showers?

Answer As a general rule, secondary containment is required for any facility, including holding tanks, containing any hazardous or toxic material. Such containment can be simply a concrete curb or berm of sufficient size to contain the full volume of the tank. For small facilities, prefabricated containment are commercially available. Design and construction of such can be achieved easily and inexpensively.

F. Operational and Organizational Issues

The mission of the NBTF includes three major components: isotope production; research and development; and education and training. The first component can be accomplished nearly anywhere; it is driven primarily by shipping to the customer. The other two components of the mission are more sensitive to location. Our advisory committee was unanimous in recommending that the NBTF not be operated by a national lab. Their reasons included excessive regulation, micromanagement by DOE (both noted in the recent Galvin report as problems), and the lack of a business mentality at the national laboratories. They recommended that another organizational structure be used to run the NBTF. Given its mission, they stated that it should be located at a university.

In soliciting input for this study, we have had the greatest variety of opinion regarding the physical location of the NBTF. Those polled were divided between a setting in an industrial park vs. a location on a university campus. We are convinced that the interaction among faculty, students, staff, and others will be enhanced by proximity to the campus. Further, we think that the NBTF should be located at a university where the medical school and medical center are integrated into the campus. This would provide access for those working at the NBTF to the greatest range of scientific disciplines from basic science (physics and chemistry) through engineering (materials science, bioengineering) and basic medical science (biochemistry, pharmacology) to clinical practice. This would enhance the NBTF as a center for nuclear medicine research and better integrate its activities and focus to radionuclides that have clinical utility. In addition, given its status as a national and international resource, the location should be within 20 minutes of a major airport to facilitate short term visits from interested users as well as same-day shipping. The campus location would also insure that there would be housing close to the site for short and medium term visitors.

We recommend that the NBTF be organized along its mission components. The primary component would be Operations. The operation of the accelerator and target areas; the processing of routine targets; the compliance with all Environmental, Safety and Health Regulations; the packaging and shipping of radionuclides and waste; and the marketing, order entry and other business activities would be handled by this section.

The second component would be Research and Development (R&D). All work in this section would be focused on the NBTF activity, i.e. isotope production. We endorse the IOM panel's conclusion that radiopharmaceutical chemistry research and other research activity should be funded by peer review grants and not NBTF operating funds. This activity would be enhanced, however, by location on a campus in which the greatest range of basic, applied and clinical research is performed to insure that the NBTF staff has daily access to this range of disciplines. We also advocate a formalized program of research activities by sabbatical scientists from academia <u>and</u> industry. The technical staff and equipment necessary to conduct a broad research program in targetry development is already in place at national laboratories and does not have to be duplicated at the NBTF. We advocate instead a strong link to industry and the national laboratories to utilize their resident expertise in targetry development.

The third component, Education and Training (E&T), should be focused on three primary activities. The first is the training and education of the NBTF staff and workers, particularly with respect to environmental, safety and health regulations. The second is the education and training of students including those who are early in their career preparation (high school and undergraduate school) and those who are more advanced (graduate students and postdoctoral fellows). A third American Chemical Society (ACS) summer school in nuclear and radiochemistry at the NBTF site would be one concrete step in this area. Another would be access to Hollander fellows. The third is training and education of those in career transition (scientists interested in radionuclide applications, technicians in industry, etc.). This could be done in collaboration with other organizations who already have activities in this area, such as Oak Ridge Institute for Science and Education (ORISE).

F.1 Operations

The most important aspect of the NBTF is its operational philosophy. One common thread running through the workshops and studies done on the NBTF and DOE's isotope production activity in general is the need for a strong commitment to performing as a reliable supplier. The primary responsibility of the NBTF is to produce radionuclides on time and in the quantity and purity specified.

The operation of an accelerator can be managed by computers. The industrial vendors of cyclotrons and the commercial users all take advantage of computer control to minimize operator time at the console, as does BLIP. The accelerator should operate 24 hours a day, 7 days a week, 52 weeks per year. The recommended operating schedule is driven by several factors. First, if the NBTF is to provide backup to commercial vendors, it has to operate on the same schedule as they do. Second, the potential for making same-day shipment of radionuclides can only be achieved by operating the facility around the clock so that shipments can be made on the first plane out in the morning. Finally, accelerators operate best when operated continuously.

We determined that processing activities will likely take place around the clock, at least Sunday through Thursday, thus insuring the facility will be staffed on this schedule. We also learned during our visits to the commercial vendors that the judicious use of Programmable Logic Controllers can greatly enhance the capacity for automated operation. We would anticipate that most of the commercial and large-scale research radionuclide irradiations would occur during the evening and night shifts requiring minimal operator supervision. The production of small-scale research and education and training radionuclides would occur during the day shift, when staffing was at its highest level. This "low level" production activity would be the most labor intensive.

The philosophy concerning maintenance varied among the companies that we consulted. There was agreement that maintenance is an essential component of operations; the question was whether to perform maintenance on a scheduled basis or on an as-needed basis. For a unique facility like the NBTF with a single major accelerator, we recommend that a routine schedule of maintenance be instituted. This would include 8 hours per week for stripper maintenance and other required tasks. Once per month, the facility should shutdown for 48 hours for ion source maintenance and other items that conform to this schedule based upon mean time to failure analysis. Such a schedule of maintenance should substantially reduce unscheduled outages.

Of paramount concern is the conduct of operations, i.e. running the accelerator and producing the radionuclides. We determined that the operations component of the accelerator should be run as a business, regardless of what organization is chosen for the site of the NBTF. Obviously, this has been a problem with isotope production facilities located at national laboratories which contributed strongly to our committee's recommendation that the NBTF not be located at a national laboratory. The historically low priority (and status) put on service functions at the national laboratories contributed greatly to this problem. In addition, a customer focus at the NBTF is essential for the successful attainment of its missions. Insulating and elevating the operations component from the R&D or E&T components will insure that the operations are not compromised by activities in the other two mission areas. R&D and E&T should be treated as customers and given the same quality of service as the outside customers. We recommend that this philosophy be ingrained into the NBTF operations. It is essential that intramural R&D and E&T activities not have an adverse impact on NBTF operations. This often happens at accelerators where the accelerator itself is an object of a research program. This also contributed to our recommendation that the accelerator be produced by a commercial vendor.

As part of the mandate that the NBTF be run as a business and in a business-like manner, we inevitably have carried on discussions on how to implement programs in Total Quality Management (TQM) and Continuous Quality Improvement (CQI). In an ideal case, these two goals would be part of any operation. In fact, the research focused on improving target technology and separations chemistry could easily be viewed as an ongoing commitment to these principles. But, we would also recommend that these principles be included in the operational philosophy as part of the commitment to a customer orientation. The ancillary activities in customer relations, waste handling, packaging and shipping, as well as the R&D and E&T missions could all be carried out with adherence to TQM and CQI.

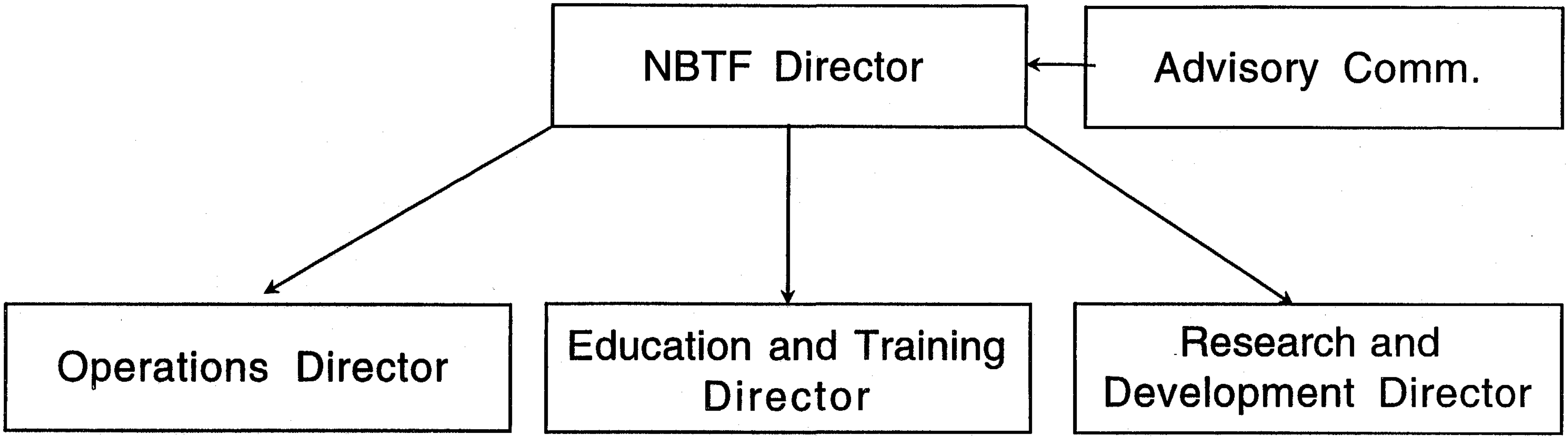
The conduct of operations is directly addressed in the guidelines for the study. We examined the role that Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) might play in the operational component of the NBTF. Our advisory committee was split on the issue of GMP. Members of the panel from industry believed a GMP program would be a substantial demand on physical resources as well as personnel. Once in place, GMP requires constant attention; it can't be dropped when it is inconvenient to maintain and re-instituted later. Unless a significant amount of radiopharmaceutical production was contemplated, they suggested that this would not be a good course of action. This suggestion also fits with our recommendation that the NBTF only being used as a radionuclide manufacturer, rather than a radiopharmaceutical manufacturer. This lowers the anxiety among those in the commercial sector that the NBTF could be turned into a subsidized competitor. Some members of the academic panel thought that by not complying with GMP in some part of the facility, the NBTF might lose potential revenue for isotope production. Given the potential for spin-off companies which created the interest in economic development by the State of Alabama in matching the DOE funding for this exercise, a recommendation was made that any retail pharmaceutical production should be done in a building remote from the NBTF.

The committee was unanimous on their endorsement of a formalized Quality Assurance & Quality Control (QA/QC) program The committee recognized that the NBTF would be used for some radionuclide production that would eventually become a radiopharmaceutical. In that case, the NBTF would have to maintain Drug Master Files (DMF). In most cases, developing and following the procedures in a DMF requires compliance with Good Laboratory Practice (GLP). The study requested a discussion of GLP. In the course of that discussion, we agreed that compliance with GLP is necessary. As the discussion deepened, however, we focused our attention more closely on ISO 9000. ISO 9000 is a quality standard that is internationally recognized. Auditing firms issue certification if they find that the facility complies with ISO 9000. In fact, many European companies now expect and specify ISO 9000 compliance in contracts. With this in mind, we opted to recommend that the NBTF be ISO 9000 certified.

