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EVALUATING THE SELECTION PROCESSES FOR THE NIH ROADMAP NANOMEDICINE INITIATIVE NANOMEDICINE DEVELOPMENT CENTERS

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Project background

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Abbreviations

CAL	Concept Approval Letter
CDM	Concept Development Memo
CDP	Concept Development Plan
CSR	Center for Scientific Review
ECG	Extramural Consultant Group
FFRDC	Federally Funded Research and Development Center
FRA	Flexible Research Authority
IDA	Institute for Defense Analyses
NDC	Nanomedicine Development Center
NEI	National Eye Institute
NIH	National Institutes of Health
NIPT	Nanomedicine Implementation Project Team
NNI	National Nanotechnology Initiative
NSF	National Science Foundation
OSTP	Office of Science and Technology Policy
RFA	Request for Applications
STPI	Science and Technology Policy Institute

1. Preface

1.1. Organization of this report

This report is organized as follows. The current section summarizes the evaluative approach of the study and the feasibility of further study. The Executive Summary (Section 2) contains a summary of the empirical findings (Section 2.2), an analysis of successes and challenges (Section 2.3), and the evaluative conclusions and recommendations of the STPI evaluation team (Section 2.4). The remainder of this report is empirical, with Sections 3 through 8 providing at-length treatments of the data that support the evaluative conclusions detailed in the Executive Summary. Accordingly, these latter sections are delineated by topic and perspective. For instance, Section 5 on the "interactivity" of the selection process (i.e., a criterion for selection process effectiveness, detailed immediately below in Section 1.2) has three sub-sections: "Applicant perspectives," "Extramural Consultant Group perspectives," and "Extramural Reviewer perspectives."

1.2. Evaluative approach

This study describes and evaluates the selection processes, including official events and meetings but also less formal interactions, which led to the eventual funding of the eight National Institutes of Health (NIH) Nanomedicine Development Centers (NDC). To discern and evaluate these processes in a step-wise manner, a number of data sources were considered. The predominant source of information is semi-structured interviews with several Nanomedicine Implementation Project Team (NIPT) officials, the director of each NDC, and with representative samples of Extramural Consultant Group (ECG) members, applicants who did not receive center funding, and extramural reviewers. Additional evaluative information is provided by longitudinal content analysis of documents, including but not limited to preliminary approval letters and NDC applications. In conjunction with the interviews, the content analysis facilitates assessment of the impact of unique aspects of the selection processes on the ideas, scientific and otherwise, proposed in the final NDC applications. Because this study is as much a descriptive as it is an evaluative effort, extant NDC program documentation (e.g., requests for applications, meeting agenda, reviewer guidelines) constitutes a third data source.

Since the overarching purpose of any process evaluation is to characterize the operation of the process and to assess the extent to which it functioned to meet process goals (i.e., not program goals, which are evaluated in an outcome evaluation), we developed a framework for the NDC selection process activities and outputs from which to determine whether the actual implementation and outcomes of the selection processes for both rounds of competition went "according to plans." The framework was a product of assessment of the NDC program's pre-implementation plans and expectations regarding the structure and activities of the selection processes, which are outlined in Section 3 of this report. The framework itself is not presented until the beginning of Section 4, which assesses how the selection processes were actually implemented.

Unusual for process evaluations, adherence of program implementation to plans and expectations is not a key parameter by which to evaluate NDC selection process effectiveness. The use of Flexible Research Authority (FRA) to structure and implement competitions for NDC funding rendered the initial plans and expectations of the NIPT less defined than those for selection processes using conventional NIH mechanisms. Therefore, the parameters of effectiveness by which this report assesses the NDC selection processes, in Sections 5 through 8, are directly related to the unique goals of the NDC selection process:

- To render the NDC selection process highly interactive, with applicants, NIPT officials, and ECG members working together to determine what type of research the program should fund and, subsequently, the eventual nature of the solicitation for full NDC applications.
- To elicit NDC applications that, in response to the full solicitation for applications, are novel and "out of the box" in their scientific and technical foci – having a clinical focus and not necessarily relying on preliminary data and findings – as well as in the organization and structure of the proposed centers, including their involvement in a collaborative network of NDCs.

