

# Purdue University National Biomedical Tracer Facility - Project Definition Phase

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*Final Report*

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## Executive Summary

The proposed National Biomedical Tracer Facility (NBTF) will house a high-current accelerator dedicated to production of short-lived radionuclides for biomedical and scientific research. The NBTF will play a vital role in repairing and maintaining the United States' research infrastructure for generation of essential accelerator-based radioisotopes. If properly designed and managed, the NBTF should also achieve international recognition as a Center-of-Excellence for research on radioisotope production methods and for associated education and training. The current report documents the results of a DOE-funded *NBTF Project Definition Phase* study carried out to better define the technical feasibility and projected costs of establishing and operating the NBTF.

This report provides an overview of recommended *Facility Design and Specifications*, including *Accelerator Design*, *Building Design*, and the associated *Construction Cost Estimates and Schedule*. It is recommended that the NBTF be established as an integrated, comprehensive facility for meeting the diverse production, research, and educational missions set forth in previous documents.<sup>1-5</sup> Based on an analysis of the projected production demands that will be placed on the NBTF, it appears that a 70 MeV, 1 mA, negative ion cyclotron will offer a good balance between production capabilities and the costs of accelerator purchase and operation. A preliminary architectural plan is presented for a facility designed specifically to fulfill the functions of the NBTF in a cost-effective manner.

This report also presents a detailed analysis of the *Required Federal, State, and Local Permits* that may be needed to establish the NBTF, along with schedules and cost estimates for obtaining these permits. The *Handling, Storage, and Disposal of Radioactive Waste* will pose some significant challenges in the operation of the NBTF, but at this stage of planning the associated problems do not appear to be prohibitive.

The draft *Business Plan for Operation of the NBTF* projects the level of recurring Federal support that will be required to operate the NBTF in a fashion that meets documented needs in the areas of education and research. The report also provides a *Projected Operating Schedule* for the NBTF isotope production program and describes and justifies the major *Proposed Product Isotopes* of the NBTF. Federal funding will be required to establish the NBTF. However, it appears that the NBTF can be operated in a fashion that adheres to the previously-proposed NBTF Mission Statement, while also insuring that the major routine radioisotope production functions are financially self-supporting.

Finally, this report documents Purdue University's *Ability to Provide Associated Education and Training* through its extensive existing programs in nuclear and radiochemistry, nuclear pharmacy, health physics, industrial pharmacy, nuclear physics, nuclear engineering, medicinal chemistry, and other related areas.

## Introduction

The National Biomedical Tracer Facility (NBTF) will serve the United States as a national resource dedicated to education, research, and the production of radionuclides for biomedical and scientific applications. The NBTF should be internationally recognized as a showcase facility in every aspect of its design and operation. This *NBTF Project Definition Phase* effort has been pursued with a commitment to designing a facility that effectively serves the biomedical, scientific, and industrial communities in the United States as described in the *NBTF Mission Statement* (see page 5).<sup>4</sup> Achieving this goal will require design and construction of excellent capital facilities, staffing these facilities with highly-qualified personnel, and implementation of a sound operating and management philosophy. This report documents the initial planning for construction and operation of such a facility.

The goals for the *Project Definition Phase* were:

1. To further refine the design, construction schedule, and cost estimates associated with a comprehensive facility for meeting the diverse production, research, and educational missions of the NBTF.
2. To examine the radioactive waste management, disposal, and other environmental issues associated with successful operation of the NBTF.
3. To develop a business and management plan for successful operation of the NBTF over its expected lifetime.
4. To assist the Department of Energy (DOE) in determining how effective such a facility would be in satisfying current and future radioisotope needs for medical, scientific, and industrial applications.
5. To assist DOE in determining whether the NBTF can be operated by the private sector (*i.e.*, outside of an existing DOE National Laboratory).

The project aims are generally unchanged from those described in our original proposal. However, as instructed by the Project Officer, the scope has been reduced to match the available level of funding by minimizing "site-specific" design and planning.

As a model planning site for the NBTF we have chosen a new segment of the Purdue Research Park that adjoins both the Purdue University main campus and the Purdue Airport in West Lafayette, Indiana. Such a site is ideally-suited to the functions of the NBTF, combining a central geographic location (with proximity to excellent shipping and distribution infrastructure) and access to strong university-based educational and research programs. In serving as host for the NBTF, Purdue University would continue to fulfill its mission as a land grant institution, logically building upon *existing* research and educational programs in nuclear and radiochemistry, nuclear pharmacy, radiopharmaceutical chemistry, industrial pharmacy, health physics, medical physics, nuclear physics, nuclear engineering, and cancer research, plus existing ties to the Indiana University Medical School and 200 MeV cyclotron facility.

## Mission of the National Biomedical Tracer Facility\*

The *National Biomedical Tracer Facility* (NBTF) will serve the United States as a national resource dedicated both to the production of radionuclides, radiochemicals, and radiopharmaceuticals for biomedical and scientific applications, and to education and training in nuclear and radiochemistry, nuclear pharmacy, nuclear medicine, health physics, and associated nuclear science and technologies. The NBTF will supply radioisotopes that are not supplied on a routine basis by industry, but which are required by physicians and biomedical researchers for use in the diagnosis and treatment of disease and the investigation of physiological processes. The NBTF will also provide radioisotopes needed in many other fields, including nutrition, agriculture, environmental studies, genetics, molecular biology, pharmacology, drug development, geology, manufacturing, and industrial calibration and testing.

This mission will be fulfilled through:

1. The production of research radionuclides for the biomedical and scientific communities.
2. The conduct of research into radionuclide production, separation, and purification.
3. The provision of education and training in techniques of radionuclide production, separation and purification; radiotracer synthesis; radiation protection and safety; and the applications of radiotracer methodologies.
4. The conduct of research in basic radiopharmaceutical chemistry, which fosters and supports the continued development of biomedical applications of radionuclides.
5. The production of radionuclides for commercial purposes in cases where these nuclides are not available to meet national needs through U.S. commercial channels.

\*This Mission Statement was developed at the Purdue University NBTF Workshop, April 28-30, 1992 and was unanimously approved by the Society of Nuclear Medicine-American College of Nuclear Physicians NBTF Task Force at their June 1992 meeting in Los Angeles.

