Evaluating technology-based public institutions: the case of radiopharmaceutical standards research at the National Institute of Standards and Technology

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Abstract:

The purpose of this paper is to illustrate, through one case study, the current state of program evaluation in the research laboratories at the US National Institute of Standards and Technology (NIST). The history of NIST's radiopharmaceutical standards research program is discussed, the methodology for data collection and analysis is detailed, and the NIST management's use of the findings from the case study is described, in an effort to move toward generalizations about best practices in program evaluation applicable to technology-based public institutions.

Keywords: National Institute of Standards and Technology | radiopharmaceuticals | evaluation

Article:

In the United States, the concept of fiscal accountability is rooted in the fundamental principles of representation of the people, by the people. However, as a more modern concept, accountability can be traced generally to the political reforms initiated by President Woodrow Wilson and specifically to the Budget and Accounting Act of 1921. This Act began the modern tradition of fiscal accountability in public institutions.[1] Building on the general concept of accountability established in the more recent Competition in Contracting Act of 1984 and the Chief Financial Officers Act of 1990, the Government Performance and Results Act (GPRA) of 1993 was passed. The focus of GPRA is performance accountability; its purpose is, among other things, to: "initiate program performance reform with a series of pilot projects in setting program goals, measuring program performance against those goals, and reporting publicly on their progress ..."

[1] This 1921 Act not only required the President to transmit to Congress a detailed budget on the first day of each regular session, but it also established the General Accounting Office to settle and adjust all accounts of the government.

It is inevitable that managers in any technology-based public institution, the National Institute of Standards and Technology (NIST) included, will become advocates for their own research agendas, and adherence to GPRA will only encourage this. Watching results on a day-to-day basis and witnessing the benefits of research and scientific inquiry to which one is committed understandably leads managers, and other participants in the research, to the intuitive conclusion that their activities are valuable.

Regardless of the veracity of this conclusion, it may not be communicated easily to others, much less quantified. Thus, when political and administrative superiors ask "But how do you know this research or technology-based investigation is effective?", managers often find themselves either dissembling or simply telling success stories. It is possible, as this case study illustrates, through the systematic application of evaluation methods, to document value and thereby produce a clear, more precise response to the question of performance accountability.

The format of this paper is as follows. First, we give an overview of the history of research activities at NIST. Then we present the findings from a recent evaluation assessment conducted on the radiopharmaceutical standards program in the Physics Laboratory at NIST. From the experiences of this assessment we describe management's use of the findings from the case study. Finally, we posit a possible set of characteristics of best practices in program evaluation applicable to technology-based public institutions similar to NIST.[2]

Brief History of NIST

The concept of the government's involvement in standards can be traced to the Articles of Confederation signed on July 9, 1778. Therein, Congress was given the "sole and exclusive right and power of ... fixing the standard of weights and measures throughout the United States." This responsibility was reiterated in Article 1 of the Constitution of the United States. In 1836, the Secretary of the Treasury was given the responsibility of distributing standard weights and measures to the governor of each state: "to the end that an uniform standard of weights and measures may be established throughout the United States."[3] In 1890, Congress first appropriated funds for an Office of Construction of Standard Weights and Measures; on March 3, 1901, Congress established the National Bureau of Standards (NBS):

> "[T]he functions of the bureau shall consist in the custody of the standards; the comparisons of the standards used in scientific investigations, engineering, manufacturing, commerce, and educational institutions with the standards adopted or recognized by the Government."

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[2] By technology-based, we mean an institution that is involved in science, R&D, technology, and other innovation-related activities. The best practices characteristics set forth at the end of this article assume that the institution under consideration is fiscally accountable, hence only issues of performance accountability are discussed. The reader is, however, warned that the characteristics of best practices in program evaluation that are discussed may not in all circumstances satisfy GPRA reporting requirements. Setting forth a GPRA template is not the intention of this paper.

[3] In 1866, Congress and President Andrew Johnson authorized the use of the metric system in the United States. In 1875, the United States participated in the Convention of the Meter in Paris, and was one of the 17 signatory nations to the Treaty of the Meter.

As part of the Omnibus Trade and Competitiveness Act of 1988, the National Bureau of Standards was re-named the National Institute of Standards and Technology.

For nearly a century, NIST (and previously the NBS) has fulfilled the terms of its creation in providing science and technical support fundamental to the success of US industry, in particular, and of the entire technical community, in general. NIST's explicit mission is (NIST, 1994, pages 5-6) "to promote U.S. economic growth by working with Industry to develop and apply technology, measurements, and standards." Accordingly, NIST's direct customer is US industry. To carry out this mission and to serve US industry, NIST supports four program areas, including a laboratory research program focused on meeting the infrastructural technology needs of industry.[4]

Radiopharmaceutical research at NIST

Background information

This section draws on Golas (1993) and Hutchinson (1996). Nuclear medicine is the branch of medicine that relies on radiation-emitting substances, called radioisotopes or radionuclides, for the diagnosis or treatment of a disease or condition. Nuclear medical and biological research can be traced to the 1895 discovery by Wilhelm Conrad Röntgen of a ray that could penetrate the human body and display bone structures.[5] Soon thereafter, in 1896, Henri Becquerel demonstrated that uranium-containing ores also emitted rays of a penetrating nature. Becquerel's student, Marie Curie, and her husband, Pierre, in 1898 identified two new radioactive elements, polonium and radium.