Process evaluations often assess whether there is exclusion of certain facets of the scientific community. In this instance, the processes implemented to facilitate unconventional interactions and novel centers proposals, because they are new and untested, pose the risk of systematically excluding some participants due to lack of exposure or due to undetected biases in the process or in the composition of the program staff. This may occur despite attempts to cover the entirety of the scientific community (e.g., by advertising an open RFA.) Accordingly, this report considers a third parameter of selection process effectiveness:

- Program coverage – the extent to which participation by the target population of scientists and engineers is achieved.

1.3. Feasibility of further inquiry

The findings of this preliminary evaluation into the selection processes used for the first two rounds of competition for the NDC program demonstrate that further inquiry is quite feasible. Based on the interviews and content analyses conducted, the selection processes can be described and evaluated per the key parameters of process "effectiveness" employed in this study: interactivity, coverage, and novelty. However, establishing feasibility does not necessarily warrant further inquiry into the NDC selection processes.

Further evaluation would include interviews with additional NIPT officials, ECG members, and extramural reviewers, as well as with additional applicants who did not receive NDC funding in either round of competition. Further evaluation would also broaden the sample of applicant documents (e.g., NDC applications) for content analysis, using additional coders to further ensure inter-coder reliability.

However, the findings of this study are resolute, with a clear story line. Accordingly, the STPI evaluation team does not believe that additional inquiry would alter the findings or evaluative conclusions presented in this report and therefore does not recommend further evaluation.

2. Executive summary

2.1. Introduction

In late 2006, the Science and Technology Policy Institute (STPI) at the Institute for Defense Analyses (IDA) began evaluation of the processes through which the National Institutes of Health (NIH) Nanomedicine Development Centers program selected the eight current Nanomedicine Development Centers (NDCs), four centers awarded in 2005 and four more awarded in 2006. During the course of this evaluation, STPI conducted a series of interviews with NDC program participants and stakeholders in addition to performing longitudinal content analysis of application documents to assess the feasibility and necessity of a broader, more in-depth evaluation of the NDC selection processes implemented to select the first two cohorts of NDCs.

In addition to the practical goal of assessing the feasibility and necessity of further evaluation, the analytic goal of this study is to identify which aspects of the selection process facilitated the solicitation and identification of applications best suited to meet the objectives of the NDC program. This evaluation includes an analysis of the use of Flexible Research Authority (FRA)[1] to select NDCs, which enabled program officials – collectively referred to as the Nanomedicine Implementation Project Team (NIPT) – and their Extramural Consultant Group (ECG) to interact with applicants and extramural reviewers at numerous points during the application process, in ways very different from standard NIH processes and practices.

The NDC program is part of the NIH Roadmap for Medical Research and is the focus of the NIH Nanomedicine Roadmap Initiative. The mission of the program is to enhance understanding of the operations of molecular structures, processes, and networks as they occur within living cells, by cataloging patterns of interactions between molecules and larger structures. Eventually, it is expected that this understanding will lead to the development of general (i.e., not specific to a particular type of cell, but applicable across a range of tissues) nanoscale tools that enable the construction of synthetic biological devices for, among other purposes, cell repair or the detection and destruction of infectious agents. Despite this emphasis on the manipulation of nanoscale biological structures for medical purposes, the analytic focus of each NDC is the biological system, not a particular technological approach or set of approaches, since multiple technologies will probably be used in resolving particular biomedical problems.

From the NIH perspective, key organizational characteristics that might help NDCs to attain the ambitious scientific, technological, and clinical goals of the NDC program include:

- A center comprised of scientists from multiple fields and disciplines, including but not limited to physicians, biologists, engineers, computer scientists, and mathematicians.
- Interaction across the NDCs to ensure resource efficiency and scientific complementarity.

[1] Use of FRA was introduced after program officials had already begun to plan the competition for selection of the first cohort of NDCs. FRA and its impact on the NDC program are described in Section 4 of this report.

While these attributes certainly are required, they are not sufficient to ensure the pursuit of the progressive, high-risk research the NDC program envisions. Accordingly, the NIPT implemented a highly interactive selection process for both rounds of competition which was designed to generate novel center proposals emphasizing progressive thinking.