## Facility Design and Specifications

**Accelerator Design and Specifications.** Our conclusions regarding design specifications for the NBTF accelerator are enumerated below (Table 1). These specifications are based on the recommendations found in the 1992 *Proceedings of the Purdue National Biomedical Tracer Facility Workshop* (Appendix 1),<sup>4</sup> with subsequent refinement to reflect the conclusions of various fact-finding documents presented as additional Appendices to the current report. These refinements take into account a more complete description of the nuclides the NBTF will be expected to produce, as well as the need to design and construct, in a timely manner, a reliable facility that will require minimal construction and operations support from DOE.

**Table 1. Recommended Design Specifications for the NBTF Accelerator**


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1. The accelerator should be a negative ion ( $H^-$ ) cyclotron.
2. The extracted proton beam energies should range from 30 to 70 MeV in 1 MeV steps.
3. Beam energy should be reproducible to 1%.
4. Beam energy spread should be less than 1%.
5. Extracted beam current should be greater than 0.75 mA, with an expectation of achieving 1.0 mA.
6. The accelerator should provide at least two high-intensity beams and two low-intensity beams, at least two of which can be operated simultaneously with separately-controllable energies.
7. The accelerator design should allow continuous, around-the-clock, accelerator operation with less than 36 hours/week routine maintenance.
8. The accelerator should operate 48 weeks per year with the remaining 4 weeks per year allowed for scheduled routine major maintenance plus (unscheduled) breakdowns.

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On the basis of strong recommendations from the three major domestic commercial radioisotope producers, whose business success has been inextricably linked to establishment of reliable accelerator facilities that operate in a cost-effective manner, a cyclotron (rather than a linear accelerator) has been specified. At least two established international cyclotron manufacturers, Ion Beam Applications (IBA) and Ebc Technologies, clearly possess the technical expertise needed to design and build the accelerator and associated targetry systems required to fulfill the NBTF mission. At this stage of the NBTF design process our plans can readily accommodate either vendor's machine. (It has been assumed that selection of a final accelerator vendor will be deferred until a final site is selected for NBTF construction. Final vendor selection would be based upon an open process involving competitive bidding for the accelerator design and construction contract.)

The cyclotron energy and beam configuration specifications are based upon the projected production requirements for this facility and a related cost-benefit analysis (Appendix 2, pages 26–30), plus the projected facility operating schedule (Appendix 3, pages 2.4 to 2.10). The proposed design will dictate that a small subset of accelerator-produced research radionuclides (e.g.,  $^{22}Na$ ,  $^{26}Al$ ,  $^{32}Si$ ,  $^{83}Rb$ ,  $^{109}Cd$ ) should continue to be produced at the Department of Energy's higher-energy BLIP or LAMPF accelerators (or their successors); the incremental cost of adding production capabilities for these nuclides at the NBTF does not appear to be merited.

An illustration of a sample accelerator layout is shown in Appendix 3, page 2.10.

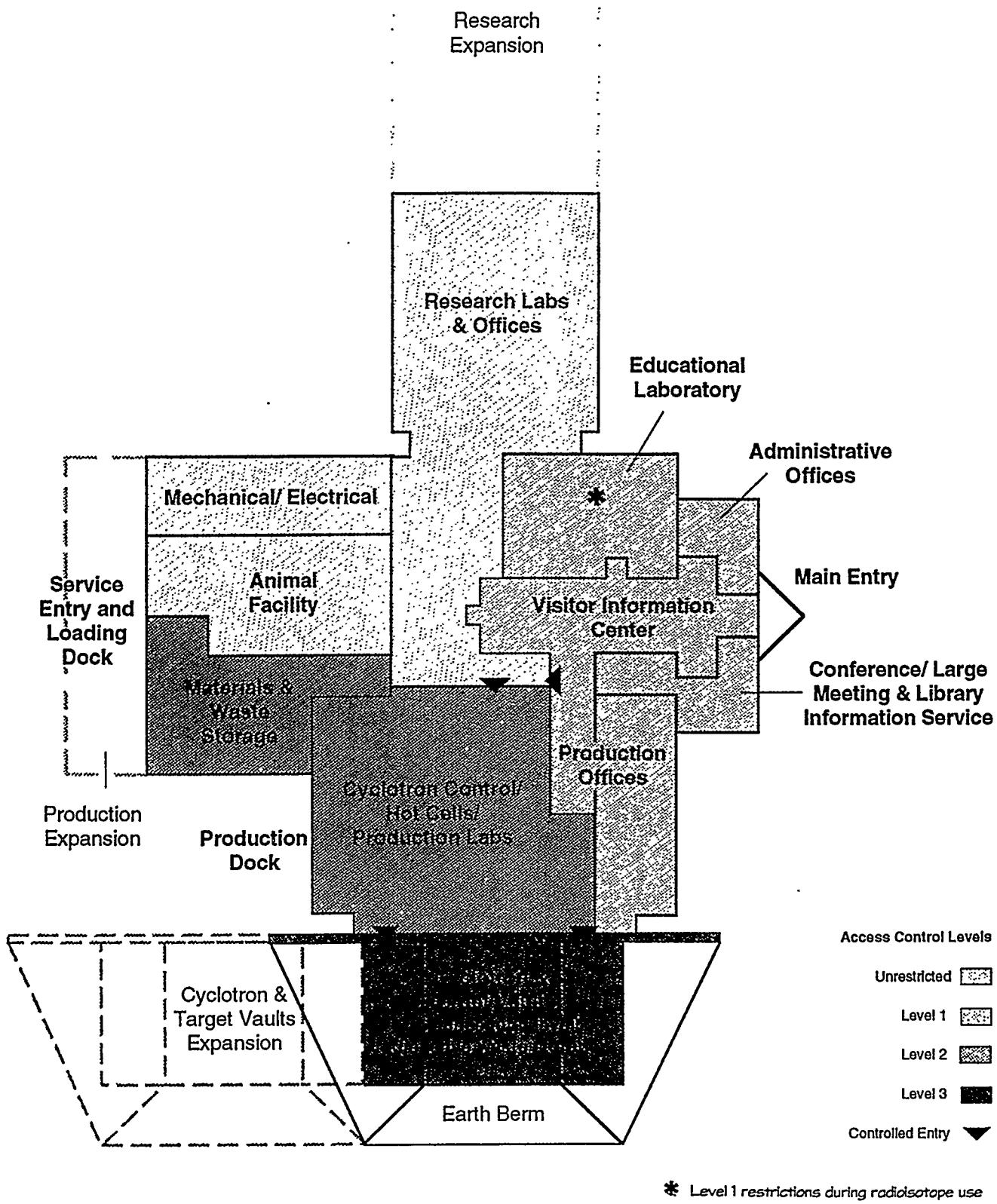
## **Building Design and Specifications.**