Soon after the turn of the century, radium and its radioactive decay product radon were found useful in treating tumors. Then, in 1925, Herrman Blumgart and Otto Yens used radioactive substances for the first time as diagnostic tracers in human subjects. In 1936, John H Lawrence and Joseph Gilbert independently undertook the first therapeutic application of a radiopharmaceutical in the treatment of leukemia.

The commercial radiopharmaceutical industry grew rapidly in the United States during the 1950s and 1960s. Disputes between manufacturers and the lack of reliability of commercial secondary standards led to widespread discontent with the available standards. The National Academy of Sciences Committee on Nuclear Science (National Research Council, 1970) studied the problem. Following their 1970 report, the radiopharmaceutical manufacturers, realizing the importance of calibrations for the short-lived radionuclides then used in nuclear medicine, initiated talks with NBS to develop necessary standard reference materials (SRMs).

According to Golas (1996), in the early 1970s SRMs were available in unsuitable physical forms and activity levels. Also, there were no standard methods for measuring the activity of a

[4] Tassey [1982] first used the term "infratechnology" to describe the infrastructure technology that resulted from laboratory research. The first major US policy statement to adopt that term was the Economic Report of the President in 1994 (Executive Office of the White House, 1994).
[5] This information draws directly from Society of Nuclear Medicine (1996a).

radionuclide, even ignoring the imprecise decay information that was available. As a result, no method existed fora pharmacy to assure the accuracy of the radiation in a prescribed dose.

In the early 1970s, there was not an established research program on radiopharmaceutical standards at NIST (then NBS), or at any other federal facility. However, in 1972, the Atomic Industrial Forum (AIF) responded to industry needs and appointed a subcommittee of Manufacturers of Radioactive Reference Standards with the objective of "obtaining a high degree of consistency and reliability in commercially available radioactive reference standards and their accompanying Certificates of Calibrations" (Seidel and Hutchinson, 1976, page 1).[6] The NBS was represented on this committee, as were all major commercial manufacturers of radiochemicals.

In 1973, following the formation of this subcommittee, a symposium was held at NBS to address the concerns of radionuclide manufacturers regarding the proposed standards. Speakers at the symposium emphasized the need for such standards, citing:

- the lack of standards for about 75% of the more than 100- radionuclides then produced by industry;
- the unusable physical form and activity levels of the few standards that were available; and
- the failure to have industry-wide adopted decay-scheme data on which to base derived standard instrument calibrations.

It was also noted at the symposium that the lack of standards was an obstacle to both the assurance of accuracy in the administration of radionuclides and the approval of new drugs by the federal Food and Drug Administration (FDA).

In response to industry-wide concerns expressed at this symposium, NBS entered into a cooperative research agreement with the Atomic Industrial Forum (AIF) (now the Nuclear Energy Institute (NEI)),

> "whereby NBS will supervise and administer on behalf of AIF a measurements technology quality assurance program which caters more specifically to the needs of the radiopharmaceutical industry" [Collé, 1976, page 71].[7]

The NBS also entered into an interagency agreement with the FDA to

> "ensure the continuous availability of national radioactivity standards at appropriate levels of activity for use by the radiopharmaceutical industry, and thus to establish a degree of uniformity in the measurements throughout the industry" (Collé, 1976, page 71).

Today, radiopharmaceutical SRMs are produced within the Radioactivity Group of the Ionizing Radiation Division of the Physics Laboratory at NIST through a cooperative research and

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[6] This committee became subcommittee N42.2 of the American National Standards Institute (ANSI).
[7] Today, this program is known as the NEI/NIST Radioactivity Measurements Assurance Program.

distribution agreement (CRADA) with NEI, and sold to the members of the NEI/NIST Radioactivity Measurement Assurance Program (MAP) and to the public.

Uses of radiopharmaceuticals in health care

In 1996, over 3,900 hospital-based nuclear medicine departments in the United States performed over 10 million nuclear procedures; about 90% of these were diagnostic and about 10% therapeutic (Health Physics Society, 1996; see also Institute of Medicine, 1995). The number of such procedures has increased from 7.7 million just a decade ago. Experts expect these numbers to increase between 5% and 10% per year over the next five years.[8]

Patients undergoing a nuclear medical examination receive a prescribed dosage of a radiopharmaceutical. This radiopharmaceutical is specifically formulated to be collected temporarily in the organ being examined. Gamma cameras and PET (position emission tomography) scanners are used to detect the radiation emitted by the radionuclide and register an image on a film or a computer for study by the nuclear medicine physician (Society of Nuclear Medicine, 1996b).