The members of the committee whose organizations had become ISO 9000 certified made several points of note. First, it would be much simpler to build ISO 9000 compliance into the NBTF from its inception rather than trying to retroactively come into compliance. All members of the NBTF team could be trained in ISO 9000 compliance. Second, while ISO 9000 provides the mechanism for producing high quality products, it does not guarantee that the products will be of high quality. Third, introducing ISO 9000 is a task that requires a lot of teamwork and commitment from management as part of a program devoted to total quality. If TQM is not a goal of management, the ISO 9000 program will not be effective. The three elements necessary to implement an effective quality program are technical input, management commitment and cultivating the proper attitude. ISO 9000 is part of the technical input. But it is obvious that a new organization can more easily adopt a TQM/CQI culture by emphasizing this as a prerequisite for employment for all members of the staff, from the director to the janitors.

This obviously does not occur spontaneously nor without support. There is strong emphasis in the IOM report and prior studies on a steady flow of funds dedicated to radionuclide production research. The importance of this is two-fold. First, any improvements in production methods will be done under this funding. In order to carry out a program in Continuous Quality Improvement, resources for the activity have to be available. Second, many of the targets developed for this accelerator will initially be unique and will need some development and testing before they go into routine use. And new chemistry for separations is being driven by the

NBTF Organizational Structure



Operations Director

- ◊ Accelerator Operations
- ◊ Product Processing
- ◊ Order Processing
- ◊ Packaging
- ◊ Shipping
- ◊ Waste Handling
- ◊ Health Physics
- ◊ QA / QC Program
- ◊ ES&H Program

Education and Training Director

- ◊ ES&H Training
- ◊ Undergraduate Research Program
- ◊ Graduate Research Program
- ◊ Postdoctoral Fellowships
- ◊ Sabbatical Leave Program
- ◊ Industrial Sabbatical Scientists
- ◊ Orientation for visitors
- ◊ Educational Outreach Program

Research and Development Director

- ◊ NBTF R&D Program
- ◊ Technology Transfer
- ◊ Industrial Outreach
- ◊ Contact for local, national, and international projects
- ◊ Coordinates with National Lab collaborators
- ◊ Manages Work For Others and CRADA activities

environmental cleanup at the national laboratories and is easily adopted in product separations. Both of these research areas need funding separate from the operations funds for the facility.

In addition, the restart of the calutrons by DOE was welcome news as it will insure that many of the enriched materials necessary for radionuclide production will be available. There was concern among the members of our advisory committee about the availability of these raw materials. Further, they suggested that a research program be instituted at the NBTF into new technology for isotope enrichment, either in collaboration with a national laboratory or as a standalone project at the NBTF.

We endorse the IOM panel's recommendation for an advisory panel. The panel will insure that the NBTF is run in a manner that meets the needs of the user community. We also recommend that regular, quadrennial site visits be held by an outside review panel delegated by DOE to review the operation of the NBTF. Our experience in using external advisors only strengthened this recommendation. The group was valuable in providing advice based upon experience and in acting as a sounding board for new ideas. The Advisory Panel would also be useful in establishing priorities for isotope production, particularly for those that would be produced at less than full cost recovery. The advisory panel would also aid in maintaining a focus on the agreed mission for the NBTF rather than as a contract producer of radionuclides for profit. While there is capacity for some contract work, this is ancillary to the primary NBTF missions.

F.2 Staffing

We have included a staffing proposal for the NBTF. This proposal was drawn from the experience of the UAB team in Education and Training, Research and Operations activities. We also received comments from the advisory committees on the proposed staffing and incorporated those suggestions in the proposal.

Position Descriptions

The positions are broken into three categories. Those whose support is 50 percent or greater from operations are listed as operations staff. Those whose support is 50 percent or greater for education and training are listed in that group. The remainder are in the research and development group.

Operations Staff

NBTF Director: Responsible for all aspects of the NBTF. Identifies and develops relationship with stakeholders in NBTF operation. Coordinates interaction with advisory committee, parent organization's administration, DOE and other funding agencies. Develops a strategic plan for the NBTF which includes integrating the three organizational units of the NBTF (operations, R&D and E&T).

Operations Director (OD): Responsible for accelerator operation and maintenance, scheduling, routine target fabrication, target processing, product packaging and shipment, waste handling and shipment. Develops production schedule and maintains compliance with that schedule. Responsible for customer orientation of NBTF including the service to the R&D and E&T functions.

Research Director (RD): Responsible for coordinating the R&D activities at the NBTF. These include interaction with DOE on NBTF R&D budget; interaction with DOE and other funding agencies on other peer-reviewed funding opportunities; coordinating R&D activities with the OD and staff; determining research opportunities that are specific to the NBTF and those that complement the NBTF operation.

Education and Training Director (ED): Responsible for coordinating education and training activities at the NBTF. These include: developing and maintaining contact with the funding agencies who sponsor the E&T work; coordinating visits by academic and industrial sabbatical scientists; supervising postdoctoral fellows and graduate students who are both NBTF-based and those who are visiting; managing the undergraduate training programs including the Nuclear Chemistry Summer School; developing the ESH training with the ESH coordinator; and training activities within the TQM and CQI operations philosophy.

Business and Marketing Manager: Responsible for the business aspects of the NBTF. These include: developing budgets for all three segments of the NBTF; grants and contract management; contract negotiations for proprietary work done on site, technology transfer, and long-term production contracts; marketing the NBTF to the stakeholders and customers, including products, physical and intellectual resource, and other opportunities for economic development; coordinates with operations director on these issues and product scheduling.

Administrative assistant: Responsible for assisting the directors in accomplishing their job goals; coordinating the visits by DOE program managers, advisory committees, site visit teams, and other stakeholders and customers of the NBTF; office manager for the NBTF; and other administrative duties for the NBTF director.

Radiochemist: Responsible for overall operation of the hot cells; target fabrication and reprocessing; oversees routine separation chemistry; supervises hot cell technician and processing technicians; works with Pharmacist to generate Drug Master Files; develops new and improved separations chemistry; works with OD to insure compliance with schedules; conduct research on new radionuclide production schemes including cross section measurement, target design, and purification chemistry.

Accelerator Physicist: Responsible for operation and maintenance of the cyclotrons, beam lines and target areas; oversight and training of the operations staff; interaction with cyclotron vendor(s); developing new target technology with radiochemist; oversight of mechanical/vacuum technician; partial oversight of electronics technician; assists OD in developing operations schedule; works with materials scientist to assess and manage heat load on targets; and assists with R&D activity based on the accelerators.

Hot Cell Technician: Responsible for routine maintenance of hot cells and their components; works with Hazardous Waste Technician to decontaminate hot cells and package waste; helps design target processing units for hot cell operations.

Processing Technicians: Responsible for cyclotron operations; target mounting and dismounting; processing targets in hot cells, glove boxes, and hot labs; primary packaging of product; target reprocessing; and routine maintenance of the cyclotron and processing areas.

ESH Coordinator: Responsible for all Education and Training of staff, students and visitors in ESH-related regulations and procedures including radiation, chemical, waste, and other hazards; manages ALARA program; manages waste minimization program; assists director in interaction with federal and state regulatory agencies.

Health Physicist: Responsible for oversight of ALARA program; coordinates routine radiation safety support activity in the NBTF operation; oversight of Radiation Safety Technicians; interaction with university safety office and with appropriate state oversight agencies.

Radiation Safety Technicians: responsible for radiation safety support in all aspects of the NBTF operation including routine lab surveys, monitoring radiation areas, surveying product shipments, waste shipments, monitoring discharges from the facility into the air, sewers and solid waste; and providing ongoing assistance to staff, students and visitors in compliance with the ALARA program.

Machinist: Supports the operations and R&D staff with design and fabrication of new equipment; assists with repair of existing equipment; works with staff, students and visitors to develop new technology; and responsible for maintenance of equipment in cold and hot machine shop.

Pharmacist: Works with production staff to develop Standard Operating Procedures, Drug Master Files, and has primary responsibility for all QA/QC activities; primary responsibility for compliance with ISO 9000; assists in formulation of new compounds; teaches staff, students, and visitors about proper aseptic technique in radiopharmaceutical production; and maintains all record keeping for inventory management system.

Computer Scientist: Responsible for installing and maintaining the computer network in NBTF; develops software for remote handling operations for NBTF; assists in developing Programmed Logic Control (PLC) modules for NBTF operation; assist in maintaining newserver for nuclear medicine community; works with pharmacologist and other scientists in developing pharmacokinetic models; and supports other computer based operations at NBTF.

Electronics Technician: Responsible for installing, maintaining are replacing electronics in NBTF; assists others at NBTF in designing and installing new electronic interfaces for production and purification operations; maintain and troubleshoot PLC network; assists OD and accelerator physicist in developing and maintaining data link within the facility.

Mechanical and Vacuum Technician: Responsible for maintaining mechanical and vacuum systems associated with the accelerator operation; works with Electronics technician to insure that hardware-software interfaces are working properly; maintains inventory of replacement parts; works with others in developing remote handling equipment; and works with hot cell technician to maintain equipment in the hot cells.

Secretaries: Responsible for handling correspondence, telephones, purchase requisitions, travel by NBTF staff and visitors and other routine clerical matters; order input; shipping clerk duties and other specific duties which align with their respective organizational unit of the NBTF.

Shipping Clerks: Responsible for receiving shipments; putting raw materials for isotope production into the inventory system; handling order processing; packaging of products and waste for shipment; maintaining all appropriate documentation for these tasks.

Hazard Waste Technician: Responsible for collection and packaging of waste for storage (radioactive) and disposal (long-lived radioactive and chemical); responsible for record-keeping and compliance with federal, state and local regulations for waste disposal.

Janitorial Staff: Responsible for care and maintenance of the building. Given the range of work at the NBTF, these positions require training beyond the normal janitorial staff. Retention of these staff is essential to minimize the training required.

Education and Training Positions

Sabbatical Scholars: Provides opportunity for scientists from elsewhere to work at NBTF. Offers cross-fertilization between resident staff and others.