*Site Selection.* The site selected for detailed investigation during the NBTF Project Definition Phase (see Appendix 4, page 1.3 and Appendix 11, page 26) provides excellent proximity to the Purdue University campus and the Purdue airport; is remote from residential housing; is seismically stable; offers substantial industrial research park space for possible location of peripheral companies that might wish to be near such a facility; offers adequate space for addition of a stable-isotope separations/enrichment facility, should DOE also decide to establish a national production laboratory for enriched stable isotopes (to meet the existing and anticipated needs of the research and industrial communities<sup>5</sup>); and is superbly accessible for shipping *via* a new four-lane highway linking the site to Interstate-65 for package delivery to the Indianapolis and/or Chicago airports (see map on page 27 of Appendix 11).

*Design Considerations.* The model site employed for this *NBTF Project Definition Phase* effort provides the opportunity to design a single, well-integrated, comprehensive facility for meeting the diverse NBTF missions. Facility design has been driven solely by intended function, setting the stage for efficient and reliable operations once the building is commissioned.

Since the National Biomedical Tracer Facility will be a national resource, our goal is to develop a design that acts as a catalyst for bringing together the production staff, the NBTF research team, visiting researchers from academia and industry, and visitors from the general public. The building must unify the diverse functional and technical requirements of radioisotope production and distribution; research to develop radionuclide production techniques and applications; and related educational activities. Thus, we have sought a design that establishes multiple levels of restricted access and functional segregation, allowing unrestricted public tours while maintaining production efficiency and reliability. Since this facility will be largely funded by the taxpayer, every effort has been made to design an economical facility without compromising its ability to achieve excellence in each of its three primary missions (production, education, and research).

In working with CRSS Architects and Constructors to develop our preliminary conceptual design for this building (Figure 1 and Appendix 4, pages 1.4 to 1.6) the Purdue team placed a high priority upon maintaining flexibility for possible future expansion of both the research and production areas. Thus, our architectural design for the Project Definition Phase readily allows for future expansion of the research wing to generate additional laboratory space (Figure 1 and Appendix 4, page 1.4, item #31). Likewise, space is provided northwest of the initial accelerator vault (Figure 1 and Appendix 4, page 1.4, item #29) for possible addition of a second accelerator, should developing research and clinical needs of the biomedical and scientific communities require the installation of either an additional <sup>1</sup>H accelerator or an alpha or <sup>3</sup>He accelerator. Hot cell spaces in the production wing are similarly designed for flexibility and future expansion. The current plan calls for installation of seven hot cells, while also including as part of the original construction the pads needed to accommodate up to four additional hot cells (Appendix 4, page 1.5, item #44).



## Purdue NBTF Floor Plan

Figure 1. Sketch of proposed facility layout.

Scale: 0 32 64



Our preliminary architectural program describing the area requirements we project for the NBTF is summarized on page 2.1 of Appendix 4 and completely enumerated on the three subsequent pages (2.2 to 2.4). These spaces include: production areas (accelerator and target vaults plus radioisotope processing, packaging, and distribution labs); research laboratories (wet labs, analytical labs, instrumentation development labs, an imaging lab, and a small animal facility to support in-house research on biomedical applications for nuclides produced by the NBTF); waste handling and storage spaces; training/educational laboratory spaces; conference rooms for enhancing faculty-industrial interactions; a public exhibit area; and building support and office spaces.

General design concepts leading to our proposed floor plan are described in Appendix 4, pages A.22 to A.33. Currently, we believe the NBTF production and research mission can be adequately fulfilled with six target vaults as shown in Appendix 3, page 2.10. However, a subsequent site-specific planning process should include examination of the flexibility that might be gained, if additional target vaults are included, and the associated incremental construction expense. Tentatively, the design calls for three (3) meters of concrete shielding for the accelerator and target vaults; however, during the site-specific design phase the adequacy of this specification will need to be confirmed by design-specific shielding calculations. Specific hot cell designs would also be further developed in the "site-specific design phase," but are expected to be modeled after those currently used in the radiopharmaceutical industry. Finally, we currently believe the NBTF production laboratories should be designed to current GMP (rather than GLP) laboratory standards, in order to insure maximum flexibility in the scope of facility operations.

### **Construction Cost Estimates and Schedule**

Table 2 presents a summary of our preliminary cost estimates for complete design, construction, and outfitting of this facility. The required real estate has been budgeted at the current market value. The additional "site development" costs include installation of storm sewers, a water main, and a high pressure gas main. The basis for the remaining design and construction cost estimate is completely detailed in Appendix 4, pages 3.2 to 3.5. Note that the quoted design and construction cost estimate *includes* the cost of cyclotron, beam transport systems, and target stations, as well as an allowance for fixed and movable equipment required to outfit the production and research laboratories.

The estimated NBTF construction costs in Table 2 are quoted in 1995 dollars. Once the final NBTF construction site is selected, an estimated 39 months will be required to complete permitting, prepare final architectural plans, order and construct the accelerator, and complete construction of the building. An additional 9 months has been allowed for cyclotron acceptance testing and commissioning. A detailed construction schedule is presented in Appendix 4, page 3.1, followed by the corresponding inflation-escalated final construction cost estimate on page 3.5.

**Table 2. Summary of Estimated Costs to Establish the NBTF (1995 dollars)**

Land (21 acres @ \$30,000/acre)	\$630,000
Site Development	\$600,000
Permits and Approvals (maximum estimated cost)	\$609,000
Enriched Stable Isotope Inventory for Target Preparation	\$5,061,000
Complete Facility Design and Construction	\$81,923,000
<b>Total</b>	<b>\$88,823,000</b>

Limited design and construction cost-sharing by the host institution and/or other related non-federal partners may be feasible. However, the exact magnitude of such cost-sharing is unlikely to be well defined prior to completion of the *site-specific* NBTF design process. We believe it is improbable that such cost-sharing would exceed the  $\pm 15\%$  design contingency included in our construction cost estimate. Therefore, at the current level of precision the costs quoted in Table 2 appear to be a reasonable projection for the amount of DOE funding required to establish a comprehensive facility for meeting the missions of the NBTF.