If a patient receives too little of the radiopharmaceutical the procedure will often have to be redone, particularly for a therapeutic procedure; if the patient receives too much, injury or death could result. In either case, there is an economic cost to imprecise measurement. It is therefore incumbent upon the nuclear pharmacist to deliver as close to the prescribed dosage as measurably possible, that is, to ensure that the patient receives x amount of radiation, where x is measured in terms of the number of atoms of the radioactive substance decaying per unit of time.

Research activities of the Radioactivity Group[9]

The Ionizing Radiation Division is one of six divisions in the Physics Laboratory at NIST. The Radioactiviy Group is one of three research groups within the Division. The Group's mission is: to develop and maintain US radioactivity standards and to confirm the standards internationally; to perform research on radioactivity decay-scheme characteristics; to develop and apply radioactivity measurement techniques; and to disseminate results using SRMs, calibrations and testing services, and cooperative industrial measurement traceability programs.

To date, NIST has produced the 28 radiopharmaceutical standards listed in Table 1.[10] Also shown in Table 1 is the primary diagnostic use of each of the radionuclides.

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[8] This forecast was provided by experts within the Radioactivity Group at NIST. See also Institute of Medicine (1995).

[9] This section draws directly from Golas (1996) and Physics Laboratory Brochure (1998).

[10] Some of these standards are no longer produced or are produced only rarely for a user to verify response rates. The letter at the end of the SRM number indicates how many times the substance has been produced (for instance, A=1, B=2, and so on).

Table 1. Radiopharmaceutical standard reference materials (SRMs) produced at NIST

Radionuclide	SRM number	Diagnostic/therapeutic use of relevant organ
Chromium-51	4400N	Diagnosis of blood cell survival
Iodine-131	4401V	Thyroid and other organs
Tin-113-Indium-113m	4402C	[Replaced by Indium-111]
Strontium-85	4403B	Bone studies
Thallium-201	4404S	Cardiac studies
Gold-198	4405B	Synovectomy, treatment for rheumatoid arthritis
Phosphorous-32	4406N	*In vitro* tracers/biotechnology
Iodine-125	4407T	*In vitro* clinical chemistry
Cobalt-57	4408F	Standard for calibration of imaging instruments
Selenium-75	4409D	Biochemical tracer
Technetium-99m	4410V	Imaging of multiple organs
Iron-59	4411B	Hemoglobin studies
Molybdenum-99	4412U	[Parent of Technetium-99]
Mercury-197	4413A	*In vitro* tracer studies
Iodine-123	4414C	Thyroid and other organs
Xenon-133	4415T	Lung imaging studies
Gallium-67	4416Q	Gastrointestinal tract imaging
Indium-111	4418A	Radioimmunotherapy
Mercury-203	4418A	*In vitro* tracer studies
Ytterbium-169	4419C	Brachytherapy
Lead-203	4420B	*In vitro* tracer studies
Gold-195	4421A	Tracer for new therapeutic agents
Chlorine-36	4422A	Beta-particle standard
Stronium-90	4423A	Beta-particle standard
Sulfur-35	4424A	Cell kinetics and metabolism; biochemical tracer
Samarium-153	4425B	Bone palliation agent
Strontium-89	4426A	Bone palliation agent
Yttrium-90	4427A	Radiolabelled antibody therapy

Source: Institute of Medicine (1995) and information provided by experts within Radioactivity Group at NIST

Table 2. Current participants in the NEI/NIST radioactivity measurement assurance program

Bristol-Meyers Squibb Company
DuPont Merck Pharmaceuticals Company
Institute of Nuclear Energy Research (Taiwan)
Mallinckrodt Medical, Incorporated
Medi+Physics, Incorporated
Nordion International, Incorporated
Packard Instruments, Incorporated
Syncor International Corporation
US Food and Drug Administration

Source: Golas (1996) and the Radioactivity Group at NIST

A radiopharmaceutical standard produced at NIST is typically accurate to within ±1% at the one standard deviation level; that is, all standards produced at NIST are calibrated within ±1 % of the actual decay rate of the substance. In other words, NIST's calibration error on these SRMs is ±1%. These calibrated SRMs are provided to the radiopharmaceutical manufacturing companies

that belong to the NEI/NIST MAP for an approximate fee of US$600.00 per ampoule.[11,12] The current members of the MAP are listed in Table 2.