Table 1. NIH Nanomedicine Development Centers

Award year	Center	Lead institution
2005	Center for Protein Folding Machinery	Baylor College of Medicine
2005	National Center for Design of Biomimetic Nanoconductors	University of Illinois – Urbana-Champaign
2005	The Cell Propulsion Lab	University of California – San Francisco
2005	The Nanotechnology Center for Mechanics in Regenerative Medicine	Columbia University – Morningside
2006	Nanomedicine Center for Nucleoprotein Machines	Georgia Tech Research Corporation
2006	Phi29 DNA-Packaging Motor for Nanomedicine	Purdue University
2006	The Center for Cell Control	University of California – Los Angeles
2006	NDC for Optical Control of Biological Function	University of California – Lawrence Berkeley National Laboratory

2.2. Findings in brief

The empirical findings from this report are presented in full in Sections 3 through 8 and are summarized below. Because this study is based predominantly on interview data, there are many quotations throughout the report. The questions that elicited these various quotations were open-ended and carefully crafted so as not to lead, while adhering to the rules of validity and reliability.[2] The methods and discussion guides employed for this study are detailed in Appendices B through D at the end of the report.

The results from the interviews and content analyses demonstrate the NDC program to be "unique" for the NIH, with mixed effects regarding the above parameters for selection process effectiveness. It is important to note that the presentation of these findings is empirical – based entirely upon what was reported during interviews and what the content analyses detected. Further, no quantitative decision rules were used for inclusion or exclusion of particular findings.

[2] Interview questions are considered "valid" when there is congruence between the question and the concept it is purported to ask about; interview questions are "reliable" when they are interpreted consistently across the interviewer and interviewees. See Singleton Jr., R.A. and B.C. Straits *Approaches to Social Research Third Edition*. Oxford: Oxford University Press, 1999.

In other words, both unique and common perspectives are included. Indeed, such richness of data is the primary advantage of qualitative case evaluation.[3]

2.2.1. Adherence to original plans and expectations

As mentioned above, the extent to which implementation of the NDC selection processes adhered to initial plans and expectations is not a major concern due to the use of FRA and the attendant flexible nature of NIPT officials' initial plans and expectations. Nevertheless, the structure for implementing the NDC selection processes was premeditated and clear, and implementation steps were performed according to plans. However, initial expectations concerning what precisely was to occur during each phase of the selection processes were considerably less clear. This was especially the case during the first round of competition. In interviews with members of the NIPT, the general expectation was that the first round process would be highly interactive, soliciting novel center proposals that rely more on progressive thinking than conventional center proposals (e.g., for the NIH P50). The findings for proposal novelty are reviewed in brief below.

2.2.2. Interactivity

The NDC selection processes were highly interactive when compared to standard NIH processes and practices. Of the participants and stakeholders interviewed – including members of the NIPT, the ECG, as well as applicants and extramural reviewers – all described the interactions as "unique" and "frequent." However, not all of the interactions were perceived as constructive, but rather as instructive and some even described specific interactions (i.e., at the Concept Development Plan [CDP] meeting, described below in Section 4) as "contentious." Specifically, most of the applicants and reviewers interviewed did not feel that their input was heeded by the NIPT, despite the stated intention by the NIPT to do so. In contrast, NIPT and ECG members generally felt that both the applicants and extramural reviewers did not understand the goals of the NDC program, specifically the goal of novel, "out of the box" proposals with a vision of how the knowledge gained could be applied clinically. Perhaps most important, the interviews and content analyses did not demonstrate that the interactions had a major impact on the scientific, technical, and clinical foci, or the goals and experimental approaches, of the proposed centers. Accordingly, although the NDC selection processes were highly effective at facilitating interactions, these interactions did not always have clear and consistent outcomes.

[3] It is important to note that in a qualitative case study, statistical inferences need not and cannot be made. For example, the perspective of one NIPT member could be of greater insight and value to the program than a common (and perhaps contrary) perspective shared across all extramural reviewers. Accordingly, the findings in this report are presented as-is. When they are interpreted in later sections of this Executive Summary, weight is given to the perceived evaluative value of the perspective and not to the number of interviewees supporting that perspective. However, some highly "valuable" perspectives may be shared across numerous interviewees.

2.2.3. Program coverage

Measuring program coverage almost always relies on a reliable idea of who does and who does not comprise the target population. Due to the breadth and newness of the concept of "nanomedicine," however, the target population is sufficiently broad to defy definition per discrete disciplinary boundaries. A majority of those interviewed felt NDC program coverage to be adequate, for both rounds of competition. When asked whether areas of science and engineering that they thought promising avenues of inquiry for nanomedicine were absent from the application pools, most responded that program coverage was adequate.