A *Draft Project Management Plan Outline* for the remainder of the NBTF design and construction process is presented in Appendix 5. This plan will be completely developed in a subsequent site-specific design phase and will detail project management responsibilities as well as cost and schedule control methods.

### Required Federal, State, and Local Permits

A detailed description of the Federal, State, and Local permits that may be required for construction and operation of the NBTF is provided in Appendix 6. The maximum of the estimated \$176,000 to \$609,000 cost to obtain these permits is included in the estimated costs quoted in Table 2 for Facility establishment. A summary of the basis for these estimates is presented in Table 3-1 at the end of Appendix 6. This analysis includes separate cost ranges for preparation of pre-permit application documents, the initial application, response to agency comments, and final application submittal, for the spectrum of permits that *may* be required. The broad range of this estimate is the result of currently undefined areas of scope and uncertainties associated with agency review comments. As plans for the NBTF are further refined, it is expected that some of the listed permits will be determined to be not applicable. Also, the quoted estimates do not include possible regulatory expenses/operating costs that may be associated with the production and sale of FDA-regulated radiopharmaceutical precursors.

The timetable for the permitting process is shown in Figure 3-1 of Appendix 6.

## Handling, Storage, and Disposal of Radioactive Waste

Radioactive waste streams that are expected to result from the major projected NBTF "production" activities are detailed in Appendix 2, pages 24 and 25, and Appendix 3, pages 3.14 to 3.18. Work practices will be structured to minimize both the amount of waste that is produced and the exposure to staff handling that waste. The waste radionuclides that pose the most concern will be Co-57 and Zn-65, due to their half-lives and the relatively large quantities that are likely to be produced (Appendix 3, pages 3.14 to 3.17). Since the availability of low-level radioactive waste disposal facilities is beyond the control of the NBTF managers, space has been allowed in the proposed architectural plan to allow storage of all radioactive waste for decay.

Large quantities of radioactive material will be generated by the irradiation of targets and the processing of the targets. This waste will need to be stored in shielded containers and vaults. When the radiation levels are reduced, this material may be further processed to reduce its volume prior to disposal at a low-level waste facility. Segregation of material with short half-lives will be done to take full advantage of the decay-in-storage (DIS) option. Final surveys will need to be performed to ensure that no measurable radioactivity is released to conventional waste disposal facilities, such as sanitary landfills.

A larger volume of solid waste will be generated from research activities at the NBTF. While lower in radioactivity, this waste needs to be disposed of at a low-level waste facility. Segregation of waste will be done to utilize the DIS option for the short-lived radionuclides. For combustible and biological materials, an incinerator should be used to reduce the volume of the waste. The ash will need to be stabilized prior to disposal at a low-level waste facility.

Drainage from sinks in rooms that house radioactive materials will need to be routed to holding tanks where sampling will be performed to ensure that this liquid meets the appropriate emission standards. Liquid waste from research will need to be collected in containers at the point of generation. This waste should also be consolidated in holding tanks and held for decay until applicable release limits are achieved. Handling of liquid waste should be minimized to keep worker exposure low and to reduce the possibility of spills.

Mixed waste will need to be minimized through design of chemical processes. When possible, non-hazardous chemicals should be used in target processing and radiochemical production. When this is not feasible, the smallest volume of chemical necessary to meet the task should be used. Mixed waste should be stored separately to prevent inadvertent mixing with other types of waste. For short-lived radionuclides, the DIS option should be used, followed by proper disposal of the remaining hazardous chemicals. Long-lived mixed waste will need to be disposed of *via* a licensed waste facility.

During the operation of the cyclotron, machine components and shielding will be unavoidably activated. Design, maintenance, and operations should be such that this radioactivity can be minimized. Activated components that must be replaced during operation will need to be stored on-site in shielded areas. Further processing, such as dismantling and compaction, may be used to keep volumes as low as possible. These operations would be

performed when the level of radioactivity has decayed to acceptable levels.

Since radioactive waste disposal is anticipated to be quite expensive when waste facilities are sited, an aggressive waste minimization strategy should be utilized. When feasible, reusable glassware, laboratory equipment, and personnel protective equipment will be used. Procedures will need to be developed to prevent contamination, spills, and other incidents that may increase the amount of radioactive waste that is produced. Preventive maintenance of the facilities and equipment will also need to be used to reduce catastrophic failures that could result in increased volumes of radioactive waste.

Complete procedures for the handling, storage, and disposal of radioactive waste will be further developed as part of the overall *NBTF Safety Plan* in a future site-specific planning phase. An initial draft of this safety plan is provided as Appendix 7.

## Business Plan for Operation of the NBTF

We recommend that the NBTF be established under the auspices of a private not-for-profit NBTF Corporation or foundation. This NBTF Corporation would oversee both construction of the NBTF and its subsequent administration and management. Through grants and contracts the Department of Energy would be expected to fund design and construction of the facility plus support the aspects of its operation deemed in the public interest,<sup>1-7</sup> following the financing recommendations made by the National Academy of Sciences in the 1994 report, *Isotopes for Medicine and the Life Sciences*.<sup>5</sup> This arrangement would allow the facility to be operated in an efficient, business-like, manner that is responsive to the needs of its customers, while avoiding many of the problems identified in the 1993 Arthur Andersen report, *U.S. Department of Energy-Isotope Production and Distribution Program-Management Study*.<sup>8</sup>

In developing the Purdue NBTF Business Plan we have tried to accurately define what recurring DOE support might be required for successful operation of the facility and to identify viable strategies for minimizing such recurring expenses without compromising the facility's ability to fulfill its stated missions. The *Administrative Structure* we propose for the NBTF Corporation is shown in Appendix 8, while a *Draft Business Plan* is presented in Appendix 9. (Appendix 8 also provides an interim administrative structure for management of the project from the end of a future DOE-funded Site-Specific Planning Phase through facility construction and commissioning.) The diverse production, teaching, and research missions of the NBTF will, at times, present conflicting demands on the resources of the facility. However, we believe that, with the assistance of the NBTF Board of Directors and external Advisory Panels, realistic administrative priorities and decision-making strategies can be implemented so that community confidence is maintained in the effective operation of the facility.