Not all radiopharmaceutical manufacturers are members of the MAP. Non-member companies can obtain standards from commercial laboratories for a similar fee; however, the standards produced and sold by commercial laboratories are less accurate than those produced at NIST. On average, commercial laboratories are within ±5% of the actual decay rate of the substance, but these laboratories are traceable to NIST.[13] As an example, Figure 1 shows the results of the manufacturers' measurements of iodine-131 over the past 23 years. Ninety-three percent of the results from the manufacturers are within ±5% of the NIST values.

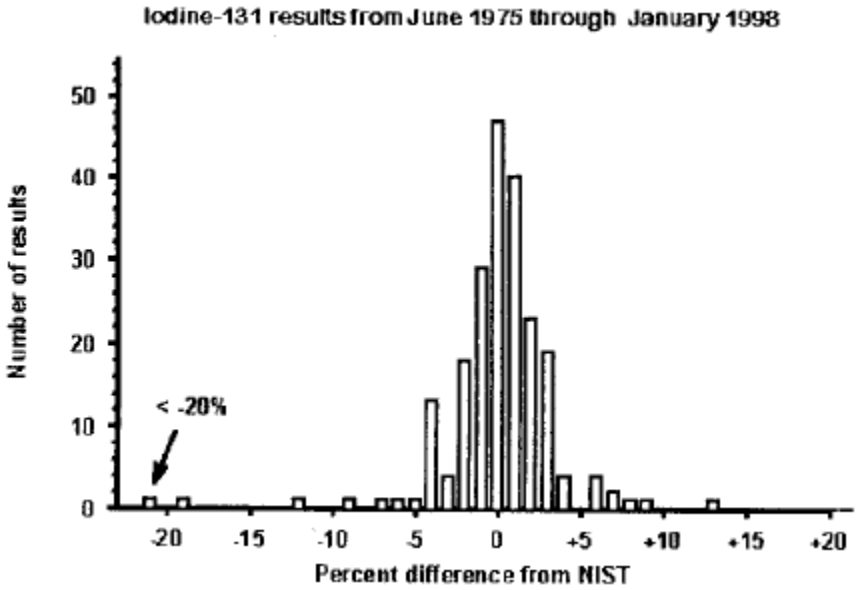

Figure 1. Radiopharmaceutical Measurement Assurance Program

Ten SRMs are produced at NIST each year, one each month following a schedule agreed upon by MAP members. The months of May and November are so-called 'open months,' during which members of the MAP can submit their own samples to NIST for calibration, as long as they contain a radionuclide already standardized by NIST. This allows companies that produce radioactive substances to have calibrated samples of radionuclides that are important to them, but that are not on NIST's current production schedule to obtain traceability.

Table 3 shows NIST's research costs related to the production of the radionuclide SRMs since 1990. While NIST initially became active in providing these SRMs in 1974, the cost data relevant to this study, as discussed below, begin with 1990. These cost data include all NIST capital, labor, and materials expenses.

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[11] In general, an ampoule is a standard NIST glass ampoule that contains 5 milliliters of solution.

[12] These revenues are divided between NIST and NEI; US$108.00 to NIST to underwrite, in part, research and the production of the SRM, and US$492.00 to NEI.

[13] This information was provided by experts within the Radioactivity Group at NIST, and it was verified during the interview stage of the study.

Table 3. NIST costs related to production of radiopharmaceutical SRMs (in US $000)

Year	NIST costs
1990	210
1991	218
1992	218
1993	265
1994	226
1995	384
1996	364

Source: Radioactivity Group at NIST

An economic analysis

Method adopted

The approach selected for evaluating the economic impacts associated with the research activities of the Radioactivity Group at NIST has been adopted from previous evaluations of other laboratory research programs at NIST and from evaluations of other public investments in infrastructure technology (see Link, 1996a; 1996b; Link and Scott, 1998). The actual NIST costs related to the production of radiopharmaceutical SRMs (Table 3) are compared to estimates of the economic benefits received by SRM users derived from a hypothetical counterfactual experiment. The experiment assumes that the first-level economic benefits associated with the Radioactivity Group's research can be approximated in terms of the additional costs that radiopharmaceutical manufacturers and patients would incur in the absence of NIST's research.

The hypothetical counterfactual experiment is used because this case study lacks comparable baseline observations. In other words, it is not the case that some members of MAP rely on NIST for only selected SRMs. Were that so, a comparison of diagnostic/therapeutic efficiency could in principle have been conducted between calibrated and non-calibrated substances.[14]

It is important to keep in mind that this study focuses on only one part of the production and distribution chain — the radiopharmaceutical manufacturer. The radiopharmaceutical itself requires a radionuclide that is produced either in a nuclear reactor or a particle accelerator. Some manufacturers operate their own reactors or accelerators, but many do not. Therefore, the radionuclides must be purchased from other laboratories such as those operated by the US Department of Energy or by universities.

