Network for Translational Research Program Evaluation Feasibility Study—Final Report

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1. Introduction

Under a Task Order[i] issued in September 2010 by the National Cancer Institute's Office of Science Planning and Assessment (NCI/OSPA) to NOVA Research Company, The Madrillon Group Inc. conducted an evaluation feasibility study to determine whether a process-outcome evaluation of the Network for Translational Research (NTR) program is warranted and to provide recommendations for its design. This report presents the findings from the feasibility study and recommendations for the evaluation questions and design for a process-outcome evaluation of the NTR program. Following this introduction, **Section 2** describes the history of the program and its position within a series of molecular imaging initiatives coordinated by the Cancer Imaging Program (CIP) and the goals and structure of the current program. **Section 3** describes the evaluation feasibility study, including the study questions, methods, and data sources used to address them. **Section 4** presents the evaluation feasibility study findings and results. **Section 5** describes the conclusions drawn from these findings and their implications for the design of a process-outcome evaluation of the NTR program. **Section 6** presents recommendations for the design of a process-outcome evaluation study, including proposed evaluation questions, general design for the study, conceptual framework, key variables, data collection methods, and an analysis plan.

[i] The Madrillon Group Inc. (under a subcontract from NOVA Research Company) is providing program evaluation expertise and support to the National Cancer Institute's Office of Science Planning and Assessment under the contract entitled *Task Order Services to Support the NCI's Office of Science Planning and Assessment, Part I. Program Evaluation Support.*

2. Background

During the past two decades, our understanding of human disease has been revolutionized by advances in basic molecular biology. These advances have enabled scientific achievements such as sequencing of human genes, identification of molecular pathways, determination of protein-specific causes of diseases, and use of cell lines that allow for rapid testing of new drugs and therapies. Discoveries in molecular biology have also triggered advances in related technologies, including imaging sciences.

The use of imaging techniques has become a critical element in the care of patients with various forms of cancer. Prior to the development of these imaging techniques, clinicians had few options for the diagnosis and staging of cancers other than direct observation via exploratory surgery or limited radiological examination. Development of what are now considered to be traditional imaging techniques began in the late 1960s and 1970s, with the advent of modalities such as computed x-ray tomography (CT), ultrasound (US), magnetic resonance imaging (MRI), and developments in nuclear medicine. These techniques operate primarily by imaging differences in tissue density or water content. While they are not invasive in the way that earlier methods were, they nonetheless do produce some alteration in the surrounding tissues.

Molecular imaging emerged from the intersection of molecular biology with *in vivo* development in imaging technology. Molecular and functional imaging techniques permit the visualization of cellular functions and molecular processes in living organisms without producing alterations in them. Molecular imaging differs from traditional imaging approaches in that it uses probes known as biomarkers to help image particular targets or pathways. Biomarkers interact chemically with their surroundings and alter the image according to molecular changes occurring within the area of interest. Because these images can be captured at a cellular and even molecular level, *in vivo* molecular imaging approaches offer the potential for producing earlier and more precise diagnoses of diseases such as cancer and cardiovascular disease as well as promoting improved understanding of the molecular pathways of these diseases.

Exhibit 1. A Brief History of the Cancer Imaging Program

1996—NCI establishes the Diagnostic Imaging Program (forerunner of the Cancer Imaging Program)

1997—NCI convenes the Imaging Sciences Working Group

1998—NCI identifies imaging technology as an "extraordinary opportunity" in its Bypass Budget (FY 1998-FY2003)

1998—Small Animal Imaging Research Resources Program first announced

1999—In Vivo Cellular and Molecular Imaging Centers Program first announced

2001—Diagnostic Imaging Program name changed to Biomedical Imaging Program

2002—Network for Translational Research – Optical Imaging Program first announced

2003—Biomedical Imaging Program name changed to Cancer Imaging Program

2007—Network for Translational Research – Optical Imaging in Multimodal Platforms Program announced

2.1. The Promise of Molecular Imaging

The development of molecular imaging technologies has enormous potential for clinical, scientific, and economic impacts. Direct imaging of the molecular changes underlying diseases would have a major impact on patient care by allowing much earlier detection of disease, even at "pre-disease states," allowing intervention at a point in time when the outcome is most likely to be affected. For example, in most cases, detection of Stage 1 cancers is associated with a greater than 90 percent five-year survival rate; when lesions are detected even earlier (at the premalignant stage), treatment is often curative.[1]

At the same time, the development and validation of these technologies underscore two critical points about the nature of medical innovation in the twenty-first century. First, the scientific and technological impetus for molecular imaging emerged from the active intersection of several fields of research and technology development: molecular biology and chemistry, biomedical engineering, radiology, and surgery, among others. This type of multidisciplinary attack on a major scientific and technological problem is becoming increasingly the norm in addressing biomedical challenges. Secondly, the development of molecular imaging techniques illustrates the critical importance of translational research for moving the discoveries and innovations of basic science into actual tools and products that can be applied in clinical settings.

Exhibit 2. Imaging Science Goals of NCI

1. Develop and validate imaging technologies and agents.
2. Develop imaging techniques that can help to identify the biological properties of precancerous or cancerous cells and aid the prediction of clinical course and response to interventions.
3. Develop minimally invasive technologies that can be used in interventions and assessment of treatment outcomes.
4. Foster interactions and collaborations among imaging scientists and basic biologists, chemists, and physicians to advance imaging research.
5. Create infrastructures to advance research in the development, assessment, and validation of new imaging tools, techniques, and assessment methods.

2.2. Molecular Imaging Initiatives at the National Cancer Institute

Much of the impetus and funding for the research translation of molecular imaging technologies is attributable to the National Cancer Institute at the National Institutes of Health (NIH). Since the mid-1990s, NCI has supported a series of research initiatives aimed at identifying and developing these techniques and moving them from the bench to the clinical environment. Many of these initiatives have been coordinated by the Cancer Imaging Program at NCI. A brief timeline of several of these initiatives is presented in **Exhibit 1**. Two of these initiatives will be discussed below in more detail.

2.2.1. NCI's Imaging Sciences Working Group

On July 17-18, 1997, NCI convened an Imaging Sciences Working Group (ISWG) as part of a broader strategy to identify intellectually fertile areas for new investment relating to particular areas of cancer research. The strategy involved bringing together diverse scientific and clinical communities that did not often get to interact with each other. The ISWG's focus was on traditional imaging techniques and concepts of the molecular basis of cancer, with special emphasis on the detection of subtle genomic and molecular changes.

As a "committee of the whole," the ISWG identified several issues that would frame subsequent discussions and recommendations. First, they agreed that imaging technology needed to emphasize the detection of the dynamics of cell metabolism and function, rather than issues concerning the improvement of anatomic resolution, per se. This would require developing new instruments and new types of contrast media and radiopharmaceuticals. In particular, the ISWG recognized that there would need to be parallel advances in MR spectrometry, new imaging techniques such as optical imaging, and the exploitation of single-photon and PET imaging and ultrasound. Second, the ISWG recognized the importance of involving partnerships between government, academia, and industry as a means of facilitating product development. A third major area of broad agreement was the need for enhanced training of professionals in imaging sciences research at both the entry level and for experienced researchers seeking to enter the field. The ISWG formed seven task groups to address these issues.

Several initiatives emerged from the work and recommendations of the Imaging Sciences Working Group. Arguably the most important of these was the identification of imaging science as an area of "extraordinary opportunity" in the NCI Bypass Budgets for FY 1998-2003. This action identified imaging sciences as a major scientific priority, resulting in substantially increased research funding and the issuance of several Requests for Applications (RFAs) for later programs such as the Small Animal Imaging Research Resources Program (SAIRP) and the In Vivo Cellular and Molecular Imaging (ICMIC) Program. NCI established several goals[2] for its development of imaging sciences research, as shown in **Exhibit 2**.

2.2.2. The Network for Translational Research Optical Imaging (NTROI) Program

By 2002, the biomedical imaging research community had become increasingly interested in a newer group of imaging technologies known broadly as optical imaging. NCI hosted several workshops at which participants described various *in vivo* biophotonics technologies that appeared to hold promise for application to the early detection, diagnosis, and assessment of cancer and other diseases. These *in vivo* optical imaging and/or spectroscopy technologies and methods appeared to offer exciting possibilities for clinical application with a wide range of cancers. They also offered potential advantages over traditional imaging technologies on at least two fronts. First, the optical measurements they could provide extended across a wide range of resolution, from molecular and cellular levels up to tissues and organs. Second, some of these methods complemented advances in targeted or activated optical contrast agents that offered better sensitivity and specificity at molecular levels than other imaging technologies.

If these technologies were to achieve their promise, a major funding and developmental effort would be required. The Biomedical Imaging Program (BIP) at NCI therefore issued RFA-CA-03-002 to establish the Network for Translational Research—Optical Imaging program. Using the U54 cooperative agreement mechanism, BIP created a network of interdisciplinary, interinstitutional research teams (Specialized Research Resource Centers) for the purpose of supporting a translational research initiative focusing on optical imaging and/or spectroscopy *in vivo*. The program funded three research teams, with each team including investigators from at least two institutions; additional investigators from national laboratories, industry, or intramural laboratories at NIH participated in these teams as well. Each team received funding for a five-year period; a total of $3 million in total costs was provided for Year 1, and $18 million in total costs was provided for all five project years.

The stated goal of NTROI was to organize a consortium with flexibility in scope and funding incentives to support inter- and intra-team research collaboration to encourage translational research. In this context, translational research was defined as the development of a consensus process and methodology to move the application of emerging optical imaging and spectroscopy methods and their intrinsic or extrinsic (agent-mediated) contrast mechanisms closer to use in clinical oncology or research with human or animal models. The program had two objectives: (1) accelerate translational research by developing a consensus-based approach to improving methods for system integration, optimization, and validation of next-generation optical imaging, spectroscopic methods, and contrast agents; and (2) validate the new optical imaging methods with specific cancer applications.

To accomplish these objectives, the NTROI program was funded as a cooperative agreement, with guidance provided through a Steering Committee comprising Principal Investigators (PIs) and NCI program staff scientists. The three research teams were to originate and propose at least three primary research projects, and additional developmental projects as desired. It was also hoped that the teams might collaborate on common primary projects or pilot studies.

2.2.3. The Current Network for Translational Research Program

No formal evaluation of the NTROI program was conducted; however, discussions with program scientist staff members at the Cancer Imaging Program[ii] suggested that the NTROI program was at best a mixed success. Two lessons learned from the NTROI experience were that there needed to be a shift in technological focus from the original single-modality imaging methods emphasized in NTROI to multimodal imaging platforms, and that the desired level of inter-team collaboration could easily be undercut by the strength of existing institutional research silos.

The period during which the NTROI program operated witnessed a number of advances in medical imaging that resulted from the combination of different imaging techniques (multimodal imaging platforms). The idea is that each imaging modality has its own unique strengths and limitations. Each imaging technology uses different principles of physical interaction with tissue and, where appropriate, different molecular probes. By combining two modalities in a single integrated platform, the selected modalities can complement each other, with the strengths of one technology offsetting the limitations of the other, theoretically leading to increased overall performance in sensitivity and specificity. The challenge lies in developing a single platform that successfully integrates two imaging technologies. Another reason the creation of combined-technology platforms may be an attractive strategy is that in such platforms, one technology can be considered new and the other can be considered well-established. It therefore becomes possible to use the results from the more established technology as a surrogate standard for the validation of the newer imaging modality. Optical imaging is seen as an ideal modality to combine with other, more traditional imaging technologies. For example, it could be highly advantageous to operate multimodal imaging at widely different resolution scales. One modality can perform a traditional measurement at the organ level to identify a suspicious location, while an optical imaging technology can then be used to highlight cellular-level events.[3]

In 2007, the Cancer Imaging Program first announced the Network for Translational Research-Optical Imaging in Multimodal Platforms (RFA-CA-08-002). This new five-year program (hereafter called the Network for Translational Research, or NTR) funded four multidisciplinary, multi-institutional research centers; applicants were strongly encouraged to propose teams that involved at least one other academic institution and one or more industrial partners. Like its predecessor program, the NTR was funded through a U54 cooperative agreement, and is guided by a Steering Committee composed of PIs from each center and NCI program staff scientists. Representatives from other Federal agencies were also invited to participate, including the Food and Drug Administration (FDA), the Centers for Medicare and Medicaid Services (CMS), the National Institute of Standards and Technology (NIST), the NCI caBIG initiative, and other relevant NCI programs. In addition to the Steering Committee, there is an External Advisory Committee with representatives from industry and academia.

2.2.3.1. Program Goals

The overall mission of the Network for Translational Research is to develop, optimize, and validate multimodal molecular imaging platforms and methods so that they can enter single- or multisite clinical trials with human subjects. The goal of the NTR program is to accelerate the translational research of *in vivo* multimodal imaging and/or spectroscopic platforms from the laboratory to the preclinical level and, ultimately, to the clinical level.

[ii] Meeting on September 21, 2010 between members of The Madrillon Group Inc. evaluation team and the NCI Cancer Imaging Program.

2.2.3.2. Program Structure

The NTR program is organized as a network. As stated in the RFA:[iii]

> *"The overarching purpose for the Network is to facilitate the conduct of translational research in the area of multimodal imaging and spectroscopy and validation of such approaches for clinically relevant applications. It is desirable that the academic and industrial communities work together where appropriate to develop consensus approaches for validation of multimodal imaging technologies that satisfy unmet needs in the clinical environment. Such consensus on validation approaches is expected to accelerate the dissemination of new imaging applications/platforms into clinical practice by shortening the time and effort associated with formal procedures of their evaluation and approval by regulatory agencies (notably FDA.)"*

The NTR program has a "hub-and-spoke" structure with several components. These components include the four research centers (the "hubs"), individual investigator-initiated research projects linked to the centers (the "spokes"), several Research Support Cores, a Steering Committee, and an External Advisory Board.

Research Centers. Four research centers were funded by the NTR program. Each center consists of a team of multidisciplinary investigators from two or more academic institutions and one or more industrial partner. Each center proposed a single primary research project focused on the development, optimization, and validation of a specific multimodal imaging platform that combined some type of optical imaging technology with one of the more traditional imaging technologies. In order to complete this project, each center also proposed several task-specific projects. Each primary project included a precise set of project milestones; the task-specific projects were planned in order to assist the center in achieving specific project milestones. The milestone system has thus provided a common framework for planning each center's work and for monitoring its progress in completing it.

Exhibit 3 shows the four NTR research centers and the technologies and organ sites each is investigating. By coincidence, the four research centers share complementary research goals and imaging platforms.

Exhibit 3. Research Centers, Imaging Technologies, and Organ Application Sites*

INSTITUTION	MULTIMODAL DEVICES	MULTIMODAL PROBES	CANCER PROBLEM IMAGING MODE
Washington University	Optical; Ultrasound (photoacoustic)	Optical; nuclear	Sentinel lymph node, breast and melanoma tomography
University of Texas	Optical; Nuclear	Optical; nuclear	Sentinel lymph node, breast and melanoma tomography
University of Michigan	Optical; Nuclear	Optical; nuclear	Gastrointestinal cancers MEMS catheter
Stanford University	Optical; Ultrasound	Optical	Gastrointestinal cancers MEMS catheter

* Adapted from Tandon P, Nordstrom R J. Next-generation imaging development for nanoparticle biodistribution measurements. *WIRES Nanomed Nanobiotechnol*. 2011;3:5-10. Available from: www.wiley.com/wires/nanomed

Of the four research centers, Stanford University alone participated in the earlier NTROI Program. The remaining three centers are new to the NTR initiative.