Based on the analysis presented in Appendix 3 (pages 1.2 to 1.12), we believe the "routine production" functions of the NBTF can be operated in a fashion that generates revenues in excess of the associated recurring costs, thereby subsidizing the Facility's competing missions in education, training, and research (such as the production and distribution of essential, but financially unattractive, research radionuclides). Recurring DOE support will be required to

insure that the research and education missions of the facility are reliably met. However, the proposed business plan is structured to provide substantial incentive for the NBTF to be managed in a fashion that minimizes the need for recurring DOE support and encourages responsiveness to customer needs.

As a conceptual model for an appropriate NBTF business plan, we recommend that the NBTF budget be divided into the following expense categories:

- Core Facility Operating Expenses (utilities, maintenance, core personnel, safety program, waste disposal, insurance, *etc.*)
- Core Research and Development Budget (production research, pilot project funding, *etc.*)
- NBTF Education and Training Programs Budget
- Decommissioning Cost Budget (annual escrow account deposit)
- Applications Research and Development Budget

These expenses must be met by the following sources of revenue:

- Isotope Sales Revenue
- Core Operating Expense and Research Support from DOE (includes start-up costs, general building support and maintenance costs, production-research funding, pilot-project research funding, and decommissioning-cost escrow account deposits)
- DOE-Funded Education and Training Grant (amount and scope subject to triennial performance review)
- Tuition Revenue from Short Courses and other Training Programs
- Technology Transfer Revenues
- Extramurally-Funded (Peer-Reviewed) Research Grants for Applications Research and Development Programs

The amount and duration of the "*Core Operating Expense and Research Support*" from DOE would need to be negotiated prior to facility commissioning. We would recommend an initial 10-year renewable commitment from DOE that would guarantee a "base level" of operations funding sufficient to cover the difference between the "total NBTF core operating expenses" and a "negotiated projection of expected base sales revenue." To minimize taxpayer expense and to provide incentive for effective facility management, we recommend that the actual amount of the negotiated base support in any given year be *reduced* by an amount equal to a fraction (perhaps one-half) of the "prior year's technology transfer revenue" plus a fraction (perhaps two-thirds) of the "prior year's sales revenue in excess of the negotiated projection of base sales revenue." The remaining prior-year revenues from technology transfer and "radioisotope sales in excess of the negotiated projection of base sales" would be allocated to a discretionary budget, under the control of the Executive Director, for use in enhancement of NBTF educational and research programs. Thus, effective management of the production and distribution functions of the NBTF

would lead to a direct reduction in taxpayer support, while also generating resources that can be used to improve facility programs.

A detailed analysis of building operating costs is provided in Appendix 10, while staff salary projections are included in Appendix 8. Research costs that should be incorporated into the DOE-supported core NBTF operating budget include the costs associated with in-house activities to develop new production and purification methodologies; costs associated with research to expand the selection of radionuclides that the NBTF can make available to the research community; and costs associated with small "seed" grants to support meritorious pilot projects of internal and external researchers. As recommended in the *Isotopes for Medicine and the Life Sciences* report,<sup>5</sup> it is our expectation that "applications research" by NBTF faculty and staff (i.e., research to explore new applications for materials the NBTF can produce) should generally be subjected to external peer review and funded by established external public and private sources, rather than through the NBTF core budget.

The plan for NBTF management and operations should include a formal mechanism whereby external researchers can request "custom" production of radionuclides (to satisfy unusual, but scientifically meritorious, needs). Thus, infrastructure funding needs to be provided to allow the NBTF to solicit and regularly receive requests for radionuclides not on the current "routine" production list. It is assumed that procedures will be implemented to allow such external requests to be: (1) expeditiously screened to assess whether the NBTF is technically capable of fulfilling the need; (2) evaluated to estimate the internal costs and programmatic implications associated with fulfilling the request, including establishment of a plausible timetable for being able to satisfy the need; and (3) reviewed by a Pilot Project Review Panel for assessment of the scientific merit of the request. The Associate Director for Research and Education, with guidance from the Executive Director and the Scientific Advisory Committee, would then prioritize the request and subsidize its fulfillment using resources from a recurring "pilot-project" discretionary administrative budget.

Development of reliable figures for projected NBTF sales revenue (and associated waste disposal costs) is somewhat problematic, due to uncertainties over the exact nature and quantity of materials the NBTF will ultimately be called upon to produce. Our projections for anticipated isotope sales and sales revenue (Appendix 9) are based on analysis of recent sales records for the DOE Isotope Production and Distribution Program (Tables 3 and 4) and external consulting reports solicited in the course of the current *Project Definition Phase* effort (Appendix 2 and Appendix 3). Budgeting for radioactive waste disposal is made more problematic by the current lack of disposal sites for low level waste. While provision has been made to allow on-site storage of radioactive waste for decay, the *Draft Business Plan* also currently allows \$200,000 for off-site annual radioactive waste disposal costs (assuming off-site disposal of 20 waste barrels per year at \$10,000 per barrel).

The October 14, 1993 DOE Request-for-Applications for the *NBTF Project Definition Phase* specifically calls for development of a plan to reimburse the government for the costs of NBTF construction. Unfortunately, this requirement fundamentally conflicts with the stated purpose and mission of the NBTF as developed in both the DOE-funded 1991 SNM/ACNP *National Biomedical Tracer Facility Planning and Feasibility Study*<sup>2</sup> and in the 1992 *Proceedings of the*