Once the radiopharmaceuticals are prepared at the manufacturer, they are shipped to the clinic or hospital. At this point, it is the responsibility of the radiopharmacist to dispense the bulk shipment into individual doses for the patients. Finally, the radiopharmaceutical is administered to the patient by the nuclear medicine technician.

At each of these steps in the distribution chain, it is important to maintain good measurement and quality assurance practice because any errors introduced, especially early in the distribution chain, are quickly multiplied before the drug is given to the patient.

[14] Data could not be obtained from manufacturers of radiopharmaceuticals that are not members of the MAP.

Previous experience with the collection of information related to the economic benefits associated with NIST's laboratory research suggests that the most efficient, and presumably the most accurate means to collect data is through semi-structured, interactive telephone interviews. Accordingly, the Radioactivity Group identified a contact person in each of the seven manufacturing companies in the MAP listed in Table *2.* In effect, this group defined the domestic industry of radiopharmaceutical manufacturers for this study.

The radionuclide industry is of modest size. Based on data from the Department of Commerce's Bureau of the Census in its 1992 Census of Manufacturers, SIC industry 2835 is diagnostic substances. In 1992, the value of product shipments from this four-digit industry was US$6,177.1 million. The five-digit SIC industry 28352, *in vivo* diagnostic substances, had a value of product shipments of US$1,051.8 million in 1992. The value of product shipments of *in vivo* radioactive reagents (diagnostic and therapeutic), SIC 2835220, was US$323.2 million in that year.

Prior to the telephone interview, each identified participant was sent electronic mail from the Radioactivity Group introducing the study, soliciting participation in the study, and assuring confidentiality of individual responses. Each identified participant was asked to consider two general topics prior to the telephone interview. The first related to what their company would do under the hypothetical counterfactual situation where NIST ceased to produce SRMs. The second related to how the industry would adjust to such a situation and what the consequences would be.

Results of interviews

Each identified manufacturing individual was interviewed, from which the following conclusions were made.

- Without NIST's Radioactivity Group's involvement in SRMs, it would take between five and ten years for some industry group or association to form and become accepted as *a de facto* standard-setting body. The total (summed over the seven companies) expected transaction costs during this transition period would be at least US$1.3 million per year. This amount represents the additional labor costs expected to be required on the part of manufacturers to resolve measurement disputes between manufacturers and customers, and the associated additional measurement equipment needed by manufacturers. The expressed expectation was that these costs would increase between 4% and 10% per year until a steady-state situation was reached. During this five to ten-year transition period, the level of accuracy at the manufacturing stage would decrease from the current ±3 % to between +5 % and 10% because of the lack of accurate reference materials and measurement methods. At the hospital, the accuracy of dosages would fall from the current ±10% to at least ±15%.
- Reliance on foreign national laboratories for SRMs has never been considered because of the measurement quality at NIST. Thus, no respondent could reasonably assess the likelihood that the industry would turn to a foreign national laboratory for SRMs in the hypothetical counterfactual situation.

These findings are summarized in Table 4.

Table 4. Summary of findings from interviews with MAP manufacturing members

Hypothetical counterfactual situation	Range of responses
In the absence of NIST's readiopharmeceutical research, how long would it take an industry group or association to form and become accepted as a *de facto* standard setting body?	Between five and ten years
During this five- to ten-year transition period, what would happen to the accuracy of radiopharmaceuticals at the manufacturing stage?	Accuracy would decrease from ±3% to between ±5% and ±10%
During this five- to ten-year transition period, what would happen to the accuracy of radiopharmaceuticals administered by hospitals?	Dosage accuracy would decrease from ±10% to at least ±15%

Thus, the radiopharmaceutical manufacturers interviewed believe that without NIST's current efforts regarding SRMs, an industry association would evolve over a five to ten-year period to replicate NIST's current role and level of accuracy in SRMs; during this transition period manufacturers would experience sizable transaction costs and patients would receive less accurate dosages of radionuclides. The economic costs to manufacturers during this transition period are estimated to be at least US$1.3 million per year, to increase at a rate not less than 4% per year; and patient dosages of radioactive substances would fall by at least 5 percentage points, from ±10% to ±15%.[15]

Quantification

To quantify, in dollar terms, the economic cost of decreased accuracy, the Radioactivity Group identified three recognized experts at renowned US medical centers as candidates for telephone interviews. Each was interviewed, and as a group they expressed the following opinions:

- A decrease in the accuracy of a radioactive substance from ±10% to ±15 % would require that, on average, 1% of all diagnostic procedures be re-done due to too low a dosage (for instance, imprecise imaging) at an estimated average cost of between US$500 and US$750 per diagnostic procedure.
- A decrease in the accuracy of a radioactive substance from ±10% to ±15% would require that, on average, 3% of all therapeutic procedures be re-done due to too low a dosage (for instance, ineffective treatment) at an estimated average cost of US$1,500 to US$2,500 per therapeutic procedure.
- The health implications (for instance, organ damage) of too high a dosage could not be estimated because such consequences would not be known immediately. It is probable, however, that substantial long-term economic costs would be associated with this type of misadministration.