Investigator-Initiated Research Projects. Investigators at each research center (and other qualified individuals) have been encouraged to pursue additional research projects that build upon the primary project at a specific research center. Such projects could include the use of the center's multimodal platform with a separate type of cancer, or other variations on the primary project or its task-specific projects. These research projects are to be funded separately from the NTR project using existing NIH funding mechanisms. This linkage of independent research to the NTR primary projects is referred to as a

[iii] NCI RFA-CA-08-002: *Network for Translational Research (NTR): Optical Imaging in Multimodal Platforms.* Release Date 2007 Oct 12.

"hub-and-spoke" organizational model, in which the research center primary project serves as the "hub" and the independent investigator-initiated research projects are the "spokes" that emanate from it.

Research Support Cores. One important difference between the current NTR program and NTROI is the existence of intercenter Research Support Cores. At the first meeting of the NTR Steering Committee, the members voted to establish Research Support Cores with representatives from each of the four centers. While each center has one or more internal research support cores that provide specialized services unique to its own specific infrastructural needs, the Research Support Cores were established for the explicit purpose of opening communication and promoting collaboration on problems and barriers of common concern and interest. The Research Support Cores have been described by some of the PIs as the "workhorses" of the Network, providing an important forum for consensus building and problem-solving. The Cores are autonomous and set their own agendas and priorities. Each Core has its own elected chairperson. Individual members report on monthly activities to their respective PIs, and the Cores report on their activities to the Steering Committee. The Research Support Cores were developed to ensure cross-center communication and collaboration.

NTR Steering Committee. Consistent with the cooperative agreement model, central guidance for the project rests with the Steering Committee. Membership on the Steering Committee is held by the four PIs and NCI program staff scientists. The Committee holds periodic teleconference calls and meets formally in conjunction with "Face-to-Face" meetings, which have been held on an annual basis. Three such meetings have been conducted to date; the most recent meeting was held in February 2011.

External Advisory Board. In addition to the Steering Committee, the Cancer Imaging Program established an External Advisory Board. Members of this Board include individuals with expertise and experience in the imaging industry and other experts.

2.2.3.3. Objectives of the NTR Program Evaluation Feasibility Study

The Network for Translational Research initiative (consisting of the earlier NTROI program funded in 2003 and the current NTR program funded in 2008) represents an important programmatic innovation in accelerating the translation of complex biomedical technology from basic science discoveries to the early stages of clinical testing, application, and commercialization. Translational biomedical research poses numerous challenges that have been difficult to overcome in the past. The NTR program includes several structural elements designed to address some of these challenges in an innovative manner. First, the program requires that the four research teams include individuals from multiple disciplines, and that the teams demonstrate an overall multidisciplinary approach. Second, each team must include industrial partners—companies with specific expertise in issues and solutions relevant to the team's primary project. This requirement attempts to ensure that the team maintains a balance between academic research and the types of information and evidence necessary to move a multimodal imaging platform from academia to commercialization. Third, the Network includes several Research Support Cores (currently there are four) that involve investigators from each of the four centers and industry in efforts to reach consensus on solutions to basic obstacles in the translational path.

While individual elements of this program structure are not by themselves unique to the NTR, their combination in one program offers a promising model that could be applied in other technological development initiatives. The NTR program model has already stimulated considerable interest at the FDA, which is considering this approach for some of its initiatives. An evaluation of the NTR program could provide evidence on whether this program model works and whether (and how) these structural elements contribute to its success.

For those reasons, the evaluation feasibility study was commissioned to address three objectives: (1) determine whether an evaluation of the program is feasible and warranted; (2) determine what form that evaluation should take and how best to conduct it; and (3) gather baseline data on the NTR program's current functioning.

2.2.3.4. How the Evaluation Feasibility Study Results Will Be Used

The findings from this study will be used to inform decision-making at the Cancer Imaging Program about whether to commission an evaluation of the NTR program and how it should be designed. The results may also be used to support funding for an evaluation under the NIH Evaluation Set-aside Program. The main product of the feasibility study is a report whose audience will include Federal policy makers within the Cancer Imaging Program and NCI. The audience may also include representatives from other Federal agencies such as FDA, NIST, and CMS. The report will also provide perspectives from the research center PIs and industrial partners regarding the overall functioning of key elements of the program.

3. Feasibility Study Questions, Methods, and Data Sources

This section describes the questions examined in the feasibility study, the methods used to address these questions, and the data sources and collection approaches used to answer the questions.

3.1. Feasibility Study Questions

The questions posed for the NTR evaluation feasibility study include:

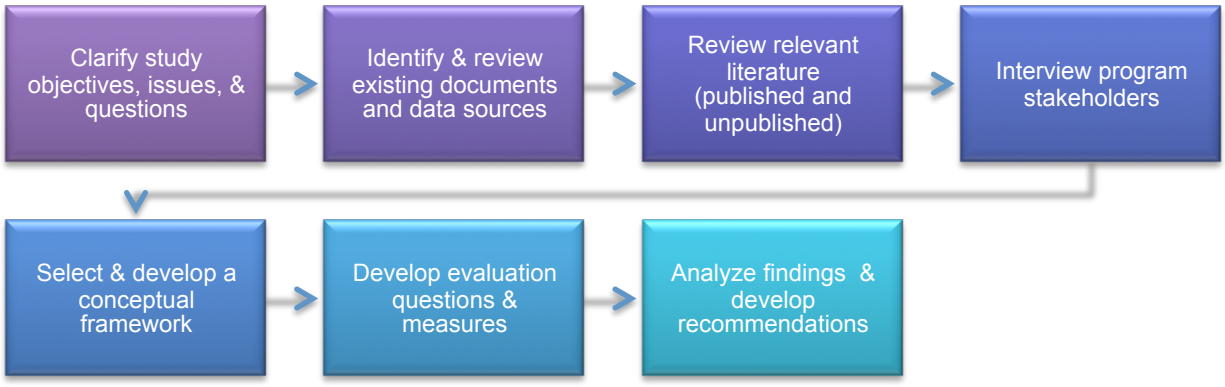
1. What are the most appropriate methods to evaluate the NTR program?
2. What existing data and metrics can be used to evaluate the NTR program?
3. What types of measures, study questions (variables and metrics), data collection strategies, and analysis methods should be used to evaluate the *outcomes* of the NTR program?
4. What types of measures, study questions (variables and metrics), data collection strategies, and analysis methods should be used to assess *program implementation*?
5. What clearance requirements might be necessary to conduct the NTR program evaluation?
6. What are the recommended overall process and outcome evaluation plan and design for the NTR program?
7. What is the estimated cost of the proposed process and outcome evaluation? Is the amount reasonable given the cost of the program?
8. What would be the timeline and resource requirements for conducting the process and outcome evaluation?

At the initial project meeting on September 21, 2010, Cancer Imaging Program staff scientists also expressed interest in obtaining preliminary data on the current functioning of the NTR program.

3.2. Feasibility Study Methods

The NTR Program Evaluation Feasibility Study followed a sequence of methodological steps in conducting the study, as shown in **Exhibit 4.**

Exhibit 4. Feasibility Study Methodology



3.3. Feasibility Study Data Sources

Several data sources were used in conducting the feasibility study, including documents and administrative databases; review of the published and unpublished literature; interviews with program stakeholders; and observation of the third NTR Face-to-Face Meeting on February 17-18, 2011.

3.3.1. Documents and Administrative Databases

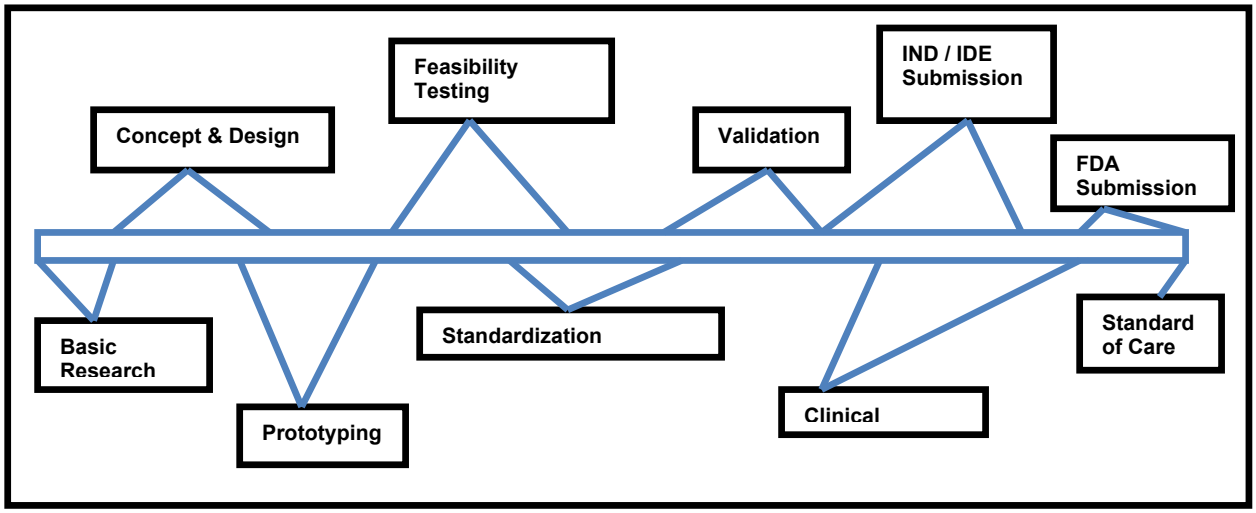
The Madrillon evaluation team reviewed existing documentation about the NTR program (see **Exhibit 5** for a list of documents). These documents included the initial RFAs for the previous NTROI program and the current NTR program, the grant applications submitted by the four research centers, the NTR Year 1 and Year 2 Reports, and minutes from several Steering Committee meetings. The evaluation team also reviewed the IMPAC II QVR database to examine existing information on the project grants, funding, and publications. The team reviewed these source materials for two reasons: (1) to provide background on the NTR program and the four individual centers and their projects; and (2) to explore the types of data that are routinely collected on the four centers and the activities of the Research Support Cores.

Exhibit 5. Documents and Administrative Databases

- **Requests for Applications (NTROI—RFA-CA-03-002, and NTR—RFA-CA-08-002)**
- **Grant applications from the four research centers**
- **NTR Year 1 Report**
- **NTR Year 2 Report**
- **Steering Committee minutes**
- **IMPAC II QVR database**

The NTR Year 1 and 2 Reports were important, as they contained detailed updates from each of the four centers on the work (and milestones) accomplished during the preceding year. The milestones were also important, since the Steering Committee had developed a translational research pipeline that was discussed as a possible tool for documenting the progress of each center on its primary and task-specific projects. That diagram is shown in **Exhibit 6**.

Exhibit 6. Translational Research Pipeline



3.3.2. Review of the Literature

The Madrillon evaluation team conducted two literature reviews. The first review focused on published literature on the role(s) of networks in accelerating translational research and on potential conceptual

frameworks that could be used to guide a process-outcome evaluation of the NTR program. The second review explored the largely unpublished literature describing past evaluations of NIH research center and network programs.

3.3.2.1. Published Literature

The objective of the review of published literature was to determine what prior research on inter-organizational networks (particularly, networks involving academia and industry) had discovered concerning whether networks promote translational research and, if so, what structural elements of such networks contributed to this acceleration. The evaluation team hoped to locate studies that might support the roles that the NTR program's structural elements (particularly, its Research Support Cores) are conjectured to play in quickening the translational research process.

A second objective was to identify useful conceptual frameworks that might guide the overall process-outcome evaluation. Two important criteria the team established for acceptable frameworks were that they should: (1) view the outcomes from research activity from a multidimensional perspective; and (2) incorporate both a process and an outcome component.

To locate these articles, the evaluation team searched major publication databases including PubMed and Scopus, using search terms such as "research impact assessment," "evaluation of research and development programs," "evaluation of R&D programs," "research payback," and the "evaluation of science and technology programs." Key words were refined based on clusters of papers found in the literature. For example, terms such as "research value mapping," "scientific and technical human capital," and "research environment" were located in this way. Manual searches were conducted of bibliographies from identified articles, and the tables of contents of specialized journals focusing on evaluation of R&D programs were searched back to the 1980s, when possible. Examples of these journals included *Research Policy, Research Evaluation, Evaluation and Program Planning, and Evaluation Review.* Over 150 articles were identified, and the individual articles were reviewed to locate general review and discussion articles and specific studies thought to be relevant for the NTR program.

3.3.2.2. Prior NIH Program Evaluations of Research Center/Network Programs

The second review focused on prior NIH program evaluations of research center/network programs. As part of a prior NCI project, the Madrillon evaluation team conducted an extensive search of NIH data sources (including Web sites, the Evaluation Office Web site, and a survey of NIH program officers). This search generated the first compilation of prior NIH evaluations of research center and network programs, successfully locating 75 documents, of which three-quarters were unpublished reports and memoranda describing the design, methods, and results from evaluations of 61 NIH programs dating from 1978 through 2009. This unique resource was used as the source for a search for relevant evaluations of research center and network programs focusing on technology development with particular emphasis on NCI. This search yielded four prior evaluations conducted since 2007.

3.3.3. Interviews with Program Stakeholders

An important part of the data collection for the feasibility study involved interviews with major program stakeholders. Two stakeholder groups were identified: (1) the four PIs of the NTR research centers, and (2) the industrial partners collaborating with the NTR research centers. A brief email was sent to each stakeholder from the Cancer Imaging Program describing the feasibility study and the purpose of the interview, soliciting cooperation with the interview, and noting that a representative from the Madrillon evaluation team would be following up to arrange a convenient time to conduct the interview. The interviews were conducted by one interviewer by telephone, and averaged 60 minutes in length. The interviews were conducted in January and February 2011, prior to the Face-to-Face Meeting.

3.3.3.1. Research Center Principal Investigators

The research center PI interview protocol (**Appendix A**) was developed by the Madrillon evaluation team and reviewed and approved by the Cancer Imaging Program. The protocol contained a series of broad, open-ended questions on the implementation of the individual research centers (factors that facilitated and/or hindered implementation), noteworthy aspects of the NTR program from the PI's perspective, the PI's experience and familiarity with NIH programs like NTR in the past, perceptions about the Research Support Cores and working with the industrial partners, and a series of questions on the design of and measures for an evaluation of the NTR program (types of outcomes and process measures to collect, evaluation questions, and whether a comparison group was appropriate for this evaluation). The data from the four interviews were analyzed qualitatively to identify major themes related to the various questions.

3.3.3.2. Industrial Partners

The industrial partners' interview protocol (**Appendix B**) was developed by the Madrillon evaluation team and reviewed and approved by the Cancer Imaging Program. The protocol contained a series of open-ended questions on the role and activities of the industrial partner/representative, perceived benefits to the company from participating in the NTR program, the NTR program as a program model for engaging academia and industry, perceptions about working with the research center, and a final series of questions on the design of and measures for an evaluation of the NTR program (types of outcomes and process measures to collect, evaluation questions, and whether a comparison group was appropriate for this evaluation).