**Table 3. Sales Records: DOE Isotope Production and Distribution Program**

Nuclide	$t_{1/2}$	Total Revenue from Sales of Accelerator-Produced Nuclides*			
		FY '93	FY '92	FY '91	FY '90
<sup>82</sup> Sr	25 d	\$1,002,987.00	\$790,988.60	\$950,524.00	\$483,840.00
<sup>68</sup> Ge	270.8 d	\$506,239.00	\$435,453.20	\$308,883.00	\$295,030.00
<sup>109</sup> Cd	1.267 y	\$197,550.00	\$175,100.00	\$120,816.00	\$110,467.00
<sup>22</sup> Na	2.6 y	\$147,400.00	\$82,348.00	\$48,992.00	\$46,831.00
<sup>67</sup> Cu	2.58 d	\$57,809.00	\$120,576.25	\$47,051.00	\$48,013.00
<sup>26</sup> Al	7.4e5 y	\$36,844.00	\$18,458.74	\$22,432.00	\$10,842.00
<sup>32</sup> Si	104 y	\$21,812.00	\$38,973.90	\$1,446.00	–
<sup>88</sup> Y	106.6 d	\$15,054.00	\$17,788.00	\$19,245.00	\$20,385.00
<sup>73</sup> As	80.3 d	\$10,371.50	\$4,794.70	\$3,758.00	\$5,020.00
<sup>148</sup> Gd	75 y	\$9,200.00	\$4,600.00	–	–
<sup>95m</sup> Tc	61 d	\$7,400.00	\$3,300.00	–	–
<sup>7</sup> Be	53.3 d	\$6,388.00	\$3,899.00	\$3,002.00	\$10,689.00
<sup>97</sup> Ru	2.88 d	\$5,760.00	–	–	–
<sup>207</sup> Bi	32.2 y	\$3,660.00	\$5,940.00	–	–
<sup>96</sup> Tc	51.5 min	\$3,510.00	\$4,166	\$248.00	\$1,400.00
<sup>48</sup> V	15.98 d	\$2,597.80	–	\$812.00	–
<sup>75</sup> Se	119.78 d	\$2,340.00	–	–	–
<sup>65</sup> Zn	244.1 d	\$2,300.00	–	–	–
<sup>127</sup> Xe	36.4 d	\$1,596.00	\$4,351.10	\$1,296.00	\$32,399.00
<sup>88</sup> Zr	83.4 d	\$474.00	–	\$648.00	\$1,161.00
<sup>28</sup> Mg	21.8 h	–	\$4,406.00	\$12,302.00	\$4,410.00
<sup>83</sup> Rb	86.2 d	–	\$4,270.00	\$2,653.00	\$5,805.00
<sup>49</sup> V	330 d	–	\$859.00	–	–
<sup>85</sup> Sr	64.84 d	–	\$382.50	–	–
<b>TOTAL</b>		<b>\$2,041,292.30</b>	<b>\$1,720,654.99</b>	<b>\$1,544,108.00</b>	<b>\$1,076,292.00</b>

\* Sales records for Brookhaven National Laboratory and Los Alamos National Laboratory combined.

**Table 4. Sales Records: DOE Isotope Production and Distribution Program**

Nuclide	$t_{1/2}$	Total Quantity of Accelerator-Produced Nuclides Sold*			
		FY '93	FY '92	FY '91	FY '90
<sup>82</sup> Sr	25 d	8794	9261.8	13366	6936
<sup>109</sup> Cd	1.267 y	3564	3604	3039	2851
<sup>68</sup> Ge	270.8 d	1951.5	1969.8	1899.6	1669
<sup>22</sup> Na	2.6 y	1701.5	1369	1645	1311
<sup>67</sup> Cu	2.58 d	789.5	2944.2	1872.9	2019
<sup>75</sup> Se	119.78 d	204	—	—	—
<sup>65</sup> Zn	244.1 d	100	—	—	—
<sup>97</sup> Ru	2.88 d	100	—	—	—
<sup>73</sup> As	80.3 d	65.7	23.01	22.1	30
<sup>127</sup> Xe	36.4 d	65	195	90	3220
<sup>88</sup> Y	106.6 d	61	63.8	78.5	85
<sup>96</sup> Tc	51.5 min	30	44	64	2 batches
<sup>7</sup> Be	53.3 d	19	9.49	6.6	57
<sup>48</sup> V	15.98 d	9.7	—	4.2	—
<sup>95m</sup> Tc	61 d	7	3	—	—
<sup>207</sup> Bi	32.2 y	188 $\mu$ Ci	420 $\mu$ Ci	—	—
<sup>88</sup> Zr	83.4 d	0.1	—	2	5
<sup>148</sup> Gd	75 y	20 $\mu$ Ci	10 $\mu$ Ci	—	—
<sup>32</sup> Si	104 y	20 $\mu$ Ci	36 $\mu$ Ci	1 $\mu$ Ci	—
<sup>26</sup> Al	7.4e5 y	0.993 $\mu$ Ci	0.53 $\mu$ Ci	0.003 $\mu$ Ci	1.0 $\mu$ Ci
<sup>83</sup> Rb	86.2 d	—	20.2	16.2	35
<sup>49</sup> V	330 d	—	3	—	—
<sup>85</sup> Sr	64.84 d	—	1	—	—
<sup>28</sup> Mg	21.8 h	—	0.4	21	10
<b>TOTAL</b>		<b>17,462.23</b>	<b>19,512.17</b>	<b>22,127.1</b>	<b>18,228.0</b>

\* Sales records for Brookhaven National Laboratory and Los Alamos National Laboratory combined.

*Purdue NBTF Workshop.*<sup>4</sup> We are committed to development of a plan for the NBTF that adheres to the spirit of both of these documents. It is clear that the NBTF can not fulfill its mandate to serve the biomedical and scientific market for "research" radionuclides and concurrently generate sufficient revenue to "repay" the government for the facility construction costs. This conclusion is independently supported by the recent National Academy of Sciences report, *Isotopes for Medicine and the Life Sciences.*<sup>5</sup> If the NBTF is properly designed and operated, the taxpayers' most substantial "return" on their investment will be in the form of an enhancement to the nation's infrastructure for scientific research and scientific/technical education; the development of new medical products and technologies; and successful technology transfer to for-profit commercial private-sector firms.

If the NBTF is to be successful in the production mission that will largely determine the financial viability of its long-term operation, customer service must be a top priority, second only to safety (Appendix 8, page 3). The model site used for this study, on the western edge of the Eastern time zone, offers a reasonably central geographic location for the NBTF that is well suited to meeting the shipping and customer service requirements of the nuclear medicine and scientific communities. The West Lafayette site is approximately 65 miles northwest of the Indianapolis International Airport and 125 miles southeast of Chicago (Appendix 11, pages 26-27). Same-day air shipments of radioactive materials for medical use can be made from the Purdue Airport *via* either scheduled commercial flights (American Airlines and Northwest Airlines) or by chartered carriers.