Industrial Visiting Scientist: This program would give industrial scientists the freedom to pursue short-term research without the constraints of working in an industrial environment. It also gives the NBTF staff the chance to receive input from those based in the private sector. This would enrich the TQM and CQI objective.

Postdoctoral fellows: Conduct research in target design and fabrication; separations technology; radionuclide generator development; and basic radiopharmaceutical chemistry.

Graduate Students: Conduct research in target design and fabrication; separations technology; radionuclide generator development; and basic radiopharmaceutical chemistry.

Undergraduate Summer School participants: Self-explanatory

Research and Development Positions

Materials Scientist: Responsible for developing new target technology in collaboration with the radiochemist and outside users; oversees research projects by graduate students and postdoctoral fellows in this area of research; responsible for primary work on heat deposition and dissipation in irradiated targets; develops new technology for target holders and associated equipment that are exposed to high radiation levels.

Inorganic Chemist: Responsible for research in the use of radiometals; provides expertise in bioinorganic chemistry, chelate chemistry, and other pertinent issues relative to the use of radiometals; assists in the development of separations chemistry; works with materials scientist on issues related to electrochemistry.

Organic Chemist: Responsible for research in the use of radioactive isotopes in synthesis; likely has research program in PET radiopharmaceuticals; assists in training of students; oversees research in halogen chemistry; and aids in developing products that can be routinely used in radiosynthesis.

Imaging Physicist: assists in conduct of biodistribution experiments; assists in pharmacokinetic experiments; performs dosimetry calculations to assess the isotopes proposed for production and distribution by the NBTF.

Pharmacologist: Responsible for developing data for dosimetry calculations for radionuclides and new radiopharmaceuticals; assist in development of new radiopharmaceuticals; assist in education and training of students in radiopharmaceutical research.

Veterinarian: assists animal technician and investigator in the design and conduct of animal experiments.

Theoretical Chemist: works with organic and inorganic chemist to define potential of drugs suggested for development; works with drug design group to identify opportunities for prospective radiopharmaceutical development; works with computer scientist to define opportunities to provide this capability throughout the NBTF.

Animal Technician: Responsible for support of R&D activity associated with NBTF; animal procurement and care during experiments; assists staff with procedures on animals; and maintenance of animal areas.

Cell Biology Technician: maintains cell cultures for in vitro experiments; assists animal technician in developing xenografts for tumor imaging and therapy experiments; works with veterinarian to determine schedule of activities.

Support for other activities on site typically can be found on a university campus. Among them are glass blowing; librarians for digital and hard copy retrieval of information, graphic arts; computing science; educational opportunities for non-doctoral staff; seminars and colloquia on topics in the basic sciences and medicine.

This staffing proposal is conservative. In a detailed analysis, there are obvious possibilities for consolidation and cost savings. These include: NBTF director also serving in a second directorial capacity; the radiochemist serving in a directorial capacity as R&D, E&T or operations director; the accelerator physicist serving as R&D, E&T or operations director; the other faculty positions also serving as R&D or E&T director; the Health Physicist serving as ESH coordinator; and consolidation of the administrative assistant and one clerical position. If located at a university, many of the technician positions could be filled by students, resulting in substantial cost savings. We recommend a university location because it provides opportunities for cost sharing. Faculty can be supported by other funding sources such as endowed chairs, university professorships, other grants and contracts, etc. These cost savings are not available at most national laboratories as they operate on full cost recovery. There are also opportunities for outsourcing some of the operations of the NBTF; this would not necessarily result in cost savings, however. Any consolidation in staffing can only be identified once candidates are recruited for the positions on the staff. Regardless, the use of faculty appointments as a mechanism for cost sharing is not available in private industry or at a national lab.

F.3 Budget

In the supplementary guidelines for the study, two scenarios were suggested for the operation of the NBTF. The first was private industry would build the NBTF and pay back the government for the cost of construction from revenues. The second was that the NBTF would be built at a National Laboratory. In this case, the our guidance from DOE was that the government would not be reimbursed for the cost of construction. We elected to examine a third scenario in which the NBTF would be university-based. As was pointed out in Section D, the cost of construction is greater if built in New York or California, site of three of the National Labs. We also wanted to examine the cost of running the NBTF under all three scenarios. We requested information on cost of staffing from three national laboratories. Investigators at BNL refused to provide the information, LANL never responded to our request, but ORNL did provide us with two different cost scenarios. After review by the Project Coordinator, the ORNL costs were in line with those at Argonne National Laboratory. ORNL polled costs at three divisions that have similar operational and staffing requirements to those found at the NBTF. We have used the information provided by ORNL to construct an operating budget for a national lab-based NBTF. Though all of the labs use different accounting methods, the differences tend to cancel out at the bottom line, i.e. they have similar costs after all loads, services, etc., are included.

The National Laboratory figures need some explanation. It is routine in costing exercises to include divisional overhead and the operational cost in the personnel cost quoted. This inflates the costs in the personnel section. Therefore, travel, supplies, etc. are not included in the later section of the budget. We also have left out staff that would be covered by lab or divisional overhead.

This budget also makes no attempt to assign the revenues that will cover the cost of operation. In the absence of firm guidance from DOE on this issue, we have estimated that an operational subsidy of $1.5 million will be required for operations in radionuclide production. This will reduce the cost of radionuclides to investigators in early stages of research. We have estimated a budget of $2 million for NBTF-related R&D activity which includes the subcontract for ORNL target development. Finally, we estimated that the Education and Training activity would require about $1 million in DOE funds. This E&T funding would support undergraduate, graduate, postdoctoral and sabbatical staff. The additional funding would result from peer-reviewed grants, industrial contracts, revenue from isotope sales, and university and state subsidies.

		Compensation (includes 26% fringe)		
	effort	National Lab.	University	Private Company
Director*	100%	$169,607	$189,000	$189,000
Ops. Dir.	100%	$169,607	$126,000	$126,000
Res. Dir.*	100%	$169,607	$126,000	$126,000
Educ. & Train. Dir.*	100%	$169,607	$107,000	$107,000
Bus. & Mktg. Mgr.	100%	$160,646	$94,500	$94,500
Admin. Asst.	100%	$87,003	$50,400	$50,400
Secretary - 4	400%	$348,012	$120,957	$120,957
Shipping Clerk	200%	$174,006	$60,480	$60,480
Radiochemist*	100%	$169,607	$90,000	$90,000
Hot Cell Tech	100%	$126,084	$45,360	$45,360
Processing Techs	600%	$756,504	$226,800	$226,800
Health Physicist*	100%		$60,480	$60,480
Rad. Safety Techs	200%		$60,480	$60,480
Accelerator Phys.*	100%	$169,607	$60,480	$60,480
Materials Scientist*	100%	$169,607	$94,500	$94,500
Machinist	100%	$76,000	$60,480	$60,480
Animal Technician	100%	$126,084	$30,240	$30,240
Pharmacist*	150%	$240,969	$135,000	$135,000
Postdoctoral Fellows*	400%	$179,200	$161,280	$161,280
Grad Res. Asst.	600%	$92,160	$113,400	$113,400
Cell Biology Tech	100%	$126,084	$30,240	$30,240
Pharmacologist*	100%	$169,607	$81,900	$81,900
Computer scientist*	100%	$169,607	$60,480	$60,480
Electronics Tech	100%	$126,084	$44,100	$44,100
Mech. & Vac. Tech	100%	$126,084	$44,100	$44,100
Undergrad. Summer school	200%	$35,000	$18,900	$18,900
Sabbatical Prog.*	200%	$339,214	$189,000	$189,000
Janitorial staff	300%			$52,500
Industry Vis. Scholar*	100%	$169,607	$131,040	$131,040
Haz. Waste Tech	150%	$189,126	$56,700	$56,700
Organic Chemist*	100%	$169,607	$94,500	$94,500
Inorganic Chemist*	100%	$169,607	$81,900	$81,900
Veterinarian	25%	$42,402	$23,625	$23,625
Imaging Physicist*	50%	$84,804	$40,950	$40,950
Theor. Chem.*	100%	$169,607	$75,600	$75,600
ESH Coordinator*	100%	$160,646	$56,700	$56,700
Total FTE	57.75	$5,461,788	$3,042,572	$3,076,172

Electricity			$920,000
Water & Deionizer			$20,000
Natural Gas			$12,000
Chilled Water			$12,000
Steam			$8,400
All Utilities	$0	$0	$972,400
Supplies and Services			
target materials [enriched isotopes]	$1,000,000	$1,000,000	$1,224,000 ¥
radiochemicals		$24,000	$24,000
Rad. Waste Disp.	$200,000	$200,000	$200,000
Haz. Waste Disp.	$100,000	$100,000	$100,000
Misc. supplies		$12,000	$12,000
chemicals		$36,000	$36,000
Telecommunications		$69,300	$69,300
Postage		$1,500	$1,500
Express Mail	$10,000	$10,000	$10,000
Shipping Service	$100,000	$100,000	$100,000
Duplication	$6,000	$6,000	$6,000
Graphic Arts	$10,000	$10,000	$10,000
Computer Equip.	$25,000	$25,000	$25,000
Software upgrades	$25,000	$25,000	$25,000
animals	$20,000	$20,000	$20,000
animal housing, etc.	$3,000	$3,000	$3,000
Health Physics supplies	$12,000	$12,000	$12,000
Machine Shop supplies	$60,000	$60,000	$60,000
Publication costs	$4,500	$4,500	$4,500
Subtotal Supplies & Services	$1,575,500	$1,718,300	$2,914,700
Maint. - Scientific Equip.	$150,000	$150,000	$150,000
Maint. - accelerators	$100,000	$100,000	$100,000
Replacement inventory. for Maint.	$250,000	$250,000	$250,000
Maint. Expense	$500,000	$500,000	$500,000
Lease for truck	$5,000	$5,000	$5,000
Lease for shipping casks	$15,000	$15,000	$15,000
Subtotal operating	$2,095,500	$2,238,300	$3,434,700

Equipment - new and replace		$750,000		$750,000		$750,000
*One trip for all scientists				$27,000		$27,000
One RT for adv. comm.		$16,500		$16,500		$16,500
Total Travel		$16,500		$53,500		$53,500
Subcontracts						
Consultants		$80,000		$80,000		$80,000
Adv. Comm.		$22,500		$22,500		$22,500
ORNL target prep.		$250,000		$250,000		$306,000 ¥
Total utils, M&S, outside serv.		$3,616,700		$2,644,300		$4,202,700
Total operating		$9,078,488		$5,686,872		$7,278,872
Overhead	43.60%	$3,958,221	44.00%	$2,502,224		$0
Equipment		$750,000		$750,000		$750,000
Total incl. Overhead		$13,786,709		$8,939,096		$8,028,872
Debt Payment	$72 million @ 8 %, 30 year term					$6,395,575
Total Obligations		$13,786,709		$8,939,096		$14,424,447

¥ If non-Federal funds purchase Services and Isotopes
an additional 22.4 % is added for DOE overhead and depreciation

Table F.1 A comparison of operation costs featuring a national laboratory, a university and a private business as contractor. The analysis assumes that the NBTF will be incorporated into an active research site with activities recommended by the IOM Panel. Therefore, some budget items included here would be covered by peer-reviewed grants and other revenue sources.