The Madrillon evaluation team obtained from the Cancer Imaging Program a list of 12 individuals representing the various industry partners collaborating with the four research centers. The list included names, companies, email addresses, and telephone numbers; 5 of the 12 individuals on the list were interviewed.

3.3.4. Observation of Third Face-to-Face Meeting, February 17-18, 2011

During the time period in which the NTR evaluation feasibility study was conducted, the Cancer Imaging Program convened and held its Third Annual NTR Face-to-Face Meeting, at which PIs and senior investigators from the four research centers, CIP program staff scientists, and invited guests from the External Advisory Board and several Federal agencies (FDA, CMS) met to review progress and discuss future plans. The Madrillon evaluation team attended both days of this meeting, including presentations by each research center on progress to date, reports from the four Research Support Cores, and discussions among the attendees (including the Federal agencies).

4. Feasibility Study Findings

This section summarizes findings from the review of documents and administrative databases, the literature review (published and unpublished literature), interviews with the major program stakeholders, and observation of the Face-to-Face Meeting.

4.1. Findings from Document and Database Review

As part of the NTR feasibility study, the Madrillon evaluation team reviewed existing documents and NIH databases to explore the utility of these sources for the program evaluation. Data from existing documents such as grant applications, summary statements, and annual progress reports, and administrative data stored in NIH databases, including IMPAC II and the electronic Scientific Portfolio Assistant (eSPA), can provide useful information on resources that grantees had available for use prior to the actual date of the award, background on team members and partners, project organization and plans, progress made each year, and publications. A major question concerning these sources is the degree to which these records are complete and sufficiently detailed to provide useful information for an evaluation. This tends to vary across programs and even within the same program over time.

Records for the NTR program appear to be reasonably complete and up to date. The evaluation team was able to locate copies of the grant applications for each of the four NTR research grants, and copies of these together with other administrative data were current for the projects. The CIP staff team compiles an annual year-end report on the NTR program, which includes the annual progress reports for the four projects and additional presentation of administrative data and developments within the program. Bound copies of these annual reports were available for the first two years of the NTR program (currently in its third year).

As one indication of the types of data that can be obtained from these sources, the evaluation team compiled the following two exhibits summarizing the types of internal research cores each research team created (**Exhibit 7**), and data on publications from 2008 through the conclusion of 2010 (**Exhibit 8**).

Exhibit 7 shows the various internal Research Support Cores the four research center teams proposed as part of their applications. These cores typically reflect specific facilities, labs, or even research centers within the local institutional environment, as opposed to new facilities developed from the grant funds. Certain cores were present at each of the four research centers. In addition to establishing an administrative core, each of the four center teams also established some type of biostatistics core and one or more types of imaging cores. The Small Animal Imaging core at Washington University is actually its Small Animal Imaging Resource (SAIR) Center program. The Stanford team is sufficiently large that it has required part of a core to manage its interactions

Exhibit 7. Internal Research Cores for Each Team

Stanford University

- **Administrative Core**
- **Chemistry of Probes & Therapeutics**
- **Instrumentation and System Integration**
- **Clinical Studies and Molecular Pathology**
- **Image Analysis, Biostatistics, and Quantification**
- **Optical Systems Development and Corporate Interactions**

Washington University at St. Louis

- **Administrative Core**
- **Human Imaging Unit**
- **Biomedical Imaging Informatics**
- **Biostatistics**
- **Small Animal Imaging**

University of Michigan

- **Administrative Core**
- **Imaging**
- **Gastroenterological Peptides**
- **Biostatistics**

University of Texas

- **Administrative Core**
- **Chemistry**
- **Preclinical Testing**
- **Small Animal Imaging**

with various corporate partners.

Exhibit 8 shows the total funding for each of the four centers and preliminary data on publications, including total numbers of publications, numbers of research publications, average citation rates by other investigators (excluding self-citations), and average journal impact factors, where available.

Exhibit 8. Selected Data on Funding and Publications

INSTITUTION	TOTAL AWARD	TOTAL PUBS	RESEARCH PUBS	AVERAGE CITATION RATE	AVERAGE JOURNAL IMPACT FACTOR
Stanford	$2,913,027	4	3	--	--
Washington	$4,350,350	55	47	8	4.0
U of Michigan	$3,438,349	3	2	2	2.9
U of Texas	$3,450,000	2	2	--	2.9
TOTAL	$14,151,726	64	54		

4.2. Findings from Literature Review

This subsection presents results from the reviews of the published literature and the review of prior NIH evaluations of research center/network programs relevant to NTR.

4.2.1. Review of Published Literature

The review of published literature addressed three questions: (1) Do networks provide any advantage for individuals or research teams pursuing translational research (and, if so, what aspects of the structure of networks contribute most to this)? (2) What guidance do internal NIH documents provide concerning translational research and its evaluation? (3) What conceptual frameworks exist that could facilitate the evaluation of a translational research program such as NTR?

4.2.1.1. Networks and Translational Research

Using Google Scholar and PubMed, a search was made of the literature on networks and translational research, using terms including “networks and translational research,” “effectiveness of networks and translational research,” “networks and innovation” and similar terms. Well over 150 articles were identified, although few of them addressed networks and translational research directly. Most focused on networks and innovation. Several review articles were identified and form the basis for the following subsection.

There is a clear consensus in the literature that networks promote innovation,[4] although important questions remain unresolved concerning how the internal structure of networks contributes to this.[5] Much of this literature can be classified into two categories based on the general focus of the study. The first category, by far the most frequently encountered, focuses on networks at an organizational level. These studies describe relationships among the various organizations within a network and how they are structured within a network. Frequently, these studies investigate an innovation output (most frequently, the number of patents or licenses over a period of time.) The second category of network studies focuses on what Keith Provan[6] and other writers have described as the “whole network.” This level of analysis takes an interorganizational approach that looks at questions such as how networks evolve and how collective outcomes are produced. Provan and colleagues define a whole network as consisting of three or more organizations connected in ways that facilitate achievement of a common goal. The whole-network approach uses many of the same social network analysis constructs used in studies at the organizational level, but rather than focusing on the effects of a network on a particular member organization, the emphasis is placed on describing and explaining the characteristics of the network as a

whole. Using this approach, these network characteristics can be assessed and compared across several different networks or within the same network over time. Examples of some of these network characteristics that appear particularly relevant for the NTR program are shown below in **Exhibit 9.**

Exhibit 9. Key Network Constructs Relevant to the NTR Program*

CONSTRUCT	DESCRIPTION
Density	**The number of connections among organizations within a network**
Cohesive subgroups	**The presence of numerous clusters of inter-related subgroups, often measured by the calculation of a clustering coefficient for the network as a whole**
Centralization	**The extent to which one or a few organizations within a network are more centrally connected than others**

*Adapted from Provan KG, Fish A, Sydow J. Interorganizational networks at the network level: a review of the empirical literature on whole networks. *Journal of Management.* 2007;33(3):479-516

The use of social network analysis approaches in the field of research impact assessment is growing.[7] While social network analysis is seen as a useful descriptive technique, its application in research impact assessment requires further development to move beyond simple descriptions of the relationships among members of the network. One direction this development can take is the pursuit of whole-network studies that focus on how network characteristics affect network performance. The NTR program may offer a possible opportunity for examining these issues further.

4.2.1.2. Translational Research at NCI

In 2005, NCI convened a large-scale initiative to review its activities in the area of translational research. Recognizing that the translational research enterprise was failing to keep pace with the rapidly proliferating opportunities and possibilities emergent from advances in knowledge and technology during the past 40 years of cancer research, NCI established a broad coalition of individuals representing academia, industry, the provider community, advocacy groups, FDA, and NCI staff members. The Translational Research Working Group (TRWG) was charged with developing recommendations on how NCI could best organize and promote its investment in "translational research." The TRWG issued a final report in June 2007, which in a number of ways set the stage for the NTR program.

The TRWG defined translational research as "…research that transforms scientific discoveries arising in the lab, clinic, or population into new clinical tools or applications that reduce cancer incidence, morbidity and mortality."[8] Translational research encompasses a broad continuum of research activities (see **Exhibit 10** for the conceptual framework the TRWG used in viewing this continuum); however, the TRWG focused its deliberations on the early translation phase. The Working Group identified three major challenges inherent in this phase: "identifying the most promising discoveries to move into development, accelerating the advancement of these discoveries through the highly complex developmental process as efficiently and effectively as possible, and ensuring that there is a smooth and timely transition from early stage research into later stage human trials, product commercialization and community dissemination." To address these challenges, the TRWG formulated a series of recommendations for coordination and management of translational initiatives.

Exhibit 10. Translational Continuum

BASIC SCIENCE DISCOVERY	EARLY TRANSLATION	LATE TRANSLATION	DISSEMINATION	ADOPTION
• Promising molecule or gene target • Candidate protein biomarker • Basic epidemiologic finding	• Partnerships and collaboration (academia, government, industry) • Intervention development • Phase I & II trials	• Phase III trials • Regulatory approval • Production and commercialization • Phase IV trials—approval for additional uses • Payment mechanisms established to support adoption • Health services research to support dissemination and adoption	• To community health providers • To patients and public	• Adoption of advance by providers, patients, public • Payment mechanisms in place to enable adoption

Source: President's Cancer Panel. *Translating research into cancer care - delivering on the promise.* Annual report, 2004-2005. Bethesda (MD): National Cancer Institute; 2005.

TRWG Recommendations Affecting the Structure of the NTR Program. Several of these recommendations have been incorporated directly into the structure of the NTR program. These include the use of milestones in proposed project plans for translational U-series programs, advocacy of the network model as an organizational framework for these programs, emphasis on collaborations between other academic institutions and industry through the use of associate memberships, and use of cross-team or cross-center working groups as vehicles for ensuring communication across teams, coordinating transitions between developmental stages, and solving problems.

TRWG Recommendations on Evaluation Strategies for Translational Research Programs. The TRWG report is especially relevant for the NTR evaluation feasibility study because it emphasizes the importance of evaluation as a part of effective program management. The report details a series of specific recommendations concerning how translational research programs should be evaluated. The report prefaces these recommendations by recognizing that the evaluation of translational research programs poses several challenges. First, important dimensions of performance cannot be captured by quantitative measures alone; a careful blend of qualitative and quantitative measures is necessary. Second, although translational research is highly goal-oriented, results can nonetheless be unpredictable and may depend on factors beyond the control of participants. Thus, evaluations of such programs need to incorporate an emphasis on contextual factors and unanticipated outcomes and discoveries. Finally, translational research is a complex system in which many internal and external factors interact in different ways. This means that the attribution of observed outcomes to particular policies, program structures, or management decisions may be difficult.

With these challenges in mind, the Working Group offered the following guidelines for evaluation of translational research programs. First, evaluation at the program level should address both process and outcomes. Process assessment is important to ascertain that the effort is proceeding appropriately during its initial phase while creating a basis for revising a course of action if necessary. Outcome assessment is needed to confirm that the programmatic effort is achieving its goals. Second, an evaluation of a translational research program should include three types of measures. These include program

management process measures, system process measures, and system outcome measures. Examples of measures from each of these categories are shown in **Exhibit 11**.

4.2.1.3. Research Conceptual Frameworks

In reviewing the literature on conceptual and methodological frameworks for evaluation of research programs (also called research impact assessment), the Madrillon evaluation team investigated two questions. First, how have program evaluators approached the assessment of impact from research programs (particularly biomedical research programs), and what methods have traditionally been used to conduct past evaluations? Second, what conceptual frameworks are used to guide these assessments? The evaluation team had completed an earlier review on this topic under a separate contract,[9] and therefore expanded upon that effort for this review.

Exhibit 11. TRWG Recommended Categories of Measures

Program Management Process Measures

- **Were milestones achieved on time?**
- **What obstacles were encountered in implementing project activities and how were these addressed?**

System Process Measures

- **What new structures, processes and/or behaviors were implemented, and were they effective?**
- **Is the system becoming more coordinated, more efficient, and more productive?**

System Outcome Measures

- **Is there an increase in the number of new cancer treatments, diagnostic methods, or other products that have advanced to early human testing (Stage I or II) or middle- or late-stage trials?**

Several source documents provided useful starting points, including a seminal early (1993) book by Bozeman and Melkers[10] entitled, *Evaluating R&D Impacts: Methods and Practices,* which collected a series of papers reviewing the use of various research impact assessment approaches and methods through the early 1990s, a research impact assessment toolkit developed by Ruegg and Feller[11] for the National Institute of Standards and Technology in 2003, and a number of papers describing various evaluations of biomedical research center and network programs. Among the research impact assessment methods discussed in these sources were the use of peer review, historical tracing methods, case studies, surveys, bibliometric methods, and other approaches. An additional resource was a 2004 report by the Institute of Medicine[12] entitled, *NIH Extramural Center Programs: Criteria for Initiation and Evaluation*, which includes a useful chapter on the evaluation of biomedical research center programs at NIH. This chapter recommended that NIH research center programs be evaluated on a periodic basis (for example, every five years) and that programs be evaluated against their original program objectives (accountability), and suggested possible metrics.

4.2.1.4. A Brief History of Research Impact Assessment

Georghiou and Roessner[13] traced the history of research impact assessment in the United States back to early economic studies in the 1960s and 1970s. These studies estimated the rate of economic returns from investments in research and development and explored the relative costs and benefits of supporting basic versus applied research. However, few studies at that time examined the social (noneconomic) benefits resulting from changes in technology. By the late 1970s and early 1980s, a second wave of evaluations began to explore a broader range of evaluation approaches, especially bibliometrics. During the 1980s, NIH in particular played a major role in applying bibliometric tools and methods[14] in assessing the impact of biomedical research programs. There was also increased interest in identifying and measuring noneconomic benefits and outcomes from research programs.[15] The dominant methodological approaches used during this period included expert panels, case studies, bibliometrics, and surveys. In the early 1980s, the journal *Research Evaluation* began publication as a focal point for research impact assessment studies, and by the 1990s, a community of evaluators with interest in research impact

assessment had begun to coalesce, marking its presence with a special journal issue of *Evaluation Review* devoted to the state of the art in research impact assessment.

4.2.1.5. The Research Payback Framework

While a small community of research impact assessment practitioners was slowly forming, much of the actual work during this period was extremely applied in nature. There was a strong focus on methodology and on the *outputs* from research and development programs, such as counts of publications and presentations, and the number of patents produced. In part, this emphasis on outputs rather than outcomes may have occurred because outputs were easy to count and because they occurred earlier in time than program outcomes. The development of conceptual frameworks that could incorporate broader categories of social and economic outcomes was largely minimal in the United States during this period, with the exception of an important paper by Altschuld and Zheng,[16] which examined several perspectives on the application of organizational effectiveness in research impact assessment.