Table 5 summarizes these economic benefits.

[15] Certainly, manufacturers and patients received benefits from NIST's research during the 1990 to 1996 period. However, as shown in Table 6, these benefits were not quantified because of the counterfactual methodology adopted for estimating avoided costs were NIST to cease its related research activity.

Table 5. Summary of economic benefits from radioactivity research at NIST

Category of economic benefit	Economic benefit
Reduced transaction costs between radiopharmaceutical manufacturers and their customers	Saved US$1.3 million
Increased accuracy of diagnostic procedures	Saved re-doing 1% of all procedures at an average cost of US$500 to US$750 per procedure
Increased accuracy of therapeutic procedures	Saved re-doing 3% of all procedures at an average cost of US$1,500 to US$2,500 per procedure

Table 6 replicates in the second column the NIST research costs from Table 3 from 1990 through 1996. The cost datum for 1997 is the 1997 budgeted cost amount; estimated costs (rounded) for 1998 through 2001 are based on a 5.5% annual increase, the actual increase from 1996 to 1997. The five-year forecast period is based on the opinion of radiopharmaceutical manufacturers that, in the absence of NIST, the industry would incur transactions costs and decreased accuracy for a period of five to ten years. For the sake of conservativeness, the lower bound of the forecasted range is used — five years.

Table 6. Actual and projected NIST costs and economic benefits (in US$000)

Year	NIST costs	Manufacturer benefits	Patient benefits	Total net benefits
1990	210	—	—	–210
1991	218	—	—	–218
1992	218	—	—	–218
1993	265	—	—	–265
1994	226	—	—	–226
1995	384	—	—	–384
1996	364	—	—	–364
1997	384	1,300	90,000	90,916
1998	405	1,352	94,500	95,447
1999	427	1,406	99,225	100,204
2000	450	1,462	104,186	105,198
2001	475	1,521	109,395	110,441

The third column in the table contains manufacturers' estimates of the total industry cost savings from NIST continuing its SRM activity as estimated by the transaction costs (labor and equipment costs) that manufacturers would have had to incur in the absence of NIST's radiopharmaceutical standards research. The 1997 estimate of US$1.3 million is an interview aggregate. The range of opinion on the growth rate of this amount was 4% to 10% per year. Again for the sake of conservativeness, the lower bound of the forecasted range is used — 4%.

The fourth column contains the estimated value of the cost savings to patients as a result of avoiding having to have procedures re-done because of an underdose of radiopharmaceutical. With respect to diagnostic procedures, the base estimate of 1% of 9,000,000 diagnostic procedures per year was used, valued at the lower-bound estimate of US$500 per procedure; with respect to therapeutic procedures, the base estimate of 3% of 1,000,000 therapeutic procedures per year was used, valued at the lower-bound estimate of US$1,500 per procedure. Coincidentally, the estimate of patient costs avoided given NIST's research involvement is US$45,000,000 for each procedure, or a total annual economic benefit estimate of US$90,000,000.

Based on expert opinion that such procedures will increase between 5% and 10% per year over the next five years, a conservative lower-bound rate of increase of 5% per year is imputed to the US$90,000,000 estimate. In the absence of opinion on the annual rate of increase in procedure costs, it was assumed, again for the sake of conservativeness, that per procedure costs will remain constant over the next five years.

Finally, the fifth column in Table 6 contains total net benefits, defined, by year, to be the sum of manufacturer and patient benefits less NIST costs. Net benefits are negative in value in years 1990 through 1996 because economic benefits are not realized until 1997.

The data in Table 6 are used to calculate three evaluation metrics: an interval rate of return, an adjusted internal rate of return, and a benefit-to-cost ratio. Each of these is an accepted metric for quantifying the net economic impact associated with a public research program like that within the Radioactivity Group.

A critical issue related to the calculation of the evaluation metrics is the choice of a base period and of a terminal period for the analysis. The choice of the terminal period was discussed previously with regard to a five-year forecast. However, some judgment must be exercised in determining the base period. The relevant question is: the current level of research expertise within the Radioactivity Group represents the culmination of previous efforts dating back to what year?

Certainly, knowledge depreciates over time. Based on discussion with the Radioactivity Group, we found that current economic benefits are traceable to research that began four to six years ago. Again, for the sake of conservativeness, a six-year period is used, and thus the cost data in Table 3 and Table 6 begin with 1990.