In order to attempt to keep the cost comparison uniform, we have assumed that there would be R&D and E&T activities at the privately funded NBTF. In cases in which the overhead or the manpower rate includes services or other costs, we have deleted those costs from the calculation.

Accepting the argument that there is infrastructural support at a National Lab for the NBTF, it is apparent that there is a substantial operational cost associated with this infrastructure. The comparison of production capability appearing in a recent article indicates that the NBTF would be able to produce the same amount of radionuclides in a fraction of the time required by BLIP after the upgrade or TRIUMF (9). The cost of operating BLIP accelerator alone has been approximated to be $80,000 per week at full cost recovery. On an hourly basis, this the same cost as our calculation for the NBTF including the processing staff. There would be cost savings by producing isotopes at the NBTF rather than BLIP in reduced operational expenses alone. This also neglects the cost of upgrades, renovations and new facilities at BNL that would be necessary to process the increased material produced there. At an estimated cost of $16 million for the current upgrade to BLIP and the proposed second upgrade, nearly 25 % of the cost of construction of the NBTF would be spent on a facility with a 30 year old accelerator, aging support facilities, and production capabilities one-half that of the proposed NBTF.

The difference in the operational cost between a university and a National Lab could pay for a new NBTF every 15 years. If the new facility was streamlined for production only, the savings could construct a new NBTF every 10 years. This also neglects the fact that at a university, many of the technical jobs can be filled with graduate students, either reducing the cost further or expanding the workforce at minimal incremental increase in cost. This also serves to train more people, even if their intended career is not in radiochemistry or nuclear medicine.

F.4 Research, Education and Training

Our study began with a review of existing information on the Research, Education and Training requirements for the National Biomedical Tracer Facility (NBTF) published in the National Biomedical Tracer Facility Planning and Feasibility Study (3) and the Proceedings of the Purdue National Biomedical Tracer Facility Workshop (4). Our External Academic Advisory Committee (Section K) met in Birmingham at the University of Alabama at Birmingham on September 29-30, 1994 to discuss the Research, Education and Training requirements for the NBTF. Initial recommendations were made concerning these issues, but the committee decided that the Institute of Medicine (IOM) report was crucial to provide guidance in this area. This report (5), received in December, 1994, supported the initial recommendations of the External Academic Advisory Committee.

The recommendations include a clear focus on the research and development of isotope production including target design, target cooling systems, separations chemistry, and generator development. It is our opinion that a dedicated national facility for isotope production and research is needed for the United States to maintain continued leadership in biomedical research using radioisotopes. In addition, there exists the necessary infrastructure for research and training in isotope production and nuclear medicine research as well as educational activities at a University which would not be provided at an industrial site or at a national laboratory. This opinion was supported by the members of our Industrial and Academic Advisory Committees and in our findings through visits to industrial isotope production facilities. The IOM panel also arrived at this conclusion. The panel expressed a concern that a private company could not dedicate its personnel and facilities in a manner which would sufficiently nurture the type of research and educational activities proposed for the NBTF. It was also recommended that any radiopharmaceutical chemistry research should be conducted with funds obtained from peer-reviewed grant applications rather than NBTF operating funds.

A second meeting of the External Academic Advisory Committee was held in Birmingham on January 9-10, 1995 to formulate specific recommendations for Research, Education and Training for the NBTF. Members of the Industrial and Internal Steering Committees were welcome to make comments, but the primary source of advice was the Academic Advisory Committee. The recommendations were that the facility be located on a University campus to facilitate both interactions with and participation by faculty members in a variety of disciplines including chemistry, physics, materials science and engineering, pharmacy, and nuclear medicine in order to foster meritorious research, education and training opportunities for the employees of the NBTF. The interaction among faculty, students, staff, and others would also be enhanced by the location of the NBTF on a University campus, as compared to an off-campus site or a national laboratory. The presence of a co-located Medical School and Hospital at a major research University would be an added benefit for the NBTF. The advantages of the NBTF being located on the campus of a large University with a faculty experienced in nuclear medicine and engineering techniques are also very important. This would enhance the opportunity for the NBTF to serve as a center for research and education in basic sciences (nuclear physics and radiochemistry), engineering (materials science and bioengineering), basic medical sciences (biochemistry and pharmacology), biotechnology, and clinical nuclear medicine. This would provide access to animal and histopathological testing resources as well as to patients, physicians, and allied health personnel with clinical research expertise.

As noted by the IOM panel, a close association with established research programs in nuclear medicine, radiopharmacy, radiochemistry, cardiology, neurobiology, and oncology at an affiliated University would provide NBTF scientists with continuous sources of extramural collaborations and intellectual stimulation. Our study concurred that the primary research focus of the NBTF should be on targets, target design and separations chemistry. The senior research staff of the NBTF holding Ph.D. degrees in radiochemistry and materials science and engineering should have academic appointments in the appropriate basic science or engineering departments at the affiliated University in order to foster training of undergraduate, graduate, and postdoctoral students as well as allowing visiting scientists to learn state-of-the-art radiochemical research and isotope production techniques. All categories of employees of the NBTF should be provided with education and training through courses offered at the affiliated University, and through education and training programs offered at the affiliated Universities and DOE facilities.

This education and training should be focused on three primary activities. The first is the education and training of the NBTF staff with respect to environmental, safety, and health regulations. The second is the education and training of students (high school, undergraduate, graduate, and postdoctoral fellows) in areas relevant to the operation of the NBTF through academic courses, summer school programs, and training courses. The third is the education and training of people in career transition (*e.g.* scientists or technicians from national laboratories or industry). This could be performed in collaboration with other organizations which already have activities in the area.

F4.1 Organization

F4.1.1. Research and Development

It is recommended that the NBTF be organized along its mission components (Figure 1). The primary component would be Operations, the details of which are described elsewhere in this report. The second component would be Research and Development. There should be a Ph.D. Research Director with a 75% appointment in the NBTF and a 25% appointment in a basic science or engineering department at the affiliated University. The Research Director would be responsible for the research activities in targetry development and radiochemistry (Figure 2). There should be research on the development of targets for research isotopes as well as on the development of high-beam-current targets. Further research would involve the processing of targets, and also automation in order to improve the quality of the isotopes produced and to reduce the radiation exposure to personnel in keeping with the as low as reasonably achievable (ALARA) principle. There should also be research on developing improved methods for the recovery and purification of the desired radioisotopes. Additional research staff should be affiliated with the NBTF to provide expertise in nuclear chemistry/radiochemistry research, radionuclide properties and selection, radionuclide production, radiochemical separations, radioanalytical chemistry, inorganic chemistry, automation/remote handling, organic chemistry, radiopharmaceutical chemistry, and preclinical testing to demonstrate feasibility for the new products (Figure 2). Their appointments would be either part-time or full-time at the NBTF, with the remainder of the appointment at affiliated Universities or DOE national laboratories (Table F.2).

There should be an External Research Advisory Subcommittee composed of some members of the External Advisory Committee to advise both the Director of the NBTF and the Research Director on the most important research projects to be pursued. This would be accomplished through a peer-reviewed mechanism that selects the most outstanding research programs from investigators at the NBTF and from researchers with other laboratories in the United States and abroad. The External Research Advisory Subcommittee should visit the NBTF once each year to review the research results and to set priorities for future research. The use of beam time for the production of radioisotopes for approved research programs and for the development of new techniques in approved research projects would have to be overseen by the Directors of Research and Operations of the NBTF, with advice from the External Research Advisory Subcommittee.

Figure 1

The UAB NBTF Organization

NBTF Organization

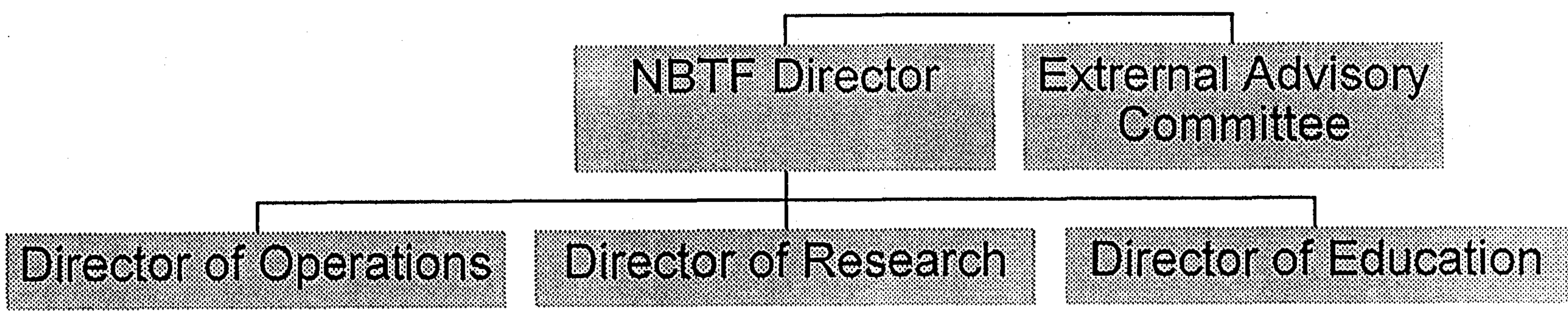
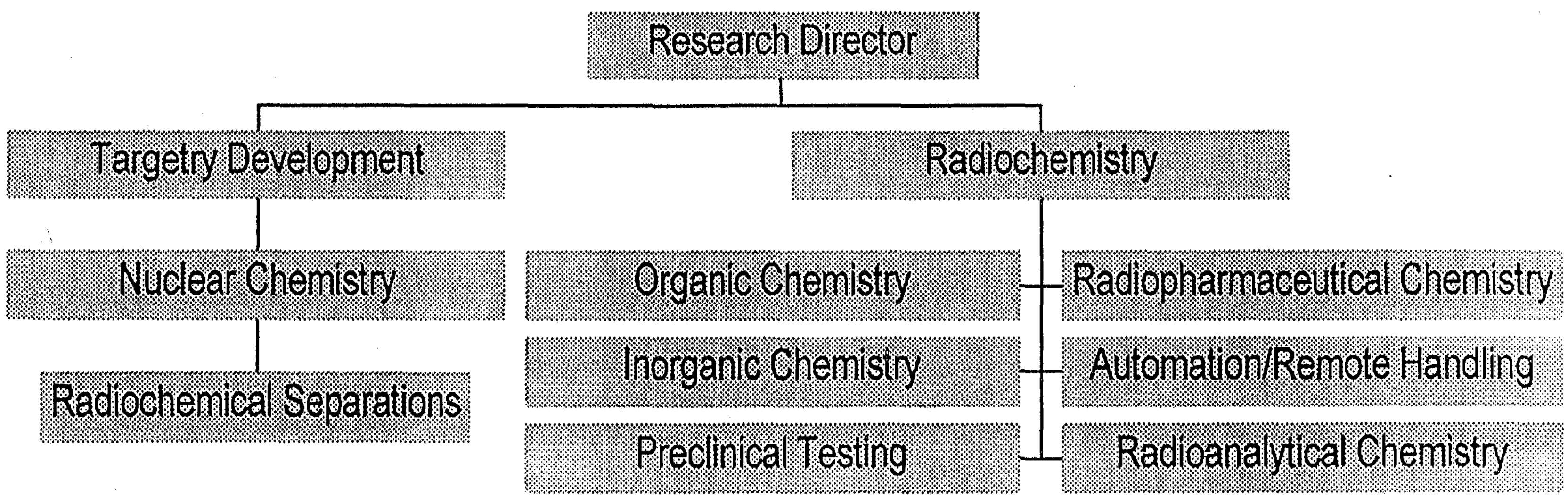