In Europe, on the other hand, thought about conceptual frameworks was taking shape. In the early 1990s, researchers at the Health Economics Research Group at Brunel University in England began to construct a conceptual framework as part of work they were conducting in a series of evaluations of health services research projects funded by the British National Health Service. The Research Payback Framework (RPF) was first described in a 1996 publication.[17] This framework was significant because it explicitly identified a multidimensional categorization of noneconomic and economic benefits arising from research activities, and provided a case-study-based methodology for assessing research impact at several levels of aggregation (individual research projects, research centers, research portfolios, and entire funding agencies). The RPF has been adapted and expanded over the years to permit evaluation of basic and clinical biomedical research, and, more recently, social science research. The RPF has been used successfully by a variety of agencies and organizations, including the United Kingdom (UK) Department of Health, the Alberta Heritage Foundation for Medical Research (Canada), the Arthritis Research Campaign (UK), the ZonMW (the Netherlands), the Health Research Board of Ireland, the UK Economic and Social Research Council, the Health and Health Services Research Fund (Hong Kong), Australian Primary Care, and the Canadian Institute of Health Research. It is currently being applied for the first time in the United States by the Madrillon Group in an evaluation of an NIH research program.

The RPF is organized around an input-process-output-outcome model with two components. The first component is a categorization of five types of economic and (largely) noneconomic paybacks that arise from research activity over time. The five categories include knowledge production, benefits to research, political and administrative benefits, health-sector benefits, and broader economic and social benefits. (See **Exhibit 12**, *Categories of Research Payback*.) The first two categories (Knowledge Production and Research Targeting and Capacity-Building) are immediate outputs from a research program. They are also considered to be academic impacts, in that their major benefit is obtained by the academic institution at which the research is occurring. The three remaining categories (Political and Administrative Benefits, Health-Sector Benefits, and Broader Economic and Social Benefits) are considered true outcomes from the research, and are sometimes called wider impacts.

The second component is a logic model (see **Exhibit 13**) consisting of nine steps (seven stages and two intervening interfaces). It is important to understand that while the model may appear linear, there are in fact multiple feedback loops that circulate among the stages. The RPF logic model captures the flow of a research project (or program) from the initial identification of a research question or problem (Stage 0); project specification and development (Interface A); inputs to the research (Stage 1); research processes (Stage 2); primary outputs from the research, which include both the knowledge production and research targeting and capacity-building payback categories (Stage 3); dissemination beyond the scientific community (Interface B); secondary outputs, including the political and administrative benefits payback category (Stage 4); adoption by practitioners and the public (Stage 5); and final outcomes, which include health-sector benefit and broader economic and social payback categories (Stage 6). As this description illustrates, the various payback categories are incorporated into the later stages of the logic model. The main role played by the RPF logic model is as an organizing schema for case studies of the research projects, centers, or program that is the focus of the evaluation.

Exhibit 12. Categories of Research Payback

Knowledge Production:

- **Publications and presentations**

Research Targeting and Capacity-Building:

- **Career development and training**
- **New researcher collaborations**
- **Research tools, methods, and models created by projects**
- **Spin-off research grants**
- **Creation of research infrastructure (new facilities, labs, etc.)**
- **Effects on host institution**

Political and Administrative Benefits:

- **Improved information base on which to make political and/or clinical decisions**
- **Incorporation of findings into clinical guidelines**
- **Inclusion in medical and/or allied health curricula or continuing education programs**

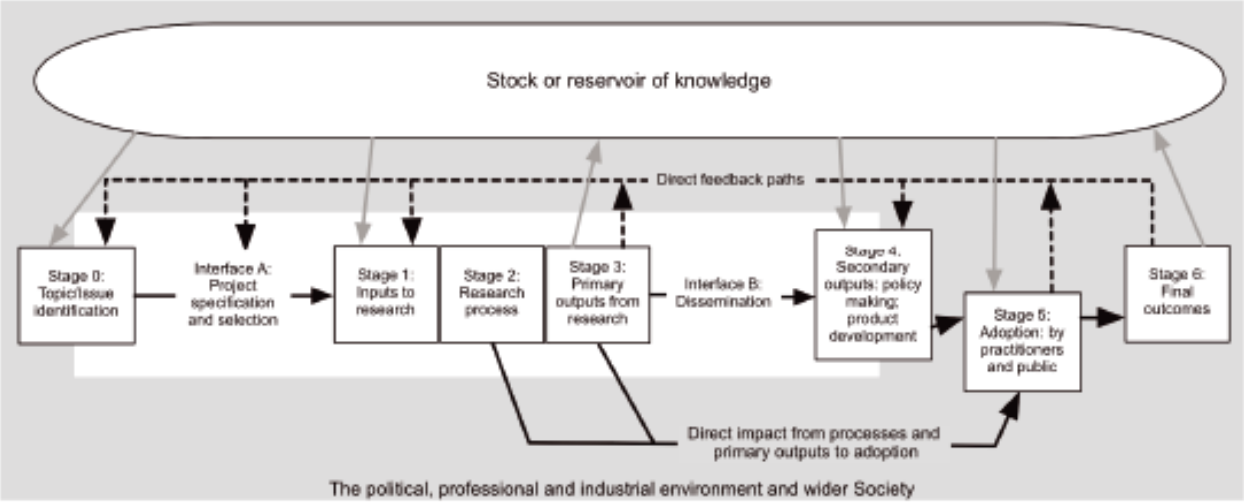
Health-Sector Benefits:

- **Improvements in health and well-being**
- **Changes to service delivery system**
- **Increased effectiveness of services**

Broader Economic and Social Benefits:

- **Income from patents and other intellectual property**
- **Cost savings to society**
- **Social and cultural benefits**

Exhibit 13. Research Payback Framework Logic Model



The RPF usually entails preparation of multiple case studies of individual research projects or centers, with the logic model serving as an organizational template for the case studies. The case studies are compiled from document reviews and interviews with one or more researcher from each project. In some cases, additional interviews have been conducted with individuals identified as potential "users" of the findings or products of the research projects. A typical RPF evaluation includes multiple case studies, with individual cases selected on a purposive sampling basis (i.e., selecting specific types of projects). As a means of comparing projects or centers within a sample, some type of scoring system is applied to the data for each outcome domain. This usually involves members of the evaluation team meeting as a group to construct ratings for each of the cases.

While the Research Payback Framework is not the only conceptual framework that has emerged during the past ten years, it offers several strong advantages over its potential competitors. It addresses outputs and outcomes that are clearly of interest to policy makers and program funding officials. It provides a well-organized approach to exploring how a project produces these outputs and outcomes through its internal logic model. It is sufficiently flexible to permit adaptation to reflect the specific structural, process, and contextual variables encountered in various programs. It has been successfully applied in evaluations of biomedical research projects and programs (both health services research and basic/clinical research) and in health technology assessments.[18] It has also been favorably compared with other frameworks[19] on a range of evaluative criteria (i.e., objectives, level of aggregation, outcome measures, timing of the evaluation, and methodology).

4.2.2. Review of Prior NIH Evaluations of Research Center/Network Programs

The Madrillon evaluation team searched its internal database of 61 prior NIH evaluations of research center/network programs to locate prior evaluations that were relevant to NIH biotechnology development programs. The four evaluations ultimately selected for this review were all commissioned by NCI between 2007 and 2009. The programs evaluated included the Small Animals Imaging Resources program, the In Vivo Cellular and Molecular Imaging Centers program, the National Technology Centers for Networks and Pathways (TCNP) program, and the Clinical Proteomic Technologies for Cancer (CPTC) initiative; relevant characteristics of these programs and evaluations are shown in **Exhibit 14**.

4.2.2.1. Comparison of Program Structure

Of the four reviewed programs, the Clinical Proteomic Technologies for Cancer Initiative most resembles the NTR program. The CPTC Initiative is more complex, including three distinct structural components that use different funding mechanisms (both research centers and individual investigator-initiated research grants). Of these three components, the Clinical Proteomic Technology Assessment for Cancer (CPTAC) most resembles the NTR program. The CPTAC component is structurally similar to the NTR program in three respects, including the funding of research centers that could include subcontracts with other institutions and companies, the use of cross-institutional working groups to identify and resolve specific technical problems, and the involvement of outside partners, including NIST, the American Association for Clinical Chemistry (AACC), the American Association for Cancer Research (AACR), and several biotechnology companies that were added as the program progressed.

Exhibit 14. Relevant Program and Evaluation Characteristics for Four NCI Programs

CHARACTERISTIC	SMALL ANIMALS IMAGING RESOURCES PROGRAM	IN VIVO CELLULAR AND MOLECUALR IMAGING CENTERS PROGRAM	NATIONAL TECHNOLOGY CENTERS FOR NETWORKS AND PATHWAYS PROGRAM	CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER INITIATIVE
Year first funded	1998	1999	2004	2006
Program structure	15 institutions funded	8 P50 centers and 16 planning grants	5 centers funded in two rounds; "Hub and Spoke" model	Three components: CPTAC—5 centers funded to develop a program network APPCS-grants to individual scientists for related projects - "hub and spoke" model PRRC—Cross-institutional system for producing standardized antigens and antibodies
Funding mechanisms	R24 (Rounds 1-3) U24 cooperative agreement (Round 4)	P50 center grants P20 planning grants	U54 cooperative agreement; PA for R01 and R21 grants	CPTAC—U24 cooperative agreements APPCS—R01, R21, and R33 grants PRRC—Interagency agreement and contracts
Did external Federal agencies participate in the program?	NO	NO	NO	YES
Was an evaluation feasibility study conducted?	YES	YES	NO	YES
Program funding cycle	Second funding cycle	Second funding cycle	First funding cycle	First funding cycle
Date of evaluation	2007-2009	2007-2008	2007	2009
Evaluation design	Cross-sectional process-outcome	Cross-sectional process-outcome	Midcourse review process	Cross-sectional process-outcome
Evaluation design highlights	• Examination of institutional environment to determine whether other types of molecular imaging programs were based there • Creation of an infrastructure equipment inventory to track types of equipment purchased or constructed	• Detailed case studies conducted on three focal centers • Embedded case studies conducted on four notable discoveries identified by Principal Investigators • Social network analysis to assess collaboration patterns	• Primarily a process evaluation to support expert panel's deliberations • Importance of identifying types and nature of collaborations taking place in program	• Role and functioning of Steering Committee (Program Coordinating Committee) • Role and functioning of CPTAC cross-center Working Groups

4.2.2.2. Timing of the Evaluation within the Program Life Cycle

Three of the four evaluations reviewed utilized evaluation feasibility studies to identify evaluation questions and develop an evaluation design; in each case, the same external contractor that conducted the feasibility study also performed the evaluation. In all four cases, the program evaluation was the first evaluation conducted on the program. In two of the cases (CPTC initiative and the TCNP program) the evaluation was conducted within the first five years of the program's launch; in the remaining two cases the evaluation occurred within ten years of program startup. The timing of an evaluation is an important consideration since it affects the likelihood that intermediate and long-range outcomes may have occurred. For the two evaluations occurring earlier in the program life cycle, the evaluations focused on process issues and included some consideration of program outputs and short-term outcomes. A major goal for these evaluations was program improvement. These first two evaluations are most similar in program life cycle stage to the NTR program, which is currently almost midway through its initial funding cycle. The third and fourth evaluations (ICMIC and SAIR) occurred eight years after the first Request for Applications was released, and also examined process issues, outputs, and short-term outcomes (SAIR also included some intermediate outcomes).

4.2.2.3. Evaluation Design Issues

Three of the four reviewed evaluations used a cross-sectional process-outcome evaluation design, while the fourth evaluation was a midcourse review conducted by an expert panel. Two of the four studies (ICMIC and SAIR) made limited use of comparison strategies, while the evaluations of CPTC and TCNP did not. In several structural elements, the CPTC case is arguably the most relevant case for the NTR program, given its mission to form a network from five research centers, its use of cross-center working groups analogous to the NTR Research Support Cores, and its limited use of a "hub-and-spoke" model of related investigator-initiated research projects.

4.2.2.4. Conceptual Issues

The prior NIH evaluations raise several conceptual and measurement issues that are relevant for the NTR program. These issues include potential overlap between the NTR program and other large-scale NCI programs, and collaboration within the NTR program. Many evaluations tend to ignore the organizational context in which the program to be evaluated is situated. One aspect of this context concerns the extent to which there are other programs with somewhat similar missions operating at the same institution. Where there are other programs operating, there are opportunities for local investigators to blend funding from multiple programs to support activities that are beneficial to all of the programs. This type of synergy can be highly beneficial in that it allows investigators to leverage resources and create cores or undertake activities that a single source of program funds would not adequately underwrite. From an evaluation perspective, however, it is important to understand when and to what extent this is occurring since it affects the degree to which some program outputs or outcomes might be attributed to the target program. Both the ICMIC and the SAIR program evaluations included consideration of this potential overlap among their evaluation questions; it would be a relevant consideration in the case of the NTR program.

A second conceptual issue that also touches upon measurement issues is collaboration. Each of the four prior evaluations addressed collaboration within the evaluated programs; however, it is clear that collaboration is an activity with several dimensions, each of which may need to be investigated. For example, it is not sufficient to simply count the number of collaborations that arise from a program's activities. It is also important to understand how these collaborations are structured, which types of individuals are collaborating, how productive these collaborations are, and what costs or barriers may exist to forming collaborations and how these are addressed by the program.

4.3. Findings from Interviews with Major Program Stakeholders

The following subsections present the findings from interviews with the four NTR PIs and the five industrial partners.

4.3.1. Findings from Interviews with Principal Investigators

The PI interviews addressed the following topics: project implementation, noteworthy aspects of the NTR program, the role of the Research Support Cores, the value of the industrial partnerships, the most important issues and questions to examine in an evaluation of the NTR program, and whether a comparison group is feasible for evaluation of the NTR program.

4.3.1.1. Project Implementation

All four PIs reported that they were either on schedule or ahead of schedule in meeting their project milestones. When asked to identify factors that have either facilitated or hindered project implementation, the PIs offered a number of ideas. Factors that facilitated implementation included the level of multidisciplinary collaboration within projects, the surrounding research environment at the university (e.g., the presence of other research centers and initiatives that could be used to leverage resources), having all of the members of the project team located under the same organizational unit (versus having individuals spread out across multiple departments), and the location of the program within the university hierarchy. Factors that posed obstacles or otherwise hindered implementation included the newness of the translational emphasis (learning curve), distance from other members of the project team (geographic dispersion), issues with Institutional Review Boards (IRBs), the complexity of the Investigational New Drug (IND) application process, the amount of validation work that had to be performed, "unexpected opportunities to refine the technology" (i.e., walking back from a wrong turn), patient recruitment, physician recruitment, and the amount of work required to pursue networking.

4.3.1.2. Noteworthy and Innovative Aspects of the NTR Program

Two of the four PIs had not participated in a research network program prior to participating in the NTR program. One of the PIs had participated in the initial NTROI program, and the other had been part of an ICMIC Center. Both of the latter agreed that there was a greater emphasis on the activities of the Research Support Cores than in previous network initiatives with which they were familiar. Other aspects of the NTR program model that PIs mentioned included the strong emphasis on valuing high-risk translational research by NIH rather than just innovation, the network they saw emerging from the four research centers and Research Support Cores, and the engagement and participation by representatives from FDA and CMS.