2.2.4. Novelty of the applications

Whether the NDC selection processes are considered to have elicited (a) applications responsive to the call for progressive proposals relying less on preliminary data and more on creative thinking or (b) applications quite similar to those elicited by conventional selection processes seems a matter of perspective. When asked about the novelty of the applications, the members of the NIPT and the ECG interviewed reported the application pools from both rounds of competition to be comprised of relatively novel proposals. When asked the same question, many of the extramural reviewers interviewed responded differently, stating that a large proportion of the proposals, including some of those awarded NDC funding, could have been funded via conventional mechanisms. However, these reviewers did not comment directly on the novelty of the scientific and technical aspects of the applications, but rather focused on the feasibility of the management of the centers. In some instances, ECG members interviewed similarly reported that they felt some of the proposals could have been funded through conventional mechanisms.

2.3. Successes and challenges

Based on the empirical findings summarized above (and presented at length in Sections 3 through 8 of this report), the processes used to select the first two cohorts of NDCs were effective in that they facilitated high levels of interaction amongst participants, solicited center proposals that some (though not all) program stakeholders perceived to be novel, and gained wide participation across the biomedical community.[4] However, with each of these successes came challenges. The most formidable of these challenges relate to divergence between the NDC processes enabled by FRA and long-standing NIH culture. Other challenges are typical when coordinating scientists and engineers from across institutions and disciplines to foster research and development in a new field of inquiry.

2.3.1. Convincing applicants and extramural reviewers to deviate from standard NIH practice

The first round saw much resistance by the applicant pool to both the structure and the expected outputs of the NDC selection process. Applicants in receipt of planning awards did not cooperate with one another as intended (i.e., approach other applicants to consolidate efforts and form larger or realigned teams; see Section 4 for a full description). Instead, they viewed one

[3] See Sections 5 through 8 for the interview and content analysis data supporting these conclusions.

another as competitors. Moreover, applicants during the first round were resistant to the idea of generating center proposals with a reduced emphasis on preliminary data and findings, but rather on progressive, "out of the box" thinking. Even after reassurance from NIPT officials, many applicants did not trust that the extramural reviewers would score favorably proposals without preliminary data and findings.

Indeed, many of the extramural reviewers reported that they scored the applications based on the demonstrated feasibility of the proposed science, regardless of whether or not the application constituted the progressive thinking encouraged by NIPT officials. This resistance occurred despite numerous tactics designed to facilitate a different approach to the reviews, including preliminary teleconferences amongst NIPT officials and reviewers, written instructions for the reviewers, and the direct intervention of NIPT officials and ECG members during the review meetings.

2.3.2. Coordinating a "network" of NDCs

Coordination of the NDCs into a collaborative network of centers was not a central goal of the NIPT at the time of the competitions and was not a formal review criterion during either round. However, mention of such coordination was included in the Request for Applications (RFA) during both rounds, and the Concept Development Plan meeting during Round 1 included a breakout session on organizing a network of NDCs. Moreover, each of the eight applications awarded NDC funding included language addressing how the proposed center would coordinate within a broader network of NDCs. This language was drafted prior to learning which proposals were to receive funding and, accordingly, constitutes little more than a general and non-binding commitment to interact with other NDCs, independent of their respective scientific, technical, and clinical foci. Further, neither the extramural reviewers nor the NIPT and ECG members interviewed reported that such coordination was a major consideration when selecting the awardees during each round of competition. Finally, each of the NDCs is comprised of investigators from multiple institutions that are not co-located – a substantial coordination challenge (intra-NDC rather than inter-NDC) in its own right. Meaningful collaboration across the current population of NDCs will require programmatic oversight and managerial engineering beyond the center selection processes.

2.3.3. Clarifying what constitutes "nanomedicine" in the context of the initiative

Since inception of the NDC program, significant progress has been made in reaching consensus as to what constitutes "nanomedicine" for this initiative amongst NIPT officials and ECG members. However, some of the NIPT officials and ECG members interviewed still do not agree with the language used to solicit NDC applications. Further, some extramural reviewers and applicants expressed confusion over the definition used in the solicitation. Due to the interdisciplinary nature of this emerging field and due to the goal of simultaneously cataloging nanoscale biological patterns and developing nanoscale tools for clinical application, arriving at a universal definition of nanomedicine is not necessary or even achievable in the short run. But there is room for rendering more explicit the preferred balance of biological research versus tool development, as well as the timeframe from these activities to clinical application.