Figure 2

Research and Development

R&D



Fraction of Effort

Position	RESEARCH FUNDING			Education Funding	
	NBTF	Peer Rev.	DOE	Other Fed	Univ. funds
Director	0.250		0.250		
Ops. Dir.					
Res. Dir.	0.500	0.500			
Educ.&Train. Dir.			0.500	0.250	0.250
Bus. & Mktg. Mgr.					
Admin. Asst.					
Secretary - 4	0.125	0.125	0.125		0.125
Shipping Clerk					
Radiochemist	0.500				
Hot Cell Tech					
Processing Techs					
Health Physicist					
Rad. Safety Techs					
Accelerator Physicist	0.500				
Materials Scientist	0.500	0.250			0.250
Machinist					
Animal Technician		1.000			
Pharmacist			0.166		0.166
Postdoctoral Fellows	0.250	0.250	0.500		
Grad Res. Asst.			0.500	0.500	
Cell Biology Tech		1.000			
Pharmacologist		1.000			
Computer scientist	0.500				
Electronics Technician					
Mech. & Vac. Technician					
Undergrad. Summer school			1.000		
Sabbatical Prog.			1.000		
Janitorial staff					
Indust. Sci. Vis. Scholar			1.000		
Haz. Waste Tech					
Organic Chemist		0.500			0.500
Inorganic Chemist		0.500			0.500
Veterinarian		1.000			
Imaging Physicist		0.500			0.500
Theor. Chem.		0.500			0.500
ESH Coordinator					

TABLE F.2 Division of support for personnel in R&D and E&T. NBTF R&D funding is referenced in first column of Research Support. NBTF-related Education Support is broken out in the third column. Any support from Operations funds is not represented in this table.

As recommended by the IOM panel, pre- and post-doctoral fellowships, faculty scholarships, and incentives for new faculty positions should be part of DOE's core support for the NBTF, supplemented by industry and government grants to both University and NBTF staff. NBTF scientists should be encouraged to apply for peer-reviewed research grants from government agencies and industry. As also recommended by the IOM panel, there should be special pricing at less than full cost for radioisotopes produced for research at the NBTF. The researchers should pay some portion of those costs through their grants, with prices negotiated annually on a case by case basis in consultation with the External Advisory Committee. Appropriate models for this are the user groups at resources used at national laboratories.

There should be an extensive research collaboration with regional academic and government facilities. An alliance of the NBTF with a DOE national laboratory would provide immediate access to expertise in radionuclide purification and processing. An alliance with a consortium of other research universities such as Oak Ridge Associated Universities (ORAU) would also be important in order to draw upon their expertise in isotope production research. The research staff would be under the supervision of the Research Director; however, it is recommended that they have joint appointments in appropriate academic departments where possible.

There should be a strong interaction with funded investigators at the affiliated Universities and DOE national laboratories, and with other regional and academic institutions that have special resources and capabilities relevant to the primary mission of the NBTF, which is isotope production. There should be outreach and technology transfer to the isotope and radiopharmaceutical industries, which is of paramount importance. We agree with the IOM panel's conclusion that radiopharmaceutical chemistry research and other related research should be funded by peer-reviewed grants and not NBTF operating funds. We also advocate a formalized program of research opportunities for sabbatical scientists from academic institutions and industry.

F4.1.2. Education and Training

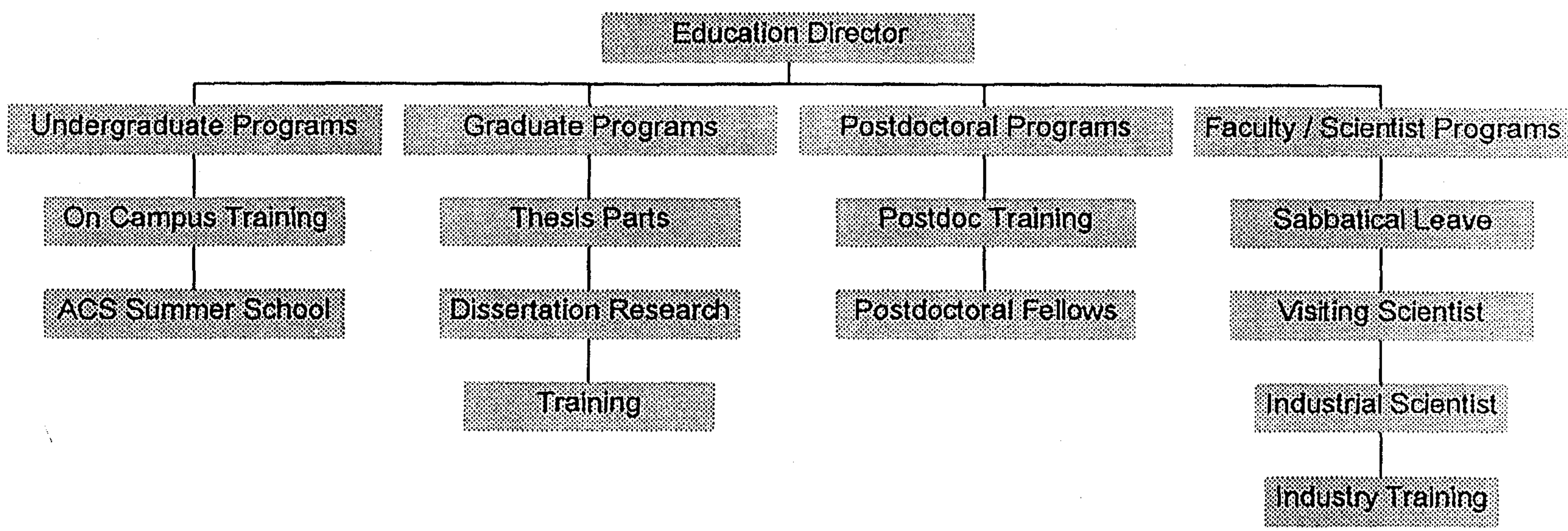
The need for training of nuclear and radiochemists is well documented (8). A workshop organized by the National Academy of Sciences examined the requirements for training chemists for nuclear medicine, the nuclear industry and related areas. They found that there was a shortfall in 1988, when the study was published, and predicted it would be worse in the next decade. Experience has shown that the report was optimistic. Retirements by chemists who were trained after the war are accelerating and many of them are not being replaced on the chemistry faculties throughout the U.S. This shortfall is not limited to the U.S. Training programs are falling short in all parts of the world. In order to assist in filling this need, we believe a strong program in education and training must be centered at the NBTF.

There should be a Director of Education and Training who would have a Ph.D. degree, a 50% appointment in the NBTF and a 50% appointment in a basic science or engineering department at the affiliated University (Figure 3). This person would be responsible for organizing all education and training activities offered by the NBTF and at affiliated Universities and DOE national laboratories. Wherever possible training courses should be certified. This should include a DOE-sponsored American Chemical Society school for undergraduates in nuclear chemistry and radiochemistry (10 weeks) at the NBTF site. The faculty affiliated with the NBTF would contribute to teaching undergraduate and graduate courses to students in degree granting programs as well as carry out training in laboratory research at the NBTF, or in the basic science or engineering departments of the affiliated University relevant to the scope of activities in the NBTF. Efforts should be made to take advantage of educational and training opportunities at other locations as well. The value that the NBTF could have towards improving internal dosimetry of radionuclides for nuclear medicine should be explored with the Oak Ridge Institute for Science and Education (ORISE) Radiation Internal Dose Information Center (RIDIC). Input from the RIDIC could be used to aid in narrowing the list of radioisotopes that would be useful in man. Any new agents developed from research at the NBTF will likely be reviewed RIDIC to receive Food and Drug Administration (FDA) approval. ORISE can also provide extensive DOE-oriented environmental safety and health compliance training for the worker population.

Collaborative arrangements should be formalized between the NBTF and affiliated Universities and DOE national laboratories. There should be education and training in radiation protection

Figure 3

Education and Training



techniques and regulations, isotope production, target processing and mounting, the use of hot cells, radiochemistry (analysis and synthesis), and radiopharmaceutical chemistry. There should be education and training in the safe operation and maintenance of accelerator and reactor facilities, the design of new radionuclide generators, optimization of radionuclide production, training in the use of instrumentation, and the development of new applications. The specific education and training requirements for all members of the NBTF workforce need to be defined in the conceptual design phase of the study.