4.3.1.3. The Role and Value of the Research Support Cores

The respondents believed that the Research Support Cores are valuable and are working in the way that the Steering Committee had originally intended when they were established. The cores play several important roles for the four centers. They provide opportunities for an exchange of information, engage in high-level problem-solving, address regulatory hurdles, develop tools and procedures that can be used to move project work forward, and perform some of the "grunt" work that is tedious but necessary to enable everyone to move ahead. One PI noted that the Research Support Cores are the experts who have experience in other programs and provide guidance to the PIs. Another respondent noted that the cores would be more useful to a given project at some times than at others—different centers are at different stages in their projects and need different types of assistance.

There were few suggestions for how operation of the Research Support Cores could be improved. Most of the centers have designated individuals who sit in on the monthly calls from each core and

subsequently report information back to the PI; one center PI noted that it is useful to sit in on these calls as a PI because in a few cases the people participating have identified ideas for which they lack the authority to commit their project. Another respondent suggested that the cores need more direction from NIH and the Steering Committee. One PI suggested that NCI should provide each Research Support Core with its own budget. Another PI stated that it would be particularly helpful if the various Research Support Cores could meet at each of the four research centers at some point during the year; these site visits would allow the PIs the opportunity to make maximum use of the expertise in each core.

4.3.1.4. The Role and Value of the Industrial Partners

The four PIs reported that the experience of working with industrial partners as members of their project teams has been valuable. There was clear agreement on several benefits from the industrial partnerships; including increased understanding of how industry thinks and what companies want, the opportunity to share expertise and engage with leaders in their fields; the benefit of equipment, funding, and knowledge; and the opportunity to benefit from their partners' market positions and reputations. One PI noted that industrial partners are especially useful for lowering the barriers to clinical adoption of technology.

There seemed to be few perceived disadvantages or problems associated with these partnerships. One comment mentioned by two respondents was that some industrial partners can be very reticent and very proprietary about their work; in one case, a partnership has become inactive for this reason. There was strong agreement about the importance of addressing intellectual property issues before engaging in an industrial partnership.

4.3.1.5. Issues and Questions to Examine in an Evaluation of the NTR Program

The first question mentioned by each of the four PIs was whether each of the four projects has succeeded in moving its primary project into early-stage (Phase I and II) clinical trials. Beyond this basic question, several other issues were mentioned, including: (1) understanding how the Research Support Cores have contributed to success of the program; (2) what internal knowledge has been gained by each research enter from performing this project, and how this knowledge is being shared among other researchers at the participating institutions and in the wider research community; (3) how many students have earned graduate degrees and how many postdoctoral fellows have received training through each project; (4) the number and nature of new discoveries from project activities; (5) new research grants generated by the projects' activities; (6) the number of publications produced (both the actual number and the dollars of project funding per publication); (7) the number of patents filed and approved; and (8) the number of new tools, methods, and products produced by the projects.

The four PIs acknowledged that there is a need to develop both qualitative and quantitative measures for this study. While much, if not most, of the study may need to be qualitative in nature, there may be some ways to quantify some aspects of the project experience—developing estimates of how much time is saved by performing a process or procedure in a particular way, or even how many dollars were saved.

A final point that two PIs raised was that it would be useful if CIP, FDA, and CMS could jointly sponsor the evaluation of the NTR program.

The Translational Pipeline as a Monitoring Tool. One question posed in the PI interviews concerned the potential use of the translational research pipeline as a potential process measure of progress toward milestones. Only two PIs had any comments about this idea; both agreed that it can be a useful tool. One respondent noted that if the pipeline were going to be used for monitoring, it would be advisable to construct a separate pipeline for each of the specific devices and probes being tested. Moreover, it is

sometimes the case that progress is not as linear as the pipeline suggests—there can be recycling back to earlier stages in the pipeline and this recycling would not be a reversal in progress, although it might appear to be on a linear diagram.

4.3.1.6. Feasibility of a Comparison Group in an NTR Evaluation

The use of a comparison group in an evaluation design depends upon the nature of the evaluation question asked. If the question asks whether a particular program model is more effective than another model, then a comparison of the targeted program model with a similar model that differs in some important structural element would be desirable. If the question is whether the target program is better than no program at all (sometimes called the counterfactual problem), a true comparison condition is often impossible to locate. In order to determine whether the first comparative approach is feasible, it was necessary to determine whether there exists a feasible comparison group for the NTR program.

In general, the PIs are skeptical about the use of a comparison group in the form of another program. Two respondents ruled out use of a comparison group altogether. The other two emphasized that it would be very difficult to locate a comparable program, since any candidate program would need to be matched on type of technology platform, early stage of translational research, and program structure (network versus other). Comparisons with other programs might be useful for certain metrics such as research dollars per publication or research dollars per patent produced; however, it is not clear that these measures are of central importance to the project.

The four PIs agreed that it would be difficult to measure whether the absence of the NTR program would have resulted in a different set of outcomes for the projects. The main strategy mentioned by the respondents involves subjective comparisons with the past; for example, if the data submission process to the FDA occurred more quickly (and therefore at lower cost) than usual, this might be evidence that the program is helping to accelerate the process. This would have to be examined in terms of the views of people knowledgeable in the field; for example, NCI program staff.

4.3.2. Findings from Interviews with Industrial Partners

The interviews with the five industrial partners addressed several topics, including benefits to the companies from participating in the NTR program, the NTR program as a program model for engaging academia and industry, the experience of the imaging industry in Europe versus the United States, the most important issues and questions an evaluation of the NTR program should address, and the feasibility of using a comparison group.

4.3.2.1. Benefits to Industrial Partners from Participating in NTR

The respondents identified several perceived benefits from participating in the NTR program. Several respondents stressed the value of learning about a new and rapidly emerging technological field and the opportunity to build new relationships, particularly with NCI and the FDA. Respondents also noted that the program has provided an opportunity to explore whether the proposed adaptation of their imaging systems has potential as a commercial product. Universities are seen as potentially useful partners for conducting the verification and validation of imaging systems.

At the same time, however, universities are seen as having some potential liabilities as partners in this process. The industrial partner respondents were nearly unanimous in stating that academic researchers do not understand the business world and what businessmen need and want. In particular, academic researchers do not understand the product development process, which can lead to lost time and money for industry partners.

4.3.2.2. The NTR Program as a Program Model for Engaging Academia and Industry

The NTR program is seen by the respondents as a good way to foster academic-industry partnerships, and they noted that they are gratified that NCI recognized the importance of involving industry as a partner with academic researchers in the process of technology development. The respondents also noted that they appreciate the use of well-defined project milestones as a means of monitoring progress on primary projects. This use of milestones is a process with which industry is familiar and accustomed to using. One respondent noted that this use of milestones will help his company determine whether it wants to commercialize the final product.

The industrial partners were very clear about what they are seeking from the NTR program. One respondent expressed it this way: "What industry wants is the clinical and technical evidence it needs to build a business case to support the decision to commercialize a product." The respondents noted that there are several aspects of working with academic researchers that they find especially frustrating. One aspect of the academic approach mentioned by three separate respondents is the researchers' tendency to approach everything as an academic problem, rather than taking advantage of what has already been learned by industry about how to handle specific technical issues. Other respondents emphasized that academic researchers need to reduce their emphasis on publications and strive to remain focused and realistic. One example offered is the choice of biomarkers: Rather than focusing on a very small molecule which is too small to carry the dye, why not adapt a molecule that has already received FDA approval and make minor modifications to that?

4.3.2.3. The Most Important Issues and Questions for an NTR Program Evaluation

There was unanimous agreement among the industrial partners that the central question an evaluation of the NTR program should address is whether the projects have advanced to early-stage clinical trials within the five-year funding period. Other issues and questions that were raised included: (1) Have the interactions among the four research centers and Research Support Cores added value to the overall program? (2) Has the participation of the FDA and CMS added value to the NTR program? (3) What are the academic researchers learning about translational research from this project? Is there an accumulation of knowledge about procedures and processes that these research investigators are sharing within their universities and within the field more broadly that could further the development of translational research in the future, or are these lessons learned being held within the original research teams?

4.3.2.4. The Feasibility of Using a Comparison Group

As had been the case for the PIs, the industrial partners reported being generally pessimistic about the feasibility of identifying a comparison program for the NTR program, and for many of the same reasons. Three respondents stated flatly that they do not believe there is an appropriate program to compare the NTR program against; the remaining two respondents suggested either other technology development programs at NCI or two European programs (MAMMOTH—the Mammary Carcinoma Molecular Imaging for Diagnostics and Therapeutics, and MUSIS—the Intra-operative Multi-spectral Imaging Systems for Radical Tumor Resection program, both funded by the Center for Translational Molecular Medicine in the Netherlands).

4.4. Findings from Observations of Face-to-Face Meeting

The Madrillon evaluation team attended the third NTR Face-to-Face Meeting on February 17-18, 2011, in Bethesda, Maryland. The meeting included detailed presentations on current activities by each of the four PIs on the progress each was making on primary and task-specific projects, presentations by representatives from each of the four Research Support Cores, a panel and discussion with representatives from FDA and CMS, and working meetings of each of the four Research Support Cores. Based on the evaluation team's observations, the following themes and issues were evident:

- According to some observers, there has been a positive qualitative shift in the amount and depth of collaboration that is occurring at the Face-to-Face Meetings; this was particularly noticeable between the second meeting and the third meeting.
- The four research center teams are either on schedule or ahead of schedule on their primary and task-specific projects. As a result of the activities the four teams are conducting, they are making numerous unanticipated scientific discoveries, several of which were described in the PI presentations. Some teams are encountering requests from practicing clinicians to permit use of the imaging platforms with their patients as part of the clinical diagnosis/treatment process. Acceding to these requests requires the PIs to obtain permission and clearances from their IRBs to permit this use, and preparing the necessary documentation for these requests can be time-consuming.
- The Research Support Cores are generating considerable interaction and engagement on the part of both academic researchers and the industrial partners.
- Observation of the working meetings of the Research Support Cores indicated that there is overlap in the topics and issues that some of the cores are pursuing. One question that surfaced during the meeting of one core was how this overlap can be managed in order to prevent two cores from addressing the same problems. One mechanism suggested for handling such overlaps was to seek guidance from the Steering Committee.
- Closely related to this observation was the special case of the SCI-PORT data system. Examining how the issues associated with the development, implementation, and utilization of SCI-PORT by the four research center teams could provide a useful embedded case illustrating how the Research Support Cores collaborate to address common problems and issues.
- There is interest in how NCI and the Cancer Imaging Program will disseminate findings from the NTR program. It was noted that FDA is interested in the possibility of using the NTR program as a programmatic model for some of its projects, and it was mentioned that there will be an international meeting in England in July on stimulating research funding and translational research on imaging technologies, with invited representatives from the United States, Canada, and the United Kingdom.
- The regulatory agency panel discussion underscored the importance of academic researchers working with FDA and CMS at as early a stage in their project development process as possible. One message that was repeated during the course of this program segment was that researchers should not wait until they have completed their data collection to meet with FDA representatives. It is far better to meet with representatives before beginning data collection, because the representatives may be able to suggest additional types of data that should be collected, and it is easier and less costly to add measures at the beginning of a trial than to learn that additional data are needed at the conclusion of the trial.

5. Conclusions from the Feasibility Study and Implications for Design of the NTR Process-Outcome Evaluation Study

This section of the report presents the final conclusions from the feasibility study and discusses their implications for the design of a process-outcome evaluation for the NTR program.

5.1. An Evaluation of the NTR Program Is Warranted and Feasible

An evaluation of the NTR program is both warranted and feasible for the following reasons:

- Although the NTR program is the second generation of the Network for Translational Research initiative, the program has not been evaluated in the past.
- There is an urgent need to learn more about programmatic models for conducting translational technology development research.
- The NTR program model is stimulating interest at other Federal agencies in the United States and in Europe.

These points are discussed in more detail below.

The NTR program has not been evaluated in the past. The Network for Translational Research initiative consists of two programs. The first program, Network for Translational Research-Optical Imaging, was funded in 2003 for a five-year cycle. The program was not formally evaluated, although a number of lessons learned from its operation were incorporated into the current program, the Network for Translational Research-Optical Imaging in Multimodal Platforms. The current program is at the midpoint of its five-year cycle, which began in 2008 and will end in 2013. The Institute of Medicine in its 2004 report on NIH extramural research centers recommended that such programs should receive a formal external evaluation on a regular basis—at least every five to seven years. The technological focus of the program shifted from development of optical imaging as a single-modality platform to optical imaging in conjunction with traditional imaging technologies (multimodal platforms). A number of important structural changes were built into the new program model, based in part on lessons learned from the first-generation program. It is important to determine whether these changes have contributed to the program's accomplishments.

There is an urgent need to learn more about programmatic models for conducting translational technology development research. Efforts to locate research studies that examine program models for conducting translational technology development research did not identify any published studies. Translational research is a relatively new and highly complex undertaking. Understanding how research programs should be organized in order to conduct this research is important, from both program management and research investment perspectives. There is currently a widespread assumption that the use of a network program structure is an effective and desirable approach for organizing these programs. There is not, however, any published research that illustrates or demonstrates this, and an evaluation of the NTR program would provide an opportunity to provide some empirical support for this assumption.

The NTR program model is stimulating interest at other Federal agencies in the United States and in Europe. The NTR program has successfully engaged representatives from several Federal agencies, including FDA and CMS, as participants in annual meetings. There has been discussion about the NTR program model among individuals at FDA who are considering it as a possible program model for some of their research initiatives. This was stated at the most recent Face-to-Face NTR Program Meeting in

February. At that time, another individual noted that the NTR program has stimulated interest in the UK, where four major research funding agencies are sponsoring a workshop for 30 researchers and policy makers involved in the imaging technology development field in July 2011. It is important to provide a more in-depth description of the NTR program model, the operation of its structural components, and whether and how it succeeds in accomplishing its stated goal of "…accelerating the translation of *in vivo* multimodal imaging and/or spectroscopic platforms from the laboratory to the pre-clinical level to the clinical level."

An evaluation of the NTR program is also feasible for the following reasons.

- Based on its level of implementation, the NTR program has reached a level of program maturity to make an evaluation possible.
- Existing data and data sources would provide appropriate background data to support an evaluation.

Based on its level of implementation, the NTR program has reached a level of program maturity to make an evaluation possible. Programs progress through a distinct life cycle, from inception to early implementation to fully functioning maturity where all structural components are operating as intended. Delayed or incomplete program implementation can prevent the program from accomplishing its goals and objectives. The findings from the evaluation feasibility study indicate that the NTR program is fully implemented. Each of the four research centers is operating and all are making satisfactory progress on their primary and task-specific projects. The centers have established a group of Research Support Cores (currently four in number), which are meeting regularly, initiating and completing activities, and reporting to the PIs and the Steering Committee on a regular basis. The NTR program has held three annual project meetings, most recently in February 2011. Based upon a review of various program documents and the NIH IMPAC II database, the program has reached a level of program maturity sufficient for an evaluation.

Existing data and data sources would provide appropriate background data to support an evaluation. Documentation on the program is much better than that available for many NIH research programs. Annual progress reports are submitted by each PI and provide far more detail on project accomplishments and milestones than do most annual progress reports. For the past two years, the Cancer Imaging Program has assembled these reports and additional program information in a year-end report, which has proven very helpful as a background source. Data in the NIH IMPAC II QVR database on grant applications, summary statements, fiscal and administrative issues, and publications are current and up to date. While additional information would be required for an evaluation, it proved to be a straight-forward task to interview the four PIs by telephone, although it proved somewhat more challenging to reach some of the industrial partners.