2.4. Conclusions and recommendations

The NDC program implemented two center selection processes (i.e., Round 1 in 2004-2005, Round 2 in 2006) that were highly interactive, solicited center proposals emphasizing progressive thinking towards development of the field of nanomedicine, and gained wide coverage across the biomedical community. An intangible outcome of the selection processes was a degree of consensus over what "nanomedicine" means, at least within the NDC program and perhaps more broadly for the NIH Roadmap for Medical Research. Therefore, on all accounts of process effectiveness (see 1.2 above), the NDC program may be considered effective.

With these successes came some challenges (see 1.4 above), most notably the challenge of persuading applicants and extramural reviewers to deviate from standard NIH process and practice. These challenges were difficult if not impossible to avoid insofar that NIH culture is long-standing. NIPT officials, with the help of the ECG, were proactive through every phase of both funding competitions to ensure that the NDC applications adhered to program goals and were not "typical" of proposals elicited by conventional mechanisms (e.g., R01, P50). That, from the perspectives of the extramural reviewers interviewed, some of the applications resembled more conventional applications should not be viewed as a failing of the NDC selection processes, but rather more broadly (and fairly) as a function of the newness of the processes used to solicit center proposals for this new area of scientific and technical inquiry.

Based on the findings and challenges presented above, we provide two sets of recommendations. The first set of recommendations is specific to the NDC program. These recommendations are "ex post" recommendations addressing how NIPT officials may address currently some of the challenges faced during the Round 1 and Round 2 competitions (e.g., the lack of serious consideration of inter-NDC collaboration). The second set of recommendations is relevant to other NIH Roadmap initiatives that may use FRA or implement a program with comparable goals (i.e., an interactive network of centers pursuing a newly defined field of research and development). These latter recommendations are also relevant to the NDC program in the event that it solicits additional NDC proposals with subsequent rounds of competition.

2.4.1. "Ex post" recommendations for the NDC program

These recommendations address how NIPT officials may address some of the challenges faced during the competitions for NDC funding, now that the competitions are completed.

2.4.1.1. Provide incentive for inter-NDC collaboration

Initially, one of the chief "ex post" recommendations to be included in this report was to facilitate inter-NDC research projects using a program-level solicitation for joint project proposals on topics developed by the NDCs (and not by the NIPT) – requiring each proposal to include personnel from multiple NDCs and to focus on topics of mutual yet complementary interest that further the nanomedicine agenda. Further, our initial recommendation qualified that

inter-NDC collaborations should not be mandated.[5] The reasoning for this follows from the first round of competition, when there was little incentive for applicants to heed seriously encouragement from the NIPT to evaluate the potential for collaborations with one another.[6]

In 2007, the NDC program implemented such an effort, using the flexibility of FRA as a tool to manage set-aside funds that are allocated amongst the NDCs based on need or on competitive supplements. The request for competitive supplements included specific instructions encouraging inter-NDC collaborations, though proposals were not required to be collaborative.

2.4.1.2. Develop the meaning of (and broaden consensus over what constitutes) "nanomedicine"

The interviews that constitute the empirical basis of much of this report demonstrate disagreement across participant strata on a number of important issues.[7] Perhaps the one topic for which there was consensus across the participant strata was that there is room for further development of the meaning of "nanomedicine." While during the two competitions for NDC funding, it was beyond the purview of the NIPT to develop a common understanding of nanomedicine outside programmatic boundaries – and while today the NIPT is still obligated only to its constituents within the NDC program and to the broader NIH Nanomedicine Roadmap Initiative – the interview findings demonstrate that a clearer idea (though not necessarily a formal statement or definition) of what constitutes nanomedicine is in demand amongst those involved with the program.

Though the NIPT, with the aid of the ECG, reached consensus over what would be the "official" NDC program line regarding what constitutes nanomedicine and what does not, many individuals from both the NIPT and ECG reported in interviews that there remained "unofficial" disagreement over use of the term. This is not to say that such disagreement was overt or constituted a barrier during the selection processes, but rather that there is further program definition to occur. To this point, both applicants and reviewers expressed confusion over the definition used in the solicitations for NDC applications.

Of course, program definition for new fields of scientific and technical inquiry that span disciplinary boundaries and emphasize translation from the laboratory to the clinic cannot occur

[5] Empirical findings from the economics and strategic management literatures on "effective" inter-organizational collaboration in research and development suggest that the structure of these incentives should be "organic" – stemming from the mutual interests of investigators across the NDCs – rather than "top down" and orchestrated in focus and function by the NIPT. In other words, future inter-NDC collaborations should be initiated and implemented with as little programmatic interference as possible.