Interval rate of return

By definition, the internal rate of return (IRR) is the value of the discount rate, *i*, that equates the present value (PV) of a net benefit stream to zero. Mathematically, the IRR is the rate of discount, *i*, that satisfies the equation:

$$\mathrm{PV} = [(B_t - C_t)/(1+i)^0] + \cdots + [(B_n - C_n)/(1+i)^n] = 0 \qquad (1)$$

where $(B_i - C_i)$ represents net benefits in year *t,* and *n* is the number of years under consideration.

Based on the net benefit data in the fifth column of Table 6, the calculated value of *i* for which PV=0 is 1.38 (rounded), implying an interval rate of return to NIST's investments in radiopharmaceutical research of 138%.

The internal rate of return estimate of 13 8% means that 1.38 (rounded) is the value of the discount rate that equates the present value (1990 as the base year) of net benefits to zero, or in other words, the present value of total benefits to the present value of costs.

Economists and policy-makers generally use internal rate of return measures, for ongoing or completed public-sector research projects, to estimate what is referred to in the economics literature as an approximation of the social rate of return. As such, we can infer from the 138% value calculated from the data that, if 138% is above NIST's hurdle rate or generally accepted expected rate of return, then NIST radiopharmaceutical standards research program, from a social perspective, is worthwhile because the 138% value was calculated based on conservative estimates.

Adjusted internal rate of return

It is not uncommon to misinterpret an internal rate of return measure as an annual yield similar to that earned on, say, a bank deposit. One invests, say US$100, and then earns interest on that US$100 each year plus interest on the interest. That is not the case in an R&D project, in general, or in the case of NIST's radiopharmaceutical standards research, in particular.

Under an alternative set of assumptions, an adjusted internal rate of return (AIRR) can be calculated from the data to provide a rate of return that is more analogous to an annual yield (as earned on a bank deposit for example). It is important to emphasize that the AIRR is not the same as the IRR and that it is not directly comparable to the economics literature on social rates of return. Nevertheless, the AIRR remains an accepted evaluation metric.

If all net NIST costs are referenced to 1990 using a discount rate of 8.78%, the 1990 present value of NIST costs is US$2,435,720. The discount rate of 8.78% is the sum of the Office of Management and Budget's (1992) recommended real rate of discount of 7.0% plus an inflation factor of 1.78%.[16] If all economic benefits (the sum of manufacturer benefits and patient benefits) are referenced forward to the year 2001 using the same rate, the 2001 present value of industry benefits is US$596,138,530. The AIRR is the rate of return that equated a single NIST investment of US$2,435,720 in 1990 to a single benefit estimate of US$596,138,530 in 2001.

Thus, the annual compounded rate of return that corresponds to such an investment in 1990 culminating in 2001 is 65% (rounded) based on the value of x that satisfied the following relationship:

$$\text{US\$2,435,720}\ (1+x)^{11} = \text{US\$596,138,530} \qquad (2)$$

Benefit-to-cost ratio

The third evaluation metric is a benefit-to-cost ratio (*B/C*). This ratio is, by definition, the present value of all benefits to the present value of all costs, where the point of reference for both benefits and costs is the base time period, 1990. The relevant discount rate for the calculation of present value is again 8.78%. For the data in Table 6, the present value of all benefits is US$236,215,070 and the present value of all costs is US$2,435,720. Thus, the ratio of benefits-to-costs is:

[16] The Office of Management and Budget (1992) recommends using a nominal discount rate equal to a 7% real discount rate plus an inflation factor. The inflation rate of 1.78% is the Federal Reserve Board's published implicit price deflator for the past four quarters.

$$B/C = 97 - \text{to} - 1 \tag{3}$$

It should be noted that the calculated IRR of 138% from equation (1) implies a benefit-to-cost ratio of unity. Rewriting equation (1) using summation notation:

$$\text{PV} = \left[\sum_{t=0}^{n} B_t \Big/ (1+i)^t\right] - \left[\sum_{t=0}^{n} C_t \Big/ (1+i)^t\right] \tag{4}$$

where *i* is the IRR that equated PV=0.

When PV=0, then it follows that:

$$\left[\sum_{t=0}^{n} B_t \Big/ (1+i)^t\right] = \left[\sum_{t=0}^{n} C_t \Big/ (1+i)^t\right] \tag{4}$$

or that the present value of benefits equals the present value of costs, or *B/C*=1. Thus, as is the case here, when *B/C*>1 it implies that the IRR is greater than the social rate of discount used in the benefit-to-cost calculation.

Each of the above metrics was calculated under the most conservative set of assumptions possible. In every instance, when experts expressed an opinion in terms of a range of values, the most conservative end point of the range was used. Also, there are certainly costs associated with both underdose and overdose misadministrations that go beyond the direct cost of readministering a dosage (in the case of an underdose).

The benefits associated with these cost savings also have not been considered in this analysis. Were they to be considered, the estimated values of all three metrics would increase. Still, when compared to the social cost of resources used to generate the economic benefits described herein an 8.78% return on resource costs the radiopharmaceutical standard research at NIST is without question valuable to society.