5.2. An Evaluation of the NTR Program Should Include Both Process and Outcome Assessments

Based upon the recommendations of the NCI Translational Research Working Group and the types of issues and questions raised by the Cancer Imaging Program, the NTR PIs, and their industrial partners, it is clear that any evaluation of the NTR program should take the form of a process-outcome evaluation. While a process evaluation often focuses on the degree of program implementation encountered in the evaluated program, it also can include an emphasis on how the structural components of the program interact as well as their contributions to program outcomes. The evaluation feasibility study findings clearly indicate that the structural components of the NTR Program—the four research centers, the Research Support Cores, the industrial partners and representatives from Federal agencies, the Steering Committee, and the External Advisory Board—have been fully implemented and are perceived by the

major program participants to be working well. Thus the process emphasis in this evaluation should focus on how these components contribute to program outcomes, completion of each research team's primary projects, and the overall goal of accelerating the translational research process.

There are two immediate outcomes anticipated from the NTR program: the successful completion of each research team's primary and task-specific projects within the five-year funding period, and the overall acceleration of the translational research process. From the industrial partners' perspective, an intermediate outcome would be whether the information provided by each research team as a result of completing the team's primary and task-specific projects is sufficient to enable the respective partners to construct a business case supporting further commercial development of the multimodal imaging platform. Some aspects of a business case may depend upon factors outside the scope of the NTR program (for example, what additional partnering arrangements companies might need to make in order to take the technology to a commercial level), but it should be possible to determine whether partnering firms believe that the technical and clinical data they can receive from a research team are sufficiently complete and useful for application in a business case. This may require some additional time beyond the conclusion of the five-year NTR funding period.

The interview data show that a number of outputs (academic benefits) are arising from the activities of the four research teams. These include publications and presentations; development of new tools, methods, models, and processes; and considerable internal learning about how to conduct translational technology development research. This learning process includes both tacit and codified knowledge. The former includes the various lessons learned about how to complete tasks such as obtaining IRB approvals and completing IND applications, and other types of knowledge that are usually not written down but exist as an internal stock of knowledge that can serve as a useful resource for future activities and for others at the same academic institution. The codified knowledge includes internal policies and procedures, publications, and other knowledge that has been written down in some form.

5.3. The Most Appropriate Evaluation Design Is a Cross-Sectional Design

There are four broad categories of evaluation design, which include:

- **Experimental designs**, where subjects can be randomly assigned to a program or intervention versus a control group that does not receive the program/intervention (or receives a placebo)
- **Quasi-experimental designs**, where subjects cannot be randomly assigned to a program or intervention but it is possible to construct a comparison condition or identify a comparator program
- **Longitudinal designs,** in which changes in subjects or in a program are observed at two or more points over some period of time (for example, time-series)
- **Cross-sectional designs**, which produce a single "snapshot" of a program and its outcomes over a period of time.

In considering the type of design most appropriate for an evaluation of the NTR program, an experimental design can clearly be ruled out; it is not possible to randomly assign research teams to the NTR program model, given the peer-review process for selecting the funded projects. Similarly, a longitudinal design can also be ruled out. The central question is whether the four centers have completed their projects as planned within the five-year funding period—an analogy would be a baseball game, where the matter of interest is the score at the conclusion of the game, not at the half-time. This leaves two types of designs as possibilities—quasi-experimental and cross-sectional.

Quasi-experimental designs can address different evaluation questions than can cross-sectional designs. A quasi-experimental design can pose the question: Is the network program model implemented in the NTR program more effective than program model B in achieving the program's goals? To answer that question, it is necessary to identify a comparator program that is reasonably similar to the NTR program in characteristics such as a focus on early-stage translational technology development (specifically, imaging); funding level; multidisciplinary, multi-institutional teams; etc. In the Madrillon evaluation team's interviews with the NTR PIs and industrial partners, there was considerable skepticism concerning the feasibility of identifying another program that is similar enough except for program structure to provide a good comparison. Two of the four PIs and three of the five industrial partners said they do not believe that an appropriate comparison program can be identified; the remaining respondents suggested other cancer imaging programs such as ICMIC, but emphasized that the technological challenges of developing optical imaging multimodal platforms are highly specific to the field and make the NTR program unique in that regard. Another possible source of comparator programs would be institutions that unsuccessfully applied for NTR program funds; however, it is difficult to engage unfunded projects in an evaluation, and the infusion of funds provided by the NTR program might well confound any attempt at comparison.

Cross-sectional designs are often used in evaluations of research programs (for many of the reasons listed above). While the first three design categories may provide more credible evidence in some cases, it is possible to provide credible evidence using a cross-sectional design. For the NTR program, a cross-sectional design offers the best approach for evaluating the program for several reasons. First, the primary focus of the evaluation is program accountability: Did the program achieve its main goals? This is a question that can best be determined at the end of the funding cycle; thus, a single "image" of the program that includes that endpoint is exactly what is required. Second, a cross-sectional study can offer an in-depth examination of *how* a program achieved its goals. This is particularly true of case-study designs, which offer an opportunity to investigate "how" and "why" questions in detail. By careful use of "pattern-matching" analytic techniques, it is possible to present highly credible evidence triangulated from multiple sources that supports a clear and compelling narrative that policy makers find acceptable.

6. Recommendations for the Design of the NTR Program Process-Outcome Evaluation

This section presents recommendations for the design of a process-outcome evaluation of the NTR program. The recommended design for this evaluation uses a multiple-case-study approach that consists of five case studies. Four of the case studies investigate the structure, activities, outputs, and immediate, intermediate, and final outcomes for the four research center teams. The fifth case study draws upon a cross-case analysis of the four research center teams and focuses on the emergence of the larger Network in which the four projects interact with various Federal partners. As a preface to the discussion of the rationale for this design, Section 6 begins with the development of a logic model of the NTR program and then poses the specific questions the evaluation will address. Following an explanation of these questions, the multiple-case-study design is presented, along with consideration of the key variables and data sources for the studies. The analysis approach is outlined, and the section concludes with a consideration of several administrative issues, including OMB clearances and a general timeline.

6.1. The NTR Program Process-Outcome Evaluation Logic Model

A logic model is a brief (single-page) visual representation of how a program is supposed to work under certain environmental conditions in order to solve one or more problems.[20] The purpose of a logic model is to provide a simplified means of characterizing the types of outcomes a program is meant to produce while showing how the program's inputs (resources), activities, and outputs lead to these outcomes. Most logic models are linear, although programs themselves are typically not. The logic model for the NTR program process-outcome evaluation is presented as **Exhibit 15** on the following page.

The basic structure of the logic model consists of inputs, activities, outputs, immediate goals, intermediate outcomes, and final outcomes. This schema is reflected in the white boxes at the top of the diagram. The NTR program is a complex program that integrates four distinct perspectives: the individual research center teams, their industrial partners, the network that is emerging from their interactions, and the NTR program. In order to capture these perspectives, the logic model depicts two distinct, interconnected levels, represented by the orange and blue boxes in the diagram. The orange boxes show the Network and program level, while the blue boxes show the research center teams and industrial partners. For the latter, two red boxes represent individual research "spoke" grants associated with the teams. While the model is read from left to right, a series of two-headed arrows show interaction and influence between the two levels over time. A brief discussion of each element within the model is provided below.

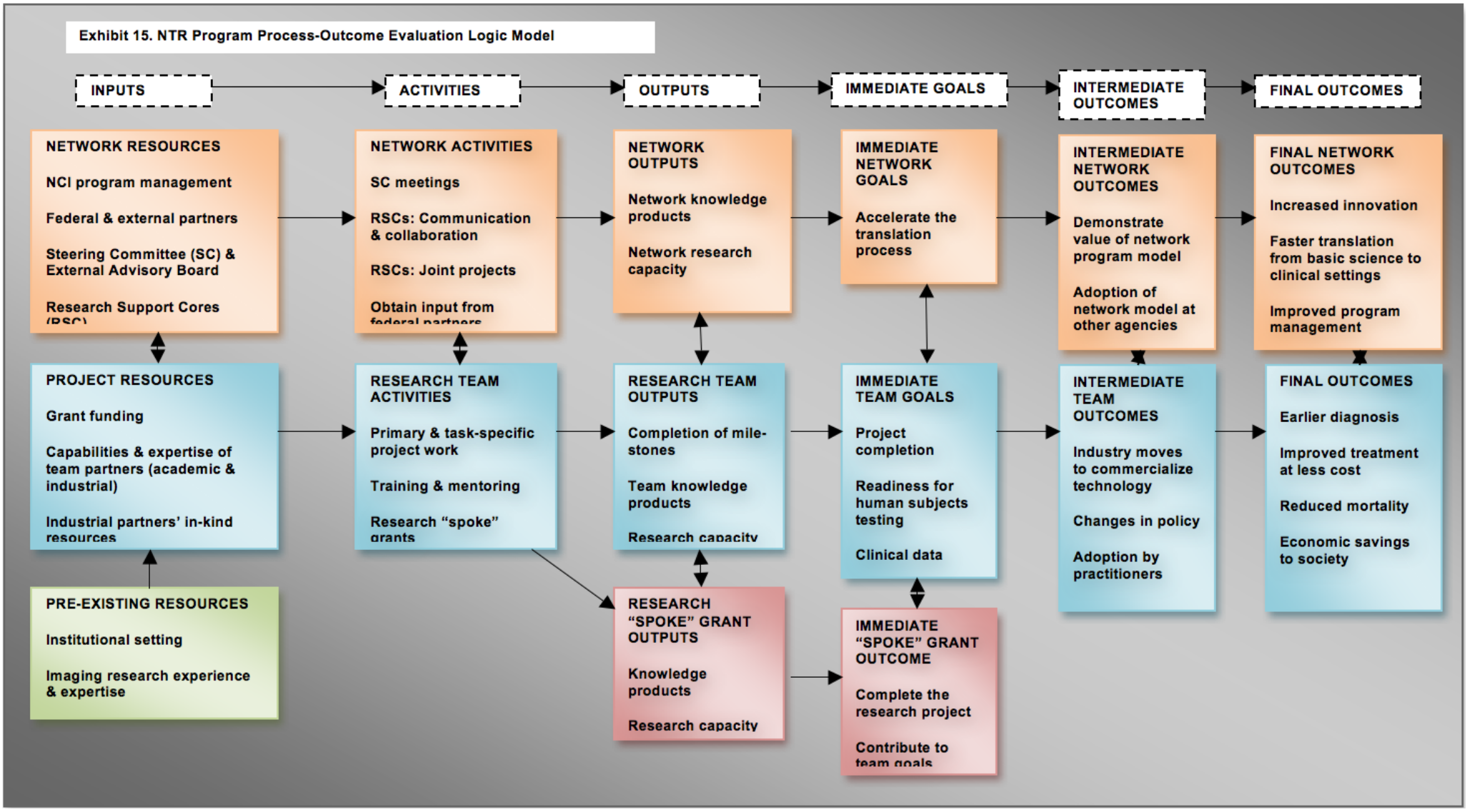
6.1.1. Inputs

Inputs represent the various resources that are available to perform the activities of the program.

6.1.1.1. Research Center Team Inputs

The research center team inputs include two categories of resources. *Pre-existing resources* are those resources that were available to each of the four awardees prior to the actual funding of the cooperative agreement award. Examples of these resources include the imaging research experience and expertise of the academic researchers, and the institutional setting in which they were operating (e.g., the presence

Exhibit 15. NTR Program Process-Outcome Evaluation Logic Model



of other types of imaging centers such as ICMIC or SAIR, or other types of programs that could provide additional resources that might be leveraged in a project application.) *Project resources*, on the other hand, are those that are brought together as a consequence of applying for the NTR grant. This includes the various academic institutional partners and industrial partners forming the proposed project team and their capabilities and expertise in various aspects of imaging research. Project resources also include various in-kind contributed resources that may be provided by these partners (especially the industrial partners). Many of the industrial partners have provided necessary resources such as fluorescent dyes or actual imaging devices as part of their contributions to the research projects. Project resources also include project funding.

An important element of these inputs is the structure that results from them. For the four research teams, the various partners in each team are connected through their involvement with the primary and/or task-specific projects. *How* these partners are connected to each other and the projects is an important question to be addressed in the evaluation, since some patterns of connections may be better suited to translational research than are others.

6.1.1.2. Network Resources

Network/program resources include overall funding for the program; the expertise, experience, and contacts of NCI Cancer Imaging Program staff scientists; the various Federal agencies that participate in the program; the External Advisory Board formed by Cancer Imaging Program staff scientists; and the Steering Committee and the Research Support Cores it formed. Some of these resources were available prior to the start of the program while others have emerged over the course of the program.

6.1.2. Activities

Activities are the specific actions that are taken using the various types of resources.

6.1.2.1. Research Team Activities

The activities of the research teams include the actual technology development work conducted on each team's primary and task-specific projects; the training and mentoring activities of graduate students, postdoctoral fellows, and junior faculty who participate in these teams; and various research "spoke" grants that are NIH-funded investigator-initiated research projects awarded either to members of a research team or to investigators external to the team who are building upon the team's project. Another set of activities here include coordination and management of the project—a not insignificant activity given that some of the research teams are widely geographically dispersed throughout the world.

6.1.2.2. Network/Program Activities

At the Network level, activities include regular meetings of the Steering Committee and the annual face-to-face project meetings, and the work of the Research Support Cores. This work includes regular communication and agenda-setting within each core, and collaboration on joint projects within and across cores. Another category of network activity involves soliciting input from and participation by other Federal agencies and international organizations with interests in this area.

6.1.3. Outputs

Outputs are the products that are generated by activities. It is at this juncture that the multidimensional categories of the Research Payback Framework enter the model. Outputs can be broken out into two subcategories: knowledge production and research targeting and capacity building. These two subcategories typically have a major influence within the local institutional site of the project and are therefore sometimes called academic benefits. However, the network structure of the program may

broaden this somewhat; for example, improvements in research capacity may benefit not only one team's host institution, but other academic institutions involved in that team as well.

6.1.3.1. Research Team Outputs

One type of output generated at the research team level is progress on the various primary and task-specific projects, as measured by the attainment of various project milestones. However, outputs also include the knowledge production and research targeting and capacity building discussed above. Knowledge production outputs at the research team level include publications and presentations developed by each team, as well as patents and licenses that are submitted and obtained as a result of work on the primary and task-specific projects. Knowledge production also includes new discoveries that are made as a result of the projects. Improvements in research targeting and capacity-building include a broad range of direct results from activities, including the numbers of students, fellows, and junior faculty mentored; the creation of new research tools, methods, instruments, and processes as a result of project work; the creation of new labs or other specialized facilities (research infrastructure); and the exchange of knowledge about how to conduct translational research (e.g., how to address various local bottlenecks, how to engage physicians as members of the team, patient recruitment approaches, etc.). Improved research targeting occurs when promising new hypotheses are identified (or previous avenues of research are closed); one way to gauge this is by examining subsequent "spin-off" grants that are generated by each project. Spin-off grants differ from the research spoke grants in that the former are based upon findings or important questions raised by the parent project, whereas the latter represent applications that are related to the original project but may have been proposed before the parent grant produced data or findings that could have stimulated the application.