As recommended by the IOM panel, DOE should fund both the research isotope production and the part of the educational and training programs at the NBTF as part of its public research and development mission. An NBTF postdoctoral program should be established. Additional funding for training costs should be sought from NSF, NIH, and industry. This is essential for the education of new investigators and technicians, and the development of new techniques and radioisotopes. There should be an effort made to include relevant education and training in radiochemistry and radiopharmaceutical chemistry from Pharmacy and Veterinary School programs, as well as to involve students from minority colleges. A training program for displaced personnel from industry and national laboratories should be instituted. A sabbatical education and training program should be established for individuals from industry and other Universities. These programs should be funded in part by DOE.

It is estimated that there would be 10 undergraduate students, 6 graduate students, 4 postdoctoral students, 1 or 2 visiting faculty from Universities, and 1 visiting scientist from industry per year affiliated with the NBTF.

An External Education and Training Advisory Subcommittee of the External Advisory Committee should be formed to provide advice to both the Director of the NBTF and the Director of Education and Training on the development of training and educational programs associated with isotope production and use. The members of the Subcommittee will be drawn from industry, other Universities, and the federal laboratory system. They should be chosen by the Director of the NBTF in consultation with the senior management of the affiliated University. This Subcommittee should meet biannually to review the training and educational programs and to provide guidance on the development of new programs.

G. Business Plan

We have spent a great deal of time determining whether private industry would build the NBTF. We have concluded that the NBTF is not economically feasible as a private undertaking. Our estimates are that a privately built and operated NBTF would run at an annual deficit of greater than $3 million per year when financing for the facility was included. Under these circumstances, it was impossible to construct a scenario in which the government was paid back for its investment. In fact, the difficulty experienced by the North Texas Research Institute in securing private funding is proof of the difficulty in a private undertaking. In contrast, we have determined that industry is quite capable of contributing to some aspects of the NBTF. The accelerator industry is well equipped to produce and maintain an accelerator that meets the specifications of this study, the IOM panel report, and prior workshops.

Ironically, the lack of regularly available radionuclides from DOE sites has dampened or eliminated the commercial market for isotopes produced by accelerators with an energy above 40 MeV. In addition, the difficulty in conducting clinical trials has also stunted the development of products using these radionuclides. We have concluded that the IOM report is accurate in predicting that any commercially successful radionuclide will generate revenue for the NBTF in the form of contracts for production in the short term and royalties in the long term.

We have determined, however, that several opportunities exist for industrial participation in the NBTF. The most direct would be if the operations function were outsourced to industry. A second mechanism for public-private partnership would be for industry to handle the marketing and sales activity at the NBTF, utilizing their existing infrastructure. Third, the NBTF can serve as a backup and supplementary supplier of accelerator-produced radionuclides for the commercial vendors. A variety of arrangements could be used to accomplish this task varying from industry employees handling the production on site to the NBTF providing the raw material to the vendor. Finally, commercial ventures could be spawned as a result of the new radiopharmaceuticals utilizing radionuclides produced at the NBTF. The latter two scenarios have the potential to generate royalty payments as described in the IOM report.

G.1 Revenue Scenarios

The business plan generated for this study necessarily contains proprietary information. As such, an abstract of the data presented in the plan will be outlined here. The plan uses data received from the Dept. of Energy, the Arthur Andersen audit of the Isotope Production and Distribution Program and the market study performed by the Hospital Financial Corporation. No attempt was made to determine independently the veracity of the figures obtained from these studies. We asked the industrial members of our advisory committee to examine these figures and inform us when they did not reflect the current market.

One of the difficulties we faced was to predict where the market would be in the year 2000, the projected first year of operation of the NBTF. The uncertainty in the future of the facilities at BNL and LANL added to this problem. Our industrial advisors said that alternate sources would be developed in the event that LANL and BNL could not meet the market demand. If lost, the task of reclaiming those customers for the NBTF would be formidable.

In order to create a business plan based on the market for NBTF-produced radionuclides, we contracted with Ernst & Young to develop the financial plan for the NBTF. In determining the feasibility of private industry constructing the NBTF, we used the following assumptions.

1. The market for the accelerator produced isotopes sold by the DOE labs would not increase in price and would grow at the following rates from their 1992 income figures:

Radionuclide	Growth Rate
Sr-82	0 %
Co-57	10 %
Ge-68	10 %
Na-22	0 %
Cu-67	15 %

2. Construction of the facility would be financed by 30 year notes at 8 %. In the first scenario, the entire amount is financed. In the second scenario, 50 % of the building is assumed to be for commercial work and thus only half the cost of construction is financed by a nonprofit entity.

3. Any activities for education, training and research would be covered by a combination of grants, contracts and institutional funds. They are not included in this analysis.

4. Of the personnel recommended in Section F, approximately half would be involved in the commercial production activity. Because the personnel involved in this activity include the technicians and clerical staff, the costs are less than half the total personnel costs for the facility.

5. Utilities and other "overhead expenses" are treated as direct costs as they would for a private business. No separate overhead is included. Salaries increase at 4 % per year; supplies and equipment at 6 % per year.

6. Total capital costs are $65 million, expended over a period of three years with operation commencing in the fourth. An additional $7 million in startup costs, primarily salaries for staff during the construction phase, are amortized over 30 years.

7. Tax effects have not been considered.

In reviewing the analysis, the argument could be made that the construction cost includes some space and resources that support the R&D or the E&T parts of the mission. If we accept this premise, and arbitrarily assign 50 % of the facility costs to these two missions and exclude depreciation and amortization as one might for a non-profit enterprise, we will still run at a deficit of over $3 million per year.

Even if one or two wildly successful radionuclides were to be developed at the NBTF, it is unlikely that they would penetrate the commercial market in this time frame. However, to examine the impact of such an activity, it is instructive to look at a couple of examples from the isotope list for the NBTF.

Assume that demand for Xe-127 is of the order of 5 Ci per month. At a production rate of 0.07 mCi/μA(11), it would require 71,500 μA per month. Assuming that we could put 500 μA on target, this would necessitate 143 hours per month of beam time. At $400 per hour for 500 μA beam time (derived by summing all of the operating costs divided by the number of hours per year of operation times 0.5 total current available), this would result in income of $57.2K per month or $686.4K per year. Assume further that the production method involves proprietary technology that would result in a royalty agreement for 5 % of the gross retail sales. With a markup on the order of 400 % from raw radiochemical costs to radiopharmaceutical (extrapolated from retail and wholesale data in the Andersen and HFC studies), this would mean that the retail market would be about $3 million per year, generating $150,000 in royalties. Note that it is not clear that the radionuclide would be competitive at this price (~ $45 per mCi, retail).

If Pb-203 also became a successful isotope for imaging, and the market was 1 Ci per week, we would need 285 μa-h for an enriched Tl-205 target or 4500 μA-h for an enriched Tl-203 target to produce it(11). The revenue range (excluding the cost of the enriched target) would be

NBTF Payback

	Year						
	2000	2001	2002	2003	2004	2005	2006
Federal Payback Model	(all figures in $ thousands)						
Scenario 1							
Revenues	3,722	4,068	4,451	4,876	5,347	5,869	6,449
Expenses							
Salaries	1,630	1,695	1,763	1,833	1,907	1,983	2,062
Benefits	424	441	458	477	496	516	536
Supplies, etc.	779	852	932	1,021	1,120	1,229	1,350
Maintenance	284	301	319	338	359	380	403
Utilities	552	585	621	658	698	739	784
Other expenses	440	467	495	524	556	589	625
Total operating	4,109	4,341	4,588	4,851	5,136	5,436	5,760
Income (loss)	(387)	(273)	(137)	25	211	433	689
* Loan Pmt.	6,396	6,396	6,396	6,396	6,396	6,396	6,396
Depreciation	2,167	2,167	2,167	2,167	2,167	2,167	2,167
Amortization	233	233	233	233	233	233	233
Net Income (loss)	(9,182)	(9,068)	(8,933)	(8,770)	(8,584)	(8,362)	(8,107)
Capital outlay	750	795	843	893	947	1,004	1,064
Deficit	(9,932)	(9,863)	(9,776)	(9,663)	(9,531)	(9,366)	(9,171)
Scenario 2	50 % of bldg. cost financed.						
Income (loss)	(387)	(273)	(137)	25	211	433	689
* Loan Pmt.	3,198	3,198	3,198	3,198	3,198	3,198	3,198
Net Income (loss)	(3,585)	(3,470)	(3,335)	(3,172)	(2,987)	(2,764)	(2,509)
Capital expenditures	750	795	843	893	947	1,004	1,064
Deficit	(4,335)	(4,265)	(4,178)	(4,066)	(3,933)	(3,768)	(3,573)

*** Annual payment on 8 %, 30 year loan**

TABLE G.1 An analysis of the revenue and expenses for a "commercial" NBTF. Scenario 1: Full cost of construction financed by a for-profit company. Scenario 2: Half of cost of construction financed by a non-profit corporation.

approximately \$400 to \$4000 per week or \$21,000 to \$210,000 per year. If we assume annual retail sales of \$1 million per year, the royalties generated would be \$50,000 per year.

We have projected recovering the costs of production in these two cases. There is no provision for recovering depreciation (debt service) nor is any markup from the cost of beam time and some nominal processing cost. If a substantial amount of technician time was involved in purification or packaging, this would increase the cost. In either case, we are merely recovering part of the operating cost at full reimbursement rather than requiring a subsidy for the production of research radionuclides.

These revenues don't provide sufficient cash flow to turn the NBTF into a moneymaking enterprise. Even reducing the cost of the construction by 50 % to reflect building a facility that will only conduct the production mission does not result in an operation that runs in the black.