It is anticipated that Federal Express will handle the bulk of NBTF overnight radionuclide shipments. Consequently, further site-specific planning should include working with Federal Express (and other overnight carriers) to insure that facility design and operations are structured from the outset to expedite package shipping and tracking. Nationwide shipping by Federal Express from the Indianapolis International Airport is particularly attractive for NBTF operations, since Federal Express is developing this Indianapolis facility as a national hub/distribution center.<sup>9</sup> In 1993 the Indianapolis Federal Express Hub employed 1,700 people who sorted 285,000 packages per day for shipment to final destinations on seven DC10s, twenty-five 727s, and nine Cessna 208 feeder aircraft. This Indianapolis Federal Express facility recently (1994) completed a \$24 million expansion that added gates to bring in more aircraft and produced a 50% increase in sorting capacity.<sup>9</sup> Thus, the Indianapolis International Airport (a 70 minute drive from the proposed NBTF site) offers an outstanding gateway to direct Federal Express flights to major cities around the country, while also offering considerable operating flexibility to the NBTF (*e.g.*, packages could be delivered to the Indianapolis Airport as late as 1:00 a.m. and still make outgoing flights for delivery around the country later that morning).

During the site-specific NBTF planning phase, the three major U.S. radiopharmaceutical manufacturers that are routinely involved in high-volume radionuclide shipping (Mallinckrodt Medical, Inc., Amersham North America, and the DuPont-Merck Pharmaceutical Company) should be consulted to investigate the technical feasibility and financial implications of sub-contracting the sales, marketing, and distribution functions of the NBTF to an experienced third party. Specifically, these firms should be consulted to determine what administrative and

financial arrangements would be necessary to involve them as a sub-contractor who would assume responsibility for the radionuclide marketing, sales, and distribution functions of the NBTF. Sub-contracting these functions would allow the NBTF to take full advantage of the existing infrastructure these firms have developed to expedite shipping of medical radionuclides, including their arrangements with commercial airlines and local ground couriers in major cities around the country.

## Proposed Operating Schedule

The NBTF accelerator design and operating schedule should allow continuous, around-the-clock, accelerator operation, 48 weeks per year. It is anticipated that the operating schedule should allow 36 hours/week for routine maintenance (Appendix 3, pages 2.1 to 2.7). Scheduled annual major routine maintenance plus (unscheduled) breakdowns are expected to require no more than four weeks per year. Staffing requirements for accelerator operations are outlined in the personnel scheme shown in Appendix 8, and more completely defined in Appendix 3, pages 1.15 through 1.21.

## Proposed Product Isotopes

The 37 radioisotopes presented in Table 5 are expected to form the core of the NBTF routine product line, based upon the recommendations of the 1991 SNM/ACNP *National Biomedical Tracer Facility Planning and Feasibility Study*,<sup>2</sup> the 1992 *Proceedings of the Purdue NBTF Workshop*,<sup>4</sup> and the analyses presented in Appendix 2 and Appendix 3. Other research radionuclides would be produced in the course of Pilot Projects and in custom irradiations; however, the initial market for such materials is expected to be small. Naturally, if the NBTF is managed in a manner that is responsive to customer needs, one can expect this "product line" to routinely undergo revision based upon market demands.

Production priorities and the sales projections used in our business planning activities are detailed in Appendix 2 (pages 9 and 10) and Appendix 3 (pages 1.2 to 1.12). The production and sales of these materials would be carried out in accordance with the provisions of the NBTF Mission Statement (page 5).<sup>4</sup>

As noted above in the discussion of accelerator specifications, the NBTF will not be an effective production source for a small number of the radionuclides currently supplied by the BLIP and LAMPF isotope production programs (e.g.,  $^{22}\text{Na}$ ,  $^{26}\text{Al}$ ,  $^{32}\text{Si}$ ,  $^{83}\text{Rb}$ ,  $^{109}\text{Cd}$ ). Depending upon market demand and the research importance of these materials, it is recommended that DOE continue to rely on the high-energy accelerators of the National Laboratories for production of these materials.

**Table 5. Recommended Major Product Radionuclides for the NBTF**


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Be-7	Ga-67	Zr-88	Nd-140
Mg-28	Ge-68	Zr-89	W-178
V-48	As-73	Tc-95m	Hg-195m
Fe-52	Se-75	Tc-96	Tl-201
Co-55	Br-76	Ru-97	Pb-203
Co-57	Br-77	In-111	Bi-205
Cu-64	Sr-82	In-114m	Bi-206
Cu-67	Sr-85	Sn-113	
Zn-62	Y-87	I-123	
Ga-66	Y-88	I-124	

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### **Ability to Provide Associated Education and Training**

Purdue University is in a position to effectively implement a program that uniquely addresses the educational objectives set for the NBTF through its existing graduate programs in Chemistry, Pharmacy, Health Physics, Nuclear Engineering, and Nuclear Physics, plus its established ties to the nuclear medicine and medical physics programs at the Indiana University School of Medicine. An outline of proposed NBTF Educational Programs is presented in Appendix 11, along with Purdue's extensive *current* undergraduate and graduate course offerings relevant to the NBTF educational mission.

Historically, Purdue's School of Pharmacy and Pharmacal Sciences has played an important and pioneering role in the development of medical applications for radiochemical and radiotracer techniques. In 1959, the School formed a Department of Bionucleonics that emphasized research and training in the medical and pharmaceutical uses of radiation and radioactive materials. The Department of Bionucleonics subsequently evolved into the School of Health Sciences and the Division of Nuclear Pharmacy in the Department of Medicinal Chemistry. The Division of Nuclear Pharmacy has for several years been the nation's leading supplier of trained nuclear pharmacists through its undergraduate and graduate programs, graduating 15-30 students per year who meet NRC guidelines for authorized user status.

Purdue's leadership role in nuclear pharmacy education has been reinforced by the creation of a "Nuclear Pharmacy Certificate Program" that provides post-graduate nuclear pharmacy training to licensed pharmacists nationwide. This program is designed for pharmacists with no prior nuclear pharmacy training who wish to acquire the background

needed to move into this practice specialty. Certificate program instruction is innovatively provided *via* a video home-study program that is combined with an "intensive" two-week on-campus laboratory training session. Since 1989, this Nuclear Pharmacy Certificate Program has trained over 100 nuclear pharmacists, several of whom have gone on to achieve Board Certification. In addition, in cooperation with Purdue's Krannert School of Management, the Division of Nuclear Pharmacy is currently offering a continuing education program on *Human Resource Management* for managers of centralized nuclear pharmacies.