Management value of case study to NIST

The management at NIST is able to use the quantitative results of this economic study to gauge the impact of NIST's research on the practice of nuclear medicine in the United States. The radiopharmaceutical standards research program in the Radioactivity Group comprises about one-third of the program of the Group. The other two-thirds deal with fundamental measurements and standards, and radioactivity standards and measurements for the nuclear fuel cycle. The latter project is mainly concerned with standards and measurements of environmental radioactivity. These two programs may be the subject of future economic impact studies.

The commercial value of the research is, however, not the only factor to consider in NIST strategic planning. NIST also enlists the support of professional associations in defining and

prioritizing measurements and standards needs. One such group, the Council on Ionizing Radiation Measurements and Standards (CIRMS), published in 1995 a report entitled "National needs in ionizing radiation measurements and standards." One of the key areas identified in that report was the need for radionuclide standards for nuclear medicine.

In the revision of that report published in 1998, CIRMS again called for standards in this area to support three specific applications. Calibrations are needed for the very short-lived (two minutes to two hours) radionuclides used in positron emission tomography. Standards are needed for the new radiopharmaceuticals used in treating bone palliation for cancer patients. Also, there is a new possibility of using radiopharmaceuticals in balloon-filled catheters to irradiate arteries following balloon angioplasty procedures. Clinical trials have shown that this procedure has great promise for preventing restenosis (reclosing of the artery) following the angioplasty. The findings in the present economic study suggest that NIST research efforts in this area will pay off handsomely in public benefits and savings to US manufacturers.

NIST's management has also considered the international marketing implications in light of the present study. NIST has led an international effort among the national standards laboratories to inter-compare radionuclide standards. Several of the important radionuclides used in nuclear medicine (Table 1) have been included in these international intercomparisons.

NIST is now planning an inter-comparison with standards laboratories in South and Central America that will involve shipment of SRMs of iodine-131 for measurement in those laboratories. If this quality assurance program set up by NIST and the US manufacturers can be extended to these Americas, it should help to increase the use of these highly beneficial diagnostic and therapeutic materials in an expanding economic market.

Toward best practices in program evaluation

Based on this case study and our other economic impact assessments at NIST, we posit in this section three evaluation elements of what might be considered as a set of characteristics for best practices applicable to any technology-based public institution. We list these below in a generic fashion. Some go beyond lessons learned from the specifics of the radiopharmaceutical standards study, but all draw on general experiences at NIST.

Certainly, the universe from which we base these characteristics is limited to only a handful of exercises within one federal laboratory, namely NIST. Obviously, not all technology-based public institutions are identical to NIST in either size or scope of research. However, in the current political environment in the United States where public accountability is becoming an operational guideline, our set of characteristics may offer a starting point for others to follow.

One, instill an institutional belief that program evaluation is important. Management must be educated to the overall gains to the institution from ongoing program evaluation (and they must also be convinced that program evaluation is not the first step toward budget reallocation). Such an *a priori* education is necessary for establishing evaluation into the culture of the institution, and (see below) into its technology planning process. The radiopharmaceutical standards study was the third such evaluation conducted within the NIST Physics Laboratory, and such economic

impact analysis has become accepted there not only in anticipation of GPRA requirements but also as sound management practice.

Two, select a standardized method for conducting program evaluation. The institution must conduct pilot evaluations as demonstrations of how to apply evaluation methods and how to learn from one evaluation exercise to the next. Subsequently the selected standardized method is institutionalized such as with NIST's federal laboratories "Guidelines for conducting and interpreting assessment studies" (see Link, 1996a). The evaluation methods must be clearly articulated to management and reasonable in terms of their implementation.

Likewise, the evaluation metrics must be conventional in the sense that they correspond to accepted evaluation practices, and (perhaps most important) they must be easily understood by the broader evaluation community. The three metrics reported in the previous section are common to all NIST assessment exercises. While the internal rate of return is perhaps more widely accepted in the academic community, it is understood among NIST upper management to be a widely accepted valuation concept. However, the benefit-to-cost ratio is probably more widely understood by scientists within the Physics Laboratory and other laboratories at NIST.

Three, execute program evaluations. Staring into the future is what technology planning is all about; program evaluation is a key to gaining understanding necessary for successful technology planning. Because no one's crystal ball is accurate, the best one can hope for is systematic and informed judgment that can be clearly explained and articulated. Technology planning that is grounded in ongoing evaluation provides two important qualities: it enables the institution to explain its mission and goals to an internal and external audience of stakeholders; and, as important, it allows the institution in time to understand its errors, to learn from them, and to incorporate that knowledge into the planning and evaluation cycle.

At NIST, only time will tell the extent to which this case study and the others like it within the Physics Laboratory will affect technology planning.

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