[6] This is understandable, given that applicants were asked to consider cross-proposal collaborations while the competition was still underway. However, during the second round of competition, there was increased incentive for consideration of cross-center collaborations insofar as there was the first cohort of NDCs (i.e., the four NDCs awarded funding in the first competition) with which to align, viewed by Round 2 applicants as being comprised of potential collaborators rather than competitors.

[7] For example, NIPT members felt that the proposals for NDCs were progressive and "out of the box," while the extramural reviewers and some of the ECG members felt that many of the proposals could have been funded using conventional mechanisms. Round 1 applicants reported that the Concept Development Plan (CDP) meeting had little impact on the scientific, technical, and clinical foci of their proposals, while NIPT members maintain that the meeting was necessary to get applicants "on track" regarding programmatic goals and expectations.

simply because one wants it to. The NDC program defined "nanomedicine" at the outset of the first round of competition to the extent possible under the difficult circumstance of defining a new field of inquiry.

The NIPT is now in the position to take advantage of learning from its experiences during the NDC selection processes as well as from learning that has occurred thus far at each of the eight NDCs. The question of what constitutes "nanomedicine" and what does not should be revisited, based on preliminary data sets and findings from the NDCs as well as on input from the ECG, extramural reviewers, and key personnel from the NDCs. A workshop or comparable forum should be held – either as part of a broader workshop or as a standalone event – to discuss further where the nascent nanomedicine "field" is and where it is headed. An output of the workshop should be a programmatic definition statement, to be distributed for comment to a broader audience.

2.4.1.3. Expand the clinical ties of the NDCs

Initially, one of the chief "ex post" recommendations to be included in this report was to expand the network ties of the NDCs by soliciting outside clinicians to collaborate with NDCs in nanomedicine development and, eventually, nanomedicine trials/testing. The reasoning behind this recommendation was that while the applicant document deliverables included in the content analysis uniformly referenced potential clinical relevance, more often than not the language was quite general with no clear statement of specific clinical applications.

The NDC program has already implemented such an effort. In November 2007, a "Call for Clinical Collaborators" was announced by the NIH Nanomedicine Roadmap. Specifically, the Call requested "letters of interest in collaboration" from clinical investigators.[8] Awardees are expected to "explore opportunities for potential medical applications that build on the science emerging from one or more of the [NDCs]." The NDC program has made approximately $2 million available with which to support three to five clinical investigators through 2009.

2.4.2. "Ex ante" recommendations for future competitions

These recommendations address how NIPT officials may avoid some of the challenges faced during the first two competitions for NDC funding, in the case that subsequent competitions to fund additional NDCs occur. These recommendations may also apply to other NIH programs that may use FRA or be aimed at funding centers with comparable goals in mind (i.e., an interactive network of centers pursuing a newly defined field of research and development).

2.4.2.1. Increase decision making transparency

Practically all of the participants interviewed who were not members of the NIPT expressed ignorance of the decision rules and methods through which the awarded applications were selected to receive NDC funding. In particular, many of the subset of extramural reviewers

[8] See http://nanomedcenter.org/funding.

interviewed were skeptical that their scores were a major consideration in NIPT officials' final decisions.

Given the unorthodox nature of the selection processes (e.g., not requiring proposals to include preliminary data and findings), it would serve the NDC program well to be clearer in its rules and methods for testing the extent to which proposals meet program goals and criteria. Codified dissemination of administrative differences and differences in review criteria may help offset some skepticism and help to align stakeholders with programmatic goals.

2.4.2.2. Do not expect competitors to cooperate

From a process perspective, the component of the NDC selection processes that stands out as unique was the CDP meeting during Round 1.[9] According to interviews and documentation, one of the purposes of the meeting was for applicant teams to share ideas, to self-identify synergies with other applicant teams, and perhaps even to make formal plans to cooperate (e.g., by combining multiple NDC proposals into a single proposal). This did not occur. All of the applicants interviewed expressed incredulity in response to this goal of the meeting.[10]

This is not to say that future competitions (whether for the NDC program or another NIH program) should not endeavor to develop an interactive network of centers focused on a unified scientific and clinical mission. However, effective research collaborations most often occur when there is mutual interest and the collaboration occurs as an outgrowth of that interest rather than when the collaboration is mandated by a program or policy. Accordingly, it is perhaps unrealistic to expect competitors to engage willingly in collaborative activities before funding has been awarded, unless there is assurance of mutual benefit (e.g., such as those found among firms in some technology-based industries). Therefore, in the future inter-NDC collaborations should be facilitated post-competition (e.g., once the NDCs, like firms in a particular industry engaging in collaborative research and development, are "established" as formal components of the NDC program).