The question of how much capacity we have for isotope production also needed to be studied. We have made an estimate of the beam time required for "commercial" isotope production based on isotope sales from DOE labs in 1993 and assumed no growth in the purchases. This analysis provides an idea of what percentage of the beam time would be used in commercial activities. Obviously, this is a conservative estimate; we anticipate that a facility that runs year-round would have higher sales, especially for the shorter-lived isotopes. The results are shown in Table G.2

We assume that the cyclotron operates 24 hours per day 7 days per week except for one 8 hour maintenance period per week for three weeks and an additional 48 hour period per month. This totals 658 hours per month. Many of these target materials are long-lived and so would be kept on target lines for irradiation when the cyclotron was not performing other runs of shorter duration. Since three of these isotopes are positron emitters, they would be irradiated and processed in the production area where shielding was maximum. We also assume that demand for Xe-127 and Pb-203 are at the level proposed in the examples above.

	mCi/mo	mCi/μAh	μA/mo	hrs/mo @500μA	\$/mCi
Na-22 (12)	167	0.003	55,556	111	\$ 268.00
Co-57 (11)	1,000	0.100	10,000	20	9.00
Ge-68 (11)	167	0.028	5,952	12	30.00
Cu-67 (11)	1,000	0.020	50,000	100	42.00
Sr-82 (11)	1,000	0.300	3,333	7	4.00
		Total	124,841	250	
			19% % capacity		
Xe-127 (11)	5,000	0.070	71,429	143	12.00
Pb-203 (11)	1,000	0.220	4,545	9	8.00
		Total	200,815	402	
			31% % capacity		
Cd-109 (12)	300	0.001	300,000	600	803.00
		If target is run individually			

Table G.2 An analysis of the beam time required to produce five of the largest selling isotopes in the DOE program. We have included three that commercial vendors have indicated would be commercially viable if produced year-round.

Since silver plate could be used as target backing and beam stop, we have not included the Cd-109 production in the capacity calculations as it would be a produced with "waste" beam in higher energy reactions. The superior heat transfer property of silver makes this a viable scheme for production even in higher current targets. If it were to be run as a single target to produce the quantities required, the cost would be quite high due to its low production yield.

As can be seen, there is some excess capacity in this breakdown for isotope production. The NBTF could be called upon during scheduled and unscheduled outages at commercial vendors as a backup or supplementary source of radionuclides. There also is room for one or two other radionuclides that had large demand. For example, if Sr-82 demand increased as a result of approval of Rb-82 for reimbursement of perfusion imaging, there is capacity to meet ten times the demand for this radionuclide.

G.2 Public - Private Partnership

In order to explore the public-private partnership possibilities presented by the NBTF, we asked one of our team members to propose an operational partnership. It provided an opportunity to draw on strengths of the industrial partner that would not likely be found on a university campus. In this particular proposal, the private partner does not have a financial interest in which isotopes are produced, i.e. which have the largest profit margins. In discussions with our advisors, we have determined that this might be a significant problem with some of the partnerships being driven by profit rather than meeting the needs of the research community. We have built the positions outlined in this proposal into the NBTF staffing outlined above. Obviously, these positions are required no matter who pays for them, so they are still part of the bottom line for the NBTF.

G.2.1 Packaging, labeling, shipping, and transporting at the NBTF

The packaging, labeling, shipping, and transporting of radioisotopes is an integral part of the operation of the NBTF. As such, Coleman Research Corporation has developed a comprehensive packaging, shipping, and transportation management plan, whose key elements are described in this section.

G.2.1.1 Physical Characteristics

The Distribution Center will be co-located with the production facility, for security and efficiency reasons. The center will include the following key areas:

- Ample storage space to store packaging supplies, product, and interim waste.
- A secure consolidation area in which material can be inspected, packaged, and stored before shipping.
- A loading dock, for the speedy and safe distribution of production materials and waste.
- Tracking area and system with ample office space for the shipping clerk and computer equipment required for label making and shipment tracking.

G.2.1.2 Personnel Requirements

The Distribution Center will be managed and operated by Coleman Research Corporation, which has extensive experience in this domain and, more particularly, is intimately familiar with regulatory requirements for the handling, storing and shipping of radioactive materials. The following personnel will staff the Distribution Center.

A Senior Manager with transportation and nuclear experience will manage the operations.

A Health Physicist will provide worker safeguards, training, and emergency response.

A Quality Assurance and Control Expert will be hired to ensure that proper controls are in place.

A Shipping Clerk will coordinate shipments of product and waste. The clerk will be responsible for address labeling, pick-up and delivery of shipments, and tracking shipments including return receipts. Marking and labeling of packages will be done in accordance with 49 CFR 172.300 and .400.

Two Material Package, and Waste Handlers, with previous nuclear medicine, or nuclear waste packaging experience will be responsible for the packaging, labeling, and loading of product materials and radioactive waste. The packages/waste handlers will be responsible for handling, packaging, and loading of shipments.

As described above, the total staff for manning the center is a minimum of six. However, needed redundancy at the lower echelons will be provided through the hiring of a third Material Package, and Waste Handler. Two of the three material handlers will be trained to replace the Shipping Clerk, during periods of absence of the latter.

A personnel management and administration manual will be developed for personnel on site during operations.

G.2.2 PACKAGING AND LOGISTICS MANAGEMENT

G.2.2.1 Regulatory Compliance

A comprehensive regulatory compliance program will be initiated and developed to insure compliance with all applicable county, city, state, and federal laws and regulations.

G.2.2.2 Carrier Selection

Transportation of radioisotopes will be accomplished with outside, contract motor-carriers. Also, mainstream air companies (such as Airborne Express, Federal Express, and UPS) will be used.

A standard operating procedure for emergency response will be established, with one person available 24 hours a day. This person will have all necessary information needed to respond to emergency situations.

A thorough quality assurance program will be established to cover materials accountability, internal and external tracking, loss and damage claims, and carrier evaluation and review program.

G.2.3 PACKAGING PROCEDURES

G.2.3.1 Applicable Regulations

All materials to be shipped will be identified in accordance with 40 CFR 261 for hazardous wastes regulated by the U.S. Environmental Protection Agency (EPA), and in accordance with 49 CFR 172 for those materials which the U.S. Department of Transportation (DOT) has designated as hazardous materials for purposes of transportation.

G.2.3.2 Packaging Types and Requirements

The hazard class will be determined in accordance with 49 CFR 173. Selection of the packaging type and packaging requirements will follow the regulations embodied in 49 CFR 173.

All packages used to ship hazardous materials will meet the general requirements described in 40 CFR 173.24 and 173.24(a).

The type of packaging used for radioactive material shipment will be in accordance with the general requirements found in 49 CFR 173.411 and the requirements for the specific shipping category. Unless otherwise specified, all shipments of radioactive materials will meet all requirements of 49 CFR 173.411 and 173.412.

G.2.3.3 Packaging, Marking, and Labeling

Each package, container, and transport vehicle containing hazardous materials will be marked in accordance with CFR 172.300.

DOT labels will identify the hazardous nature of the material within the package.

G.2.4 SHIPPING

Shipping will be done in strict conformance with 49 CFR 172.200.

G.2.4.1 Proper Shipping Names

Proper shipping name selection will include Chemical Names, Generic Description, Generic Names, and Hazard Class Names.

For Radioactive Materials, the proper shipping name will be selected after obtaining information concerning the radionuclide, activity, and material form. Limited quantity and Low Specific Activity (LSA) shipments sometimes allow a shipper to be excepted from one or more of the specification packaging, marking, labeling, and shipping paper requirements. Because of economic advantages, the applicability of these exceptions, will be checked to see if they apply to a specific shipment.

G.2.4.2 Shipper Certification and Manifest

A shipper's certification that the material is being sent in accordance with DOT regulations will accompany every shipment of hazardous material sent for transportation. Similarly, every hazardous waste shipment will be accompanied by the appropriate EPA Form 8700-22 and 8700-22A (when necessary) hazardous waste manifest, prepared in accordance with 40 CFR 262.20. The manifests will be signed, carried, and copies given to appropriate persons as required in 49 CFR 172.205.

H. Conclusions and Recommendations

The study conclusions agree nearly universally with those of the IOM Panel Report on Isotope Availability with respect to the NBTF. Those are:

1. Short term, there is no problem with the availability of commercial radionuclides produced on accelerators of energy below 40 MeV.

2. There is a clear need for a higher energy machine to provide researchers with radionuclides for new applications.

3. All of the radionuclide presented in the IOM report and the expanded table in this document can be made with an accelerator of energy of 70 MeV (the IOM panel suggests 80 MeV).

4. The beam current should exceed 750 μA. This will enable the NBTF to supply several radionuclides in large quantity while supplying small quantities of many more by simultaneous irradiations.

5. The mission of the NBTF should be production of radionuclides for the research community; research and development centered on accelerator- and generator-produced radionuclides; and education and training of people at various stages of their scientific career.

This study makes the following recommendations:

1. The NBTF should be centered around negative ion cyclotron that accelerates protons with an energy range from 10 MeV to 70 MeV and accuracy and reproducibility within ± 1.5 MeV and < 1 %, respectively A second cyclotron should be built that can accelerate He-4 with internal and external irradiation capabilities for the production of At-211 and other radionuclides that are more efficiently produced by irradiations with particles heavier than protons.

2. The NBTF should be capable of producing an extended list of isotopes beyond those outlined in earlier workshops and reports with a focus on many with shorter half life than has been traditionally available from the DOE system. Proximity to an airport is essential to provide the capability of same day shipments.

3. The NBTF should be built on a University campus. This campus should have programs in basic science and engineering, a medical school, and a medical center. Thought the NBTF has a clear mission in radionuclide production, its value as a center for nuclear medicine research will be enhanced by integration into a site in which basic, applied and clinical nuclear medicine research is performed.

4. The operations (accelerator operation and radionuclide production) of the NBTF must be run as a business. The other two missions would be treated as customers of the operations group. The goal is to provide a stable, reliable source of radionuclides that will not be adversely affected by the research or education programs. The NBTF will only produce raw radiochemicals. No radiopharmaceutical grade material should be produced on site.

5. The NBTF must be built with Federal funds with no expectation of payback to the government. The market analysis shows that there is no expectation of generating enough revenue to pay a loan, even at no interest.

6. The NBTF needs to establish and maintain a commitment to Total Quality Management and Continuous Quality Improvement from the start. Within this commitment, compliance with ISO 9000 certification, Good Laboratory Practice, and Drug Master File submissions.

7. The current Environmental, Safety and Health Guidelines on a Federal and State (Alabama) level are sufficient to insure that the NBTF can be built and operated safely. These regulations should not present an impediment to construction if they are addressed in a timely fashion. The disposal of radioactive waste may be a problem in some areas of the country. We

recommend that a site be chosen in a waste compact that is currently, and will in the future, have an operating waste disposal depository. The chosen site should also have a regulatory environment that is conducive to the movement of radionuclides.

8. The NBTF needs to forge a strong collaboration with national laboratories. There are substantial intellectual and physical resources in the area of isotope production, separation chemistry and other operating issues.

9. The NBTF presents many opportunities for public private partnerships. These range from an industrial partner handling the operations of the NBTF to spin-off companies that will process and market radiopharmaceuticals from radionuclides produced at the NBTF. The siting decision should include consideration of the economic development potential for that state.