The graduate research program in Nuclear Pharmacy emphasizes basic and applied research in radiopharmaceutical chemistry and is complemented by the Health Physics program offered by the School of Health Sciences. Currently, this research program supports graduate students and postdoctoral associates pursuing studies of the potential role for generator-produced nuclides in positron emission tomography (PET); gallium, copper, and technetium radiopharmaceutical chemistry; molecular modeling in radiopharmaceutical design; and the effects of radiopharmaceutical product formulation on tracer bioavailability. In addition, a related Medical Health Physics program offers training and research opportunities focused on dose calculation and dose delivery techniques in radiation therapy.

The Department of Chemistry in our School of Science has for many years maintained an active research and teaching presence in nuclear and radiochemistry. Three faculty members have active research programs in this field, making this one of the country's strongest remaining university-based nuclear and radiochemistry programs.<sup>7</sup> Typically, there are ten graduate students and five postdoctoral scientists working in this area. Well-equipped laboratories are available for radiochemical separations over a broad range of activity levels. A modern counting room is equipped with computerized equipment for the measurement of nuclear radiations. In addition, major experiments are mounted at MURR and many of the national accelerator facilities, including ATLAS at Argonne National Laboratory and the Fermilab Tevatron. Graduate courses are offered in radiochemistry and nuclear chemistry and a nuclear chemistry seminar complements the formal course offerings.

These programs are further strengthened and reinforced by the availability on campus of a nuclear training reactor, operated by the Department of Nuclear Engineering, and a tandem Van de Graaff accelerator, now converted into a dedicated Earth and Space Science National Facility for accelerator mass spectrometry (AMS). In addition, the Purdue nuclear pharmacy and medical health physics programs have active educational and research ties to the nuclear medicine and radiation oncology programs at the Indiana University School of Medicine. Formal ties are also currently being established that will link the Purdue School of Health Sciences Medical Technology program to the Indiana University program in Nuclear Medicine Technology.

Purdue University also offers opportunity for students to pursue a combined M.D./Ph.D. degree program in cooperation with the Indiana University School of Medicine. The program is designed to provide research training to highly-qualified students who are strongly motivated toward careers in the medical sciences. The program is adjusted to the background and particular career aims of individual students, offering a wide range of research training opportunities from numerous disciplines. Such areas include, but are not limited to, engineering, medicinal chemistry, molecular biology, and neurosciences.

The Purdue University Departments of Chemistry and Physics have also established highly-successful science education Public Outreach programs that can further support, and serve as models for, NBTF educational ventures. These programs are designed to reach students in kindergarten through twelfth grade with the goals of increasing student achievement in science, stimulating interest in science-based careers, and assisting teachers in the delivery of science education.

The most active component of the Physics Outreach Program during the past five years has been the *Physics on the Road* traveling demonstration show, which reaches approximately 25,000 students per year. This effort utilizes a dedicated van fully-equipped with demonstration apparatus purchased through a grant from the Purdue University Alumni Association. In addition, the Department of Physics annually sponsors a "Physics Funfest" show on campus that routinely attracts nearly 1000 students, parents, and teachers from the region. The Department is also establishing a Outreach Center laboratory complex and offers a "ScienceScape" summer residence camp for middle school girls.

The major outreach program sponsored by the Department of Chemistry is known as the *Purdue Instrumentation Project*. The *Instrumentation Project* is a teacher enhancement program in which teachers learn to use current laboratory equipment and then design experiments and lessons that are appropriate for their own high school students. During the school year analytical instruments, such as nuclear scalers, spectrophotometers (UV, vis, IR), chromatographs (GC, HPLC), pH meters, and conductivity meters, are then delivered to schools for student use in laboratory experiments.

The Department of Chemistry sponsors several other programs that reach pre-college students: "Chemcamp" for minority students; "Expanding Your Horizons" for middle school girls; and "Advanced Placement Chemistry." The Department also hosts two national programs for teachers: the *Science Institute for Middle School Teachers* and the *Operation Chemistry* leadership training program for building teacher-trainer teams composed of a pre-high-school science teacher, high school science teacher, university chemistry professor, and an industrial chemist.

Appendix 11 provides a more detailed narrative overview of the range of programs at Purdue University and Indiana University that can be called upon to support the NBTF mission. Strong research and training programs can readily be established as a collaborative effort between the staff of the NBTF and Purdue University and Indiana University faculty and students. These efforts would certainly include scientific and engineering support for both the targetry design and target processing research activities that must be conducted before and after the NBTF accelerator comes on-line. In particular, the 200 MeV cyclotron operated by Indiana University offers an excellent resource that is available for targetry research prior to NBTF commissioning.<sup>10</sup>

## Conclusions

The proposed National Biomedical Tracer Facility can be effectively operated by the private sector; however, the Federal government will need to provide facility construction costs as well as recurring operations support for core educational and research activities deemed of national importance.<sup>1,2,5,6</sup> It is recommended that the NBTF be established under the auspices of a private not-for-profit corporation that is charged with oversight of both the construction and operation of the facility. This corporation should manage the NBTF in a manner that, while remaining faithful to the established mission of the facility, minimizes the recurring operations support required from the Federal government. This will require an efficient, business-like approach to facility operations that seeks to minimize "overhead" expenses while maximizing productivity. It is believed that this objective can be best met if the NBTF is privately operated and the required Federal support is provided by the Department of Energy in the form of grants and contracts.

Ideally, the design of the NBTF should serve to both integrate and optimize the diverse production, research, and educational functions of the facility. Customer service and satisfaction must be top priorities of the NBTF radionuclide production program, necessitating the design of efficient, safe, and reliable facilities, as well as implementation of an effective and efficient management plan. The NBTF will be most effective in fulfilling its educational mission if it is sited at a major research university with strong academic programs in areas related to NBTF functions. Such an environment will also contribute to excellence in the research functions of the NBTF. In addition to working with faculty and students at the host institution, the NBTF staff should actively pursue research and educational collaborations with the faculty of other academic institutions and researchers at the existing National Laboratories.

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