Research "spoke" grants also generate knowledge production and research capacity outputs, and these may influence (or be influenced by) outputs from the primary and task-specific projects.

6.1.3.2. Network/Program Outputs

The Network also generates knowledge production and research capacity outputs, largely arising from the work of the Research Support Cores. These can include various publications and presentations, reports, manuals, and other examples of codified knowledge. They can also include new tools, products, methods, etc.

6.1.4. Immediate Goals/Outcomes

Sometimes called short-term outcomes, the immediate goals described here reflect the general goals of the NTR program.

6.1.4.1. Research Team Immediate Goals

At the level of the four research teams, the immediate goals of the projects are to complete their project work within the five-year period of the grant. This will entail developing, validating, and optimizing the selected imaging platforms chosen for the projects, and moving the technology development process to the point of readiness for human subjects testing. The original RFA makes clear that the teams are not expected to conduct the actual clinical trials (which may require additional time beyond the five-year period), but that the technology should be ready for this next phase of research development. Movement to this phase will require some collection of clinical data.

6.1.4.2. Network Immediate Goal

From the perspective of the larger Network/program, the immediate goal is to "accelerate the translational research process." The key issue here is the word "accelerate," which implies that the translational process would be accomplished more quickly in part due to the NTR program than it would have been accomplished otherwise. As noted during the discussion of findings and conclusions, there are no suitable comparison programs against which the pace of the translational research process for the NTR program can be compared, and it would be very difficult to project how quickly the translational process for these specific technologies would have been accomplished if the program had not been funded. For that reason, the assumption that will be made for this evaluation is the following: If ***all four*** of the research teams are able to complete their projects within the five-year period, this accomplishment will be taken as evidence that the translational research process has been accelerated.

6.1.5. Intermediate Outcomes

Intermediate outcomes are those that result from the immediate or short-term outcomes.

6.1.5.1. Research Team Intermediate Outcomes

One critical type of intermediate outcome for the NTR program is whether an industrial partner can obtain sufficient technical and clinical data to construct a business case for commercializing the multimodal platform developed by the project. At this stage, it isn't necessary that an industrial partner actually begin the process of commercialization, but it is necessary to determine whether the case for commercialization can be established based upon the data available at this point (which will be the fifth year of the project). This would mark the beginning of the hand-off to industry.

Other types of intermediate outcomes capture those addressed by the Research Payback Framework. One example at the research team level is whether there is evidence that project results are informing or changing policy (for example, whether the project has been able to advance to a point where reimbursement regulations can be established for the technology). A second type of intermediate outcome is evidence of uptake of the technology by clinical practitioners.

6.1.5.2. Network Intermediate Outcomes

There are two types of intermediate Network outcomes that may be observable within the five years of the program funding cycle. The first intermediate outcome is that the value of the Network program model as a means of organizing translational research initiatives is established. If it can be shown, for example, that all four teams have successfully completed their projects and that the structural components of the NTR program have contributed to this achievement, this would indicate that the model has value for future translational research initiatives. Related to this, if the program model is then picked up by other agencies, this would constitute a second type of intermediate Network/program outcome.

6.1.6. Final Outcomes

Final outcomes at the research team level would include the effects resulting from the successful use of the imaging technologies—earlier diagnosis, improved treatment and improved treatment monitoring, the capacity to begin treatment at an earlier stage in the disease process, reduced cost of treatment, and reduced morbidity and mortality, as well as extensive economic savings to society. These results are clearly many years away and unlikely to be observable in the process-outcome evaluation.

Final outcomes at the Network/program level would be increased innovation, faster translation from basic science to clinical settings, and improved program management. Similarly, these final outcomes are not likely to be observable during the process-outcome evaluation.

6.2. Proposed Evaluation Questions

The logic model provides a simplified overview of the NTR program, dividing it into two levels (the research teams with their industrial partners, and the Network/program level). The proposed evaluation questions focus on each of the four perspectives (the research teams, their industrial partners, the Network, and the program).

6.2.1. Research Center Team Evaluation Questions

The nine research team evaluation questions investigate the resources, structure, activities, outputs, and outcomes for each of the research teams. These questions are listed in **Exhibit 16.** It can be seen that the research team evaluation questions closely follow the logic model in **Exhibit 15**, especially questions TM1-7.

Questions TM8 and TM9 may be less self-evident than the earlier items; they are important because they address both codified and tacit knowledge. Codified knowledge is knowledge that is written down in publications, presentations, reports, manuals, and other documents. This is often publicly available knowledge. Tacit knowledge, on the other hand, represents the kind of information that is typically not written down. It includes practical knowledge about how to conduct various activities that are associated with translational research—for example, lessons learned about how to work with Institutional Review Boards and strategies for conducting specific types of research activities or working with particular problems or issues. This information can be valuable for other researchers to understand, since it may save them time and money in dealing with the same problems. In fact, in a successful project (or one with an interesting failure), this tacit knowledge may well be the kind of information that, more widely understood, can contribute meaningfully to accelerating translational research.

Exhibit 16. Research Team Evaluation Questions

TM1. What resources did each team have at the start of its primary and task-specific projects, and how did these resources contribute to the projects' outcomes?

TM2. How was each research team organized, and how did this network structure (i.e., network density, centrality, and cohesive subgroups) contribute to project outcomes?

TM3. How did each research team work with its research "spoke" grants?

TM4. How did the *network* components (especially the cores and the Federal partnerships) contribute to project outcomes?

TM5. Did each research team complete its projects within the five-year period?

TM6. What academic benefits (knowledge production and research targeting and capacity building) did each team produce?

TM7. What wider benefits (informing policy, adoption by clinical practitioners, improved health and health care service delivery, broader economic impacts) did each team produce?

TM8. What did each research team learn about how to conduct translational technology development research?

TM9. How are the teams sharing their tacit knowledge about translational research within their institutions and outside their institutions?

6.2.2. Industrial Partner Evaluation Questions

The three industrial partner evaluation questions listed in **Exhibit 17** represent questions and issues that may be important considerations if the Network program model developed here is replicated in the future. Question IP1 investigates the extent to which industrial partners have actually contributed tangible resources (equipment, dyes, biomarkers, etc.), which is an important issue to consider in developing future cost estimates for a program of this type. In the course of the industrial partner interviews, it became clear that there were a considerable number of in-kind contributions that the partnering firms were contributing to the NTR research teams. The economic value of these contributions needs to be assessed and considered in the total costs for the program.

Question IP2 focuses on one of the intermediate outcomes shown in the logic model—whether each team's efforts have resulted in sufficient information to enable the industrial partners to build a business case to support further commercialization of the platform technology. This issue was articulated by most of the industrial partners during their interviews, and determining the answer could be an important consideration in whether businesses would be willing to participate in a future initiative of this type. Question IP3 explores the types of changes (if any) that these partners would make to the program model if it were to be used in the future.

Exhibit 17. Industrial Partner Evaluation Questions

IP1. What is the economic value of the resources that industrial partners contributed to each of the four research teams over the course of the NTR program?

IP2. Did the industrial partners obtain the types of information they need to construct a business case for the potential commercialization of the selected platforms by the end of the five-year program?

IP3. At the conclusion of the project, how did the industrial partners view the value of their involvement in the NTR program?

a. Would they consider participating in a similar program in the future? Why or why not?

b. What changes would they make to the structure and activities of the NTR program model in a future initiative?

6.2.3. NTR Network Evaluation Questions

Exhibit 18. NTR Network Evaluation Questions

NE1. What structural network components emerged as the four research teams pursued their projects?

NE2. Did the four NTR research teams function as a larger network over the course of the NTR program? What level of cross-team collaboration took place, and on what types of issues, problems, and projects?

NE3. What knowledge production and research-capacity-building outputs were produced by the activities of the Research Support Cores? Were these products used by the teams?

NE4. How did the NTR network components contribute to the acceleration of translation of optical imaging multimodal platforms over and above what might have occurred in their absence?

Evaluation questions addressing aspects of the NTR network are listed in **Exhibit 18**. These four questions attempt to tease out the role(s) played by the various network structural components in the research activities of the four research teams. Question NE1focuses on the structure of the emerging network, examining the various components that emerged and how they interacted. Question NE2 investigates the extent to which the four research teams actually functioned as a larger network by focusing on the types of cross-team activities that occurred over the course of the program and whether they were used by the teams. Question NE3 examines the various outputs that were produced and the extent to which they were utilized by the research teams. Question NE4 provides an assessment of the extent to which the various network structural components contributed to the acceleration of translational research in this instance.

6.2.4. NTR Program Evaluation Questions

Two questions addressing overall reactions and impressions regarding the NTR program experience are listed in **Exhibit 19.** The first question addresses general lessons learned and insights from the operation of the NTR program by staff at the Cancer Imaging Program and other Federal agencies such as FDA and CMS. This question also includes consideration of changes (if any) that the various Federal agencies might consider in a

Exhibit 19. NTR Program Evaluation Questions

PR1. What have the various Federal participants learned from the NTR program? Which structural components would Federal staff retain and which, if any, would they not retain in a future initiative?

PR2. What changes in program policy or procedures are suggested by the NTR program experience?

PR3. What interest has the NTR program stimulated in other countries?

future initiative. Question PR2 considers a broader topic—potential changes in policy or internal procedures that might be considered by any of these Federal agencies as a result of their participation in this program. Finally, the possible effects the NTR program may have outside the United States are examined in Question PR3.

6.3. Proposed Evaluation Design

The proposed evaluation design for the NTR program process-outcome evaluation is a cross-sectional design that uses a multiple-case-study methodology. In a multiple-case-study design, separate parallel case studies are compiled for the specific programs of interest, and cross-case analysis is used to draw conclusions across the case studies. For the NTR program, there will be a total of five case studies that follow the same organizing framework based upon the elements of the Research Payback Framework. Four of the case studies will focus on the four research center teams funded by the program, while the fifth case study will investigate the emerging network developing within the program. An advantage of this approach is that it will apply a similar organizational framework for the case studies, thereby facilitating cross-case analysis. This will enable the evaluation team to address the various evaluation questions for each research team network individually and for the program as a whole.

The Madrillon evaluation team has used the Research Payback Framework in previous evaluation work. The evaluation team is currently completing the first application of the framework in an evaluation of an NIH research program for the Office of Behavioral and Social Sciences Research. In that application, the evaluation team worked with Dr. Steven Hanney of the Health Economics Research Group at Brunel University (a co-developer of the framework) to adapt the framework to the context of a U.S. research program. The Research Payback Framework has been used in a major health technology assessment[18] for the British National Health Service, but the application proposed for the NTR program would be the first time the framework has been applied in an evaluation of a translational technology development research program. The four research team case studies and the network case study will use the organizing schema displayed earlier in **Exhibit 13**, with modifications to adapt it to the specific programmatic and contextual details of the NTR program.

Data for the case studies will be collected from several sources, including existing documents and NIH databases and interviews with key individuals within the four research teams, their industrial partners, and the participating Federal partners. The data will include both quantitative and qualitative measures. Examples of the quantitative measures will include estimates of the in-kind resources provided by industrial partners and social network measures that show linkages between organizational units and primary and task-specific projects for the individual research teams (an approach known as two-mode network analysis).

6.4. Key Variables and Data Sources

A table showing key variables and sources of data is shown on the following pages as **Exhibit 20.**

Exhibit 20. Key Variables, Definitions, and Sources of Data

KEY VARIABLE NAME	DEFINITION	DATA SOURCE
PI Imaging Research Experience & Expertise	Narrative background of each of the four research team Principal Investigators—discipline, institutional location and affiliations, prior imaging research activities and grants	Document review Interview
Origin of Research Team	Description of how the specific proposed team was formed—rationale for selection of team members, whether members had worked together with this PI before, what various members are supposed to contribute	Document review Interview
Institutional Setting	Where the research team is situated within the host institution (department & school); who the PI reports to	Document review Interview

KEY VARIABLE NAME	DEFINITION	DATA SOURCE
Pre-existing Institutional Resources	What imaging and laboratory resources are available to the project; what imaging centers and related programs exist at the institution	Document review Interview
Research Team Management and Dispersion	How the research team is managed: Are all institutional team members located within a single organizational unit at institution or is there dispersion across multiple schools and campuses?	Document review Interview
Grant Funding	Total funding level for the NTR grant; any supplements	NIH Databases
Academic Partners	What individuals from other academic institutions are members of the research team? What is the rationale for their inclusion?	Document review Interview
Key Personnel on Grant	Who are the individuals listed as key personnel on the project grant? What are their degree disciplines? Are they new, early, or established investigators?	Document review
Team Multidisciplinarity	Number of degree disciplines represented in the research team	Document review
Industrial Partners	Firms included as part of the research team; their intended role(s); when they became involved with the team (from start of project or after project had already begun)	Document review Interview
Industrial Partners' In-kind Contribution to Team	Estimated economic value of any equipment, product, or technologies contributed by a firm	Interview
Team Network Density	Number of connections within the full research team	Interview
Team Network Centralization	Which team members are more centrally connected than others	Interview
Team Network Clustering Coefficient	Number of connected subgroups (clusters) within the research team network	Interview
Federal Partners	Federal agencies that are participating in the NTR network (NIST, FDA, CMS)	Interview
Non-Federal Partners	Non-Federal organizations participating in the NTR network	Interview
Research Support Cores	The name, nature, and date of origin of various Research Support Cores created by the Steering Committee	Document review
Research Support Cores—Joint Projects	The various activities and projects which each Research Support Core undertakes	Document review Interview
Federal Partners—Interactions with Teams	When, how, and how frequently Federal agencies interact with the four teams; who instigates the interaction; whether and how research teams set up meetings with FDA and CMS representatives to discuss their projects	Interview
Primary Project Team Members	Within each research team, the individuals working on the primary project, including industrial partners	Document review
Task-Specific Team Members (1, …, n)	Within each research team, the individuals working on each task-specific project, including industrial partners	Document review
Mentored Individuals	Number of students, trainees, fellows, and junior investigators who are mentored as part of the research team's activities	Interview
Research "Spoke Grants"	Number and description of any research spoke grants associated with a research team; whether the PI was a member of the research team or someone external to the team; how the spoke grant was supposed to relate to the research team activities	Document review Interview
Research Spoke Grants—Level of Funding	Total funding and Institute or Center that funded the spoke grant(s)	NIH databases
Research Spoke Grants—Key Personnel	Who are the individuals listed as key personnel on the research spoke grant? What are their degree disciplines? Are they new, early, or established investigators?	Document review
Research Spoke Grants—Academic Partners	What individuals from other academic institutions are members of the research team? What is the rationale for their inclusion?	Document review
Research Spoke Grants—Industrial Partners	Firms included as part of the research team, their intended role(s), when they became involved with the team (from start of project or after project had already begun)	Document review
Research Spoke Grants—Industrial Partners' In-Kind Contributions	Estimated economic value of any equipment, product, or technologies contributed by a firm	Interview
Research Support Cores—Frequency of Meetings	Frequency of meetings of each research support core	Document review
Research Support Cores—Projects Undertaken	List of projects undertaken by each of the Research Support Cores; their final status (completed, discontinued); whether they resulted in any type of output	Document review Interview
Research Teams—Completion of Milestones	Assessment that primary and task-specific projects have completed various predetermined milestones	Interview
Research Teams--Publications	Number and type of publications, citations (excluding self-citation); journal impact factor	NIH Databases