10. The NBTF should have an advisory committee. This committee will assist the director in defining the objectives of the NBTF within the mission; prioritizing radionuclide production, especially those isotopes produced below cost; and developing a focused research and education program.

11. The NBTF should not be operated by a national laboratory. The combination of increased cost of construction due primarily to greater regulatory scrutiny, increased cost of operations, lack of strong business orientation in isotope production (6) and the excessive micromanagement by DOE (10) all contributed to the advisory committee's recommendation on this point.

I. Glossary

ACS	American Chemical Society
BLIP	Brookhaven Linac Isotope Producer
BNL	Brookhaven National Laboratory
CEES	Coleman Environmental and Energy Systems
CQI	Continuous Quality Improvement
CRC	Coleman Research Corporation
DOE	US. Department of Energy
ED	Education and Training Director
EPA	Environmental Protection Agency
ESH	Environmental, Safety, and Health
ES&H	Environmental, Safety, and Health
E&T	Education and Training
GA	General Atomics
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
IOM	Institute of Medicine
LANL	Los Alamos National Laboratory
LLRW	Low Level Radioactive Waste
M&S	Materials and Services
NAS	National Academy of Sciences
NBTF	National Biomedical Tracer Facility
NFT	National Filter Technology
NIH	National Institutes of Health
NRC	Nuclear Regulatory Commission
NSF	National Science Foundation
OD	Operations Director
O&M	Operations and Maintenance
PLC	Programmed Logic Controller
P&L	Profit and Loss
QA	Quality Assurance
QC	Quality Control
RD	Research Director
R&D	Research and Development
TQM	Total Quality Management
UAB	University of Alabama at Birmingham

J. References

1. The Role of a High-Current Accelerator in the Future of Nuclear Medicine, Proceedings of a DOE-LANL Workshop, 1989

2. Review of the Office of Health and Environmental Research Program in Nuclear Medicine, 1989

3. National Biomedical Tracer Facility Planning and Feasibility Study. Richard A. Holmes, M.D. Society of Nuclear Medicine/American College of Nuclear Physicians, 1991

4. Proceedings of the Purdue National Biomedical Tracer Facility Workshop, 1992

5. Isotopes for Medicine and the Life Sciences, Institute of Medicine, National Academy Press, 1994.

6. U.S. Dept. of Energy Isotope Production and Distribution Program Management Study. Arthur Andersen & Co., March 1993.

7. Radiochemical Market Study, Hospital Financial Corporation, 1994.

8. Training Requirements for Chemists in Nuclear Medicine, Nuclear Industry and Related Areas, National Academy Press 1988.

9. Newsline, Journal of Nuclear Medicine, Feb. 1995.

10. Alternative Futures for the Department of Energy National Laboratories. Prepared by the Secretary Of Energy Advisory Board; Task Force on Alternative Futures for the Department of Energy National Laboratories, February 1995

11. Program Delivers Straight Talk About ISO 9000 Requirements, R&D Magazine, January 1995.

12. Radionuclide Production for the Biosciences. T.J. Ruth et al. Nucl. Med. Biol. 16:323-36 (1989).

13. National Nuclear Data Center; CSISRS Database

ACADEMIC COMMITTEE

Ken Kliewer, Ph.D.
Director for the Center of Computational Sciences
Oak Ridge National Lab
P.O. Box 2008
Bethel Valley Road
Bldg. 4500 N.
Oak Ridge, TN 37831

Michel ter-Pogossian, Ph.D.
Professor of Radiation Science
Mallinckrodt Institute of Radiology
Washington Univ. School of Medicine
660 South Euclid Avenue
St. Louis, MO 63110

Thomas E. Boothe, Ph.D.
Director of Cyclotron and Radiochemistry
Mt. Sinai Medical Center
4300 Alton Road
Miami Beach, FL 33140

Ronald Jaszczak, Ph.D.
Professor of Radiology and Biomedical Engineering
Duke Univ. Medical Center
Durham, NC 27710

George W. Kabalka, Ph.D.
Robert H. Cole Professor
Director of Basic Research at the Univ. of Tennessee Biomedical Imaging Center
1924 Alcoa Highway
Knoxville, TN 37920-6999

Ronald Manning, Ph.D.
Associate Professor of Radiology
1251 Vanderbilt
Univ. Medical Center
Department of Radiology & Radiological Sciences
School of Medicine
2222 Pierce Avenue
Nashville, TN 37232-2675

H. Anthony McBride, Ph.D.
Professor of Chemistry and Associate Dean
Samford University
School of Pharmacy
Office of Dean
800 Lakeshore Drive
Samford Hall Room 207
Birmingham, Al 35229

Alice Mignerey, Ph.D.
Associate Dean
Director of Graduate Studies for the Department of Chemistry
University of Maryland
College Park, MD 20742

Aldo N. Serafini, M.D.
Professor of Medicine & Biology
University of Miami
Department of Radiology
Division of Nuclear Medicine
P.O. Box 016960
Jackson Memorial Hospital
Miami, FL 33101

J.E. Bartels, D.V.M., M.S.
Head of the Department of Radiology
College of Veterinary Medicine
Auburn University
Auburn, AL 36849-5524

Evelyn Watson, B.S.
Program Director (Ret.)
Oak Ridge National Laboratory
104 New Bedford lane
Oak Ridge, TN 37830

INDUSTRIAL COMMITTEE MEMBERS

Ken Kliewer, Ph.D.
Director, Center for
Computational Sciences
Oak Ridge National Lab
P.O. Box 2008
Bethel Valley Road
Bldg. 4500 N.
Oak Ridge, TN 37831-6208

F.F. (Russ) Knapp, Ph. D.
Group Leader
Oak Ridge National Lab
Nuclear Medicine
P.O. Box 2008
Bethel Valley Road
Oak Ridge, TN 37831

Mr. Carmen J. Marchetti
Materials Management Coordinator
DuPont NEN Research Products
Medical Products Dept.
331 Treble Cove Road
N. Billerica, MA 01862

Mr. Peter Vermeeren
Mallinckrodt Medical Inc.
675 McDonnell Blvd.
P.O. Box 5840
St. Louis, MO 63134

Saed Mirzadeh, Ph.D.
Staff Scientist
Oak Ridge National Lab
P.O. Box 2008
Bethel Valley Road
Bldg. 4501
Oak Ridge, TN 37831

Mr. Bill Ehmig
Medi Physics
2636 S. Clear Brook Dr.
Arlington, IL 60005

Mr. Al Herbert
Medi Physics
2636 S. Clear Brook Drive
Arlington, IL 60005
708-593-6300 (ext. 222)
Fax:708-593-8010

Thomas E. Boothe, Ph.D.
Director of Cyclotron and Radiochemistry
Mt. Sinai Medical Center
4300 Alton Road
Miami Beach, FL 33140

Ronald Manning, Ph.D.
Associate Professor of Radiology
Dept. of Radiology & Radiological Sciences
Vanderbilt University
School of Medicine
2222 Pierce Avenue
Nashville, TN 37232

William Goeckler, Ph.D.
Assistant Director, Pharmaceutical Development
CYTOGEN Corp.
600 College Park East
Princeton, NJ 08540

Richard Toohey, Ph.D.
Program Director,
Radiation Internal Dose Information Center
Oak Ridge Institute for
Science & Education
140 East Vance Road
P.O. Box 117
Oak Ridge, TN 37831

Mr. Roy Brown
Director, Regulatory and Professional Affairs
Mallinckrodt Medical Inc.
675 McDonell Blvd.
P.O. Box 5840
St. Louis, MO 63134

Alan R. Fritzberg, Ph.D.
Director of Radiochemistry
NeoRx Corporation
410 West Harrison
Seattle, WA 98119

Mr. Dan Montgomery
Vice President and Q.A. Manager
Analytics, Inc.
1380 Seaboard Ind. Blvd.
Atlanta, GA 30318

Mr. Carl Seidel
Associate Director, Technical Affairs
DuPont Merck Pharm. Co.
Radiopharmaceutical Div.
331 Treble Cove Road
N. Billerica, MA 01862

Mr. Peter Holton
Manager - Cyclotron Operations
DuPont Merck Pharm. Co.
Radiopharmaceutical Div.
331 Treble Cove Road
N. Billerica, MA 01862

STEERING COMMITTEE MEMBERS

Dr. Kenneth J. Roozen
Executive Vice President, UAB
701 20th Street South
B'ham, AL 35294-0110

Mr. William Croker
Governmental Relations
701 20th Street South
Suite 880
B'ham, AL 35294-0108

Dr. James Mountz
Radiology-Nuclear Med.
625 South 19th Street
JT 256
B'ham, AL 35294-6830

Dr. Ruby Meredith
Radiation Oncology Dept.
1824 6th Avenue South
WTI 102
B'ham, AL 35294-6832

Dr. Gerald Pohost
Univeristy Hospital-Chief Services
Div. Director, Cardiology
1900 University Blvd.
THT 311
B'ham, AL 35294-0006

Dr. J. Claude Bennett
President of UAB
701 20th Street South
Suite 1070
B'ham, AL 35294-0110
205-934-4636
Fax: 975-8505

Dr. Sergio Stagnos
Vice President of Health Affairs of UAB
701 20th Street South
AB 7th Floor
B'ham, AL 35294-0107

Mr. Terry Waters
Alabama Power Company
P.O. Box 2641
600 N. 18th Street
B'ham, AL 35291-0001

Mr. Dieter R. Rietz
RUST Int'l. Corp.
100 Corporate Parkway
B'ham, AL 35242

Dr. Kenneth Pruitt
701 20th Street South
Suite 1225
B'ham, AL 35294-0112

Jim Garland
Facilities Planning
701 20th Street South
3rd Floor
B'ham, AL 35294-0103

Jim James
Director of Campus
Planning
1825 University Blvd.
B-23 MJH
B'ham, Al 35294-2010

Dr. Robert Diasio
Dept of Pharmacology
VH 101
UAB

Dr. Terry Hickey
Office of Vice President of Health Affai
701 29th Street South
UAB
B'ham, AL 35294-0107

Dr. Donald Buchsbaum
Radiation Biology
1824 6th Avenue South
WTI 674
B'ham, AL 35295-6832

Mr. Michael Garrett
Alabama Power Co.
P.O. Box 2541
600 N. 18th Street
B'ham, Al 35291-0001