KEY VARIABLE NAME	DEFINITION	DATA SOURCE
Research Teams--Presentations	Number of presentations made to scientific and professional organizations, type of organization	Document review NIH databases
Research Teams--Patents	Number of patent applications filed and number approved	Document review
Research Teams—Effects on Research Capacity	Number of team members completing graduate academic degrees; career advancement; awards and special honors; numbers of new tools, procedures, measures, models, and other products developed by team	Interview
Research Teams—Spin-off Grants	Number of new grants obtained based upon work completed on primary and task-specific projects	Interview
Research Spoke Grants—Completion of Milestones	Assessment that primary and task-specific projects have completed various predetermined milestones	Interview
Research Spoke Grants--Publications	Number and type of publications, citations (excluding self-citation); journal impact factor	NIH databases
Research Spoke Grants--Presentations	Number of presentations made to scientific and professional organizations; type of organization	Document review NIH databases
Research Spoke Grants--Patents	Number of patent applications filed and number approved	Document review
Research Spoke Grants—Effects on Research Capacity	Number of team members completing graduate academic degrees; career advancement; awards and special honors; numbers of new tools, procedures, measures, models, and other products developed by team	Interview
Research Spoke Grants—Spin-off Grants	Number of new grants obtained based upon work completed on spoke grant	Interview
Research Support Cores--Publications	Number and type of publications, citations (excluding self-citation); journal impact factor	NIH databases
Research Support Cores--Presentations	Number of presentations made to scientific and professional organizations; type of organization	Document review NIH databases
Research Support Cores--Products	Numbers of new tools, procedures, measures, models, and other products developed by Research Support Cores	Interview
Research Support Cores—Effects on Research Capacity	Extent to which products developed by Research Support Cores are used by the research teams to address problems	Interview
Research Teams—Project Completion	Assessment that all milestones for primary projects have been completed successfully	Interview
Research Teams—Platforms' Readiness for Human Subjects Testing	Assessment that the various imaging platforms are ready for human subjects testing	Interview
Research Teams—Clinical Data	Types of clinical data collected by the primary projects	Interview
Research Spoke Grants—Project Completion	Assessment that all milestones for primary projects have been completed successfully	Interview
Research Spoke Grants—Perceived Value of Contribution to Research Team	Assessment by research team PI of the nature and perceived value of the research spoke grants' contribution to the research team	Interview
Perceived Effectiveness of NTR Network Model	Views of other stakeholders concerning the perceived value and effectiveness of the NTR network model	Interview
Intention to Adopt NTR Network Model by Other Federal Agencies	Views of other Federal and non-Federal agencies regarding their interest in and intention to utilize the NTR network model	Interview
Intention to Adopt NTR Network Model Outside U.S.	Views of non-Federal agencies regarding their interest in and intention to utilize the NTR network model	Interview
Industry Partners Construct Business Case for Commercialization	Assessment of whether industrial partners can construct a business case for commercialization of the imaging platform on the basis of the technical and clinical data available	Interview
Research Team—Effects on Informing Policy	Whether and how the research team's primary project makes any contribution to informing administrative or clinical policy	Interview
Research Team—Use of Platform Technology by Clinicians	Extent to which the imaging platforms are used by local clinical practitioners; how this is accomplished	Interview
NTR Program—Achievement of Successful Translation Across Four Research Teams	Determination that all four research teams have successfully completed their primary research projects	Document review Interview

KEY VARIABLE NAME	DEFINITION	DATA SOURCE
NTR Program—Effects of Program on Federal Partners	Evidence that participating Federal partners are using results from the NTR program within their agencies, including policies and procedures that might be reviewed in light of NTR experience	Interview
Research Team—Wider Benefits from Project	Whether the research team's primary project has led to wider benefits in one or more of the following areas: improvements in health and well-being, changes in clinical practice and health care service delivery, potential broader economic and social benefits	Interview
NTR Program—Wider Benefits from Program	Whether the NTR program has successfully demonstrated a program model that could be replicated at other agencies pursuing translational technology development research; whether the model is perceived as contributing to a faster and more efficient translational research process	Interview

6.5. Data Analysis Plan

The guiding logic for the analysis of each case study is called *pattern matching*. In pattern matching, an empirically derived pattern of data is compared with a predicted pattern. If the observed and predicted patterns coincide, the results strengthen the internal validity of the case and the arguments it is advancing. In this instance, the predicted pattern is the *program theory* described by the logic model. If the logic model describes how a program is supposed to work, the program theory describes why it is supposed to work—why were these resources, activities, and outputs supposed to lead to these results. As an example, **Exhibit 21** presents a simplified version of the general program theory underlying the research team level of the NTR program. The function of the case studies is to organize the qualitative and quantitative data that support each element within this program theory. If the data support these general assertions, the case is considered to be established.

Exhibit 21. Simplified Version of NTR Program Theory

1. **The four funded research teams have the necessary technical expertise, experience, and resources to complete their projects.**
2. **Problems and barriers exist that are beyond the resources or expertise of individual teams to address.**
3. **By forming a larger network, the four research teams can:**
   a. **Identify common problems**
   b. **Work collaboratively to overcome these problems**
   c. **Generate products and processes that each team can apply in the context of its work.**
4. **Combining the products and solutions generated by the larger network, each team can complete its primary and task-specific projects within the allotted five-year timeframe.**
5. **If all four teams complete their projects within the allotted five-year timeframe, it will represent a faster pace of technology development than would have occurred without the program's resources.**

As described in the preceding section, the data collected for the case studies will include both qualitative and quantitative data. The qualitative data will be analyzed using basic content analysis techniques.[21] This involves the identification of themes from qualitative material, which are then coded. The quantitative data will be explored through descriptive statistical procedures (e.g., calculation of means, standard deviations, medians, etc.). In each instance, the data will be organized under the appropriate element of the program theory.

6.6. Administrative Issues

6.6.1. OMB Clearance

OMB clearances are required in instances in which a specific data collection process is to be used with more than nine individuals. In this instance, it could be argued that an OMB clearance may not be necessary. There are only four research center teams in the program. Within each research center team, there will be several categories of individuals from whom data will be collected, and separate data collection protocols will be developed for each category (e.g., Principal Investigator, task-specific project

leaders, industrial partners, etc.); however, the number of individuals in each of those categories will be less than nine.

6.6.2. Timeline

The NTR program process-outcome evaluation would require a two-year funding period. The evaluation would begin at the Year 4 midpoint (roughly March 2012) and conclude in March 2014. This would extend about six months beyond the conclusion of the NTR program in August, 2013; the extended period would be necessary to track any last-minute actions by Federal partners that might bear upon the completion of the four primary projects (for example, approvals of 510k applications, etc.).

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Appendix A: Network for Translational Research Evaluation Feasibility Study: Protocol for Principal Investigator Interviews

Date of Interview: Length of Interview (minutes):
Principal Investigator:
Telephone Number:
Institution:
Lead Network Institution Grant Number:
Name of Primary Interviewer: JES
Others Participating in Interview (if any):

Good (morning/afternoon), my name is _____.
Thank you for taking the time to talk with us about your participation in the Network for Translational Research Program. As you know from the email correspondence, we are conducting an evaluation feasibility study on behalf of the Cancer Imaging Program at the National Cancer Institute. The purpose of this study is to determine the feasibility of conducting a process and outcome evaluation of the NTR program. This interview will be used to gather data on program implementation and inform the future evaluation of the NTR program. Please note that the interview information collected from you and other program participants will only be presented in summary form and individual responses will not be shared. Before we start, do you have any questions?

INDIVIDUAL RESEARCH CENTER COMPONENTS

1. To what extent have you been successful in implementing your ***research center*** within the timeframe you had originally estimated in the 2008 grant application? Are there any components that have required more time to implement than you anticipated?

a. What factors, structures, and/or events have helped you most in implementing the various components of your **research center**?

b. What factors, structures, and/or events have hindered or slowed your efforts to implement the center?

2. Which aspects or components of your **research center** (if any) do you believe are unique and/or highly innovative? In what way(s)?

THE NETWORK FOR TRANSLATIONAL RESEARCH PROGRAM AS A COOPERATIVE AGREEMENT

3. Have you participated as a research investigator in a research center or network program with NIH in the past? Which program?

a. **IF YES**: In what way or ways is the structure or implementation of the NTR program different from the organization of other cooperative agreement programs in which you have participated?

b. **IF NO**: What aspects of the structure or implementation of the NTR program seem to be particularly noteworthy or innovative?

I'd like to ask you about your perceptions of two of the structural elements of the NTR program—the Working Groups and the Industrial Associate Partners.

WORKING GROUPS

4. Keeping in mind that the primary goal of the NTR program is to accelerate the translation of multimodal imaging platform technology from the laboratory to clinical practice, what role(s) do the five **Working Groups** play in this acceleration?

a. How are they supposed to contribute to *accelerating the translation process*?

b. How are they supposed to support the *research centers*?

5. As a member of the Steering Committee that established these five Working Groups, do you think that the Working Groups are performing their functions in the ways that the Committee originally envisioned?

a. Is there anything that you would change about the Working Groups to improve their value to the research centers?

b. How does information move from the individual Working Groups to you as the Principal Investigator at the research center level?

c. What kinds of costs (in terms of time, effort, etc.) do you see associated with the activities of the Working Groups?

d. What kinds of benefits have you seen from the activities of the Working Groups?

(i) For whom are these benefits (e.g., the research center, the NTR program as a whole)?

INDUSTRIAL PARTNERS

6. The second program element I'd like to ask you about is the participation of industrial partners. Since your research center was funded under the NTR program, based on the information we have, you have added a total of ___ industrial partners to your center. Is this correct? Yes ____ No ____

a. How do you identify potential Industrial partners? What outreach activities do you conduct to identify potential partners? Is there a formal affiliation process?

b. What kinds of benefits for your research center have you noted from having industrial partners?

c. As a member of the Steering Committee that established this mechanism, how did you hope that this program element would contribute to accelerating the translation of multimodal imaging technology from the laboratory to clinical practice?

d. Is this program element operating as you expected it to operate?

e. From your perspective, do you think that the industrial partners are being successfully integrated into the activities of the Working Groups? What problems have you encountered in this integration process (if any) and how have you addressed them?

EVALUATING THE NETWORK FOR TRANSLATIONAL RESEARCH PROGRAM

The Cancer Imaging Program at the National Cancer Institute is interested in planning for a process and outcome evaluation of the NTR program.

PROGRAM IMPLEMENTATION

7. What do you think are the most important aspects of the program's implementation that should be assessed in an evaluation?

a. What is the best **way to measure** the implementation of these activities?

b. **At what point in time** do you think it would be best to measure these activities?

PROGRAM OUTCOMES

8. What do you think are the most important outcomes that should be assessed in an evaluation?

a. What is the best **way to measure** these program outcomes?

b. **At what point in time** do you think it would be best to measure these outcomes?

COMPARISON GROUPS

9. One of the issues we often face in designing evaluations of programs like the NTR program is whether to use a comparison group. Keeping in mind that the primary goal for this program is to accelerate the translation of a complex imaging technology from the laboratory to clinical practice, in your opinion, does it make sense to compare this program with another program? Why, or why not?

a. What program would you suggest as a potential comparison program?

b. If we do not use a comparison group, how do you think we could best determine whether the NTR program has succeeded in accelerating research translation more quickly than would have occurred if the program had not been funded?

Appendix B. Network for Translational Research Evaluation Feasibility Study: Protocol for Industrial Partner Interviews

Date of Interview: Length of Interview (minutes):
Industrial Partner:
Telephone Number:
Company:
Affiliate Network Institution Grant Number:
Name of Primary Interviewer:
Others Participating in Interview (if any):

Good (morning/afternoon), my name is _____.

Thank you for taking the time to talk with us about your participation in the Network for Translational Research (NTR) program. As you know from the email correspondence, we are conducting an evaluation feasibility study on behalf of the Cancer Imaging Program at the National Cancer Institute. The purpose of this study is to determine the feasibility of conducting a process and outcome evaluation of the NTR program. This interview will be used to gather data on program implementation and inform the future evaluation of the NTR program. Please note that the interview information collected from you and other program participants will only be presented in summary form and individual responses will not be shared. Before we start, do you have any questions?

BACKGROUND—YOUR COMPANY AND YOU

1. What is your role at _____? How long have you been employed there?

2. Had your company worked with university researchers prior to your association with the NTR Program? In what capacity?

INITIAL ENGAGEMENT WITH THE NETWORK FOR TRANSLATIONAL RESEARCH PROGRAM

3. When and how did your company first learn about the NIH Network for Translational Research program?

4. What benefits did your company expect to gain from participating in the NTR program? At what point in time did you expect these benefits to begin to accrue?

5. When you first joined the program, what did you understand that you would be expected to do?

a. Have those activities changed since you first joined? (If YES: In what ways?)

b. What would you say have been the most important contributions you and/or your company have made to the activities of your Working Group since joining?

c. Can you provide me with a rough estimate of how much time (in hours per month) you spend on activities associated with your participation in the NTR program?

d. How satisfied is your company with its involvement in the NTR program?

6. How much contact do you have with other industrial partners in the NTR program?

   a. What types of relationships have you established with other industrial partners affiliated with your research center? (Use list of types of relationships—information exchange, joint projects, etc.)

   b. To what extent have you been successful in establishing new working relationships with industrial partners outside those engaged with your research center?

7. How well do you believe these partnerships between the NTR research centers and their industrial partners are working at this time?

a. Are there aspects of these partnerships that could be improved? (If so, how, or in what ways?)

b. Do you believe the NTR program is an effective model for stimulating research and technology development between universities and industry? Why (or why not?)

EVALUATING THE NETWORK FOR TRANSLATIONAL RESEARCH PROGRAM

The Cancer Imaging Program at the National Cancer Institute is interested in planning for an evaluation of this program.

PROGRAM IMPLEMENTATION

8. What do you think are the most important aspects of the program's implementation that should be assessed in an evaluation?

a. What is the best **way to measure** the implementation of these activities?

b. **At what point in time** do you think it would be best to measure these activities?

PROGRAM OUTCOMES

9. What do you think are the most important outcomes that should be assessed in an evaluation?

a. What is the best way to measure these program outcomes?

b. At what point in time do you think it would be best to measure these outcomes?

COMPARISON GROUPS

10. One of the issues we often face in designing evaluations of programs like the Network for Translational Research is whether to use a comparison group. Keeping in mind that the primary goal for this program is to accelerate the translation of a complex imaging technology from the laboratory to clinical practice, in your opinion, does it make sense to compare this program with another program? Why, or why not?

a. What program would you suggest as a potential comparison program?

b. If we do not use a comparison group, how do you think we could best determine whether the NTR program has succeeded in accelerating research translation more quickly than would have occurred if the program had not been funded?