2.4.2.3. Ensure alignment between programmatic and applicant expectations, continually

The NDC selection processes were designed as step-wise processes (especially during the first competition) to allow applicant teams ample time to develop their proposals for NDC funding. As applicants submitted "interim" (i.e., pre-NDC application) document deliverables, NIPT officials and ECG members evolved their plans and expectations for moving forward in the selection process. While there was frequent and extended communication between the NIPT

[9] During this meeting, applicants who were approved to continue in the competition (after submission of a 5-page proposal and, upon approval from NIPT officials, receipt of a $50,000 planning award) met with one another as well as with NIPT officials and ECG members for a two-day workshop.

[10] There were varying reasons for such expressions. First, at the time of the meeting, no one knew which center proposals were to be funded. Many applicants expressed concern over allying with "losing" proposals. Second, the competition was "on" and the applicants did not want to "show all of their cards." Last, the amount of money to be allocated per NDC seemed to applicant teams enough to support themselves, but not themselves in addition to the research agenda of additional personnel from other teams.

and applicants throughout, many of the Round 1 applicants interviewed entered the "CDP meeting" phase of the selection process with different expectations than did the NIPT and ECG.

Specifically, in response to the CDPs that applicants submitted during Round 1, the NIPT altered their plans for the CDP meeting. Initially, one of the chief reasons for the meeting was to gather input from the applicant teams as to what the eventual limited competition NDC RFA should look like and to determine if the plans for the RFA were reasonable given the state of the science. After receiving the CDPs, NIPT officials realized that many of the applicant teams still had "missed the point" of proposing progressive research plans that included tough challenges and "out of the box" ideas that are usually not funded by NIH. Accordingly, the majority of the discussion during the CDP meeting was spent conveying the goals and intent of the program by members of both the NIPT and the ECG.

Many of the applicants interviewed expressed dissatisfaction with this aspect of the CDP meeting. They went in expecting to help the program develop its mission and identity, but left having had little opportunity to provide such input. Universally across the participant strata, the CDP meeting was described as contentious, though some NIPT officials interviewed reported that the meeting started contentiously but ended amicably. If applicants had entered the meeting with different expectations – for instance, with the expectation of receiving critical feedback on their CDPs and how to align better their ideas for an NDC with the goals and expectations of the NDC program (which is precisely what occurred during the meeting) – the CDP meeting may have been described by applicants as helpful and instructive rather than as contentious. Coupled with the expectation for applicants to develop collaborations with each other during the meeting (see above), from the perspectives of the applicants interviewed, the CDP meeting was disruptive rather than helpful.

2.4.2.4. Allow more time for process planning

From the outset of the NDC program, and despite the intended interactive nature of the selection processes, there seems to have been insufficient clarity in the communications between the NIPT and applicants and between the NIPT and extramural reviewers. Indeed, most of the above recommendations address in one way or another increasing the transparency of programmatic expectations and decision making so that applicants, reviewers, and the NIPT can continually be "on the same page." If the above recommendations were combined into a singular meta-recommendation, it perhaps would read "Articulate, and then *re*-articulate, programmatic goals and expectations."

Perhaps some of the need for "re-articulation" may have been avoided if there had been ample time for process planning. The NDC program was not originally charged with the use of FRA. Once FRA was granted, NIPT officials essentially scrambled to figure out how to use it during program implementation (which was already underway). Many of the NIPT members interviewed reported feeling that the process planning was rushed.

Future implementations could benefit from more time for planning. Some of the extramural reviewers and ECG members interviewed mentioned that they felt many of the NDC applications to be fundable via conventional mechanisms. This is partially owing to long-

standing NIH process and practice and therefore not entirely under the control of the NDC program (or any other centers program). However, the observation makes the need for extended process planning and design all the more apparent.

2.4.2.5. Anticipate the above challenges and then some

Do not expect the process to go perfectly. This report highlights the strengths and challenges of developing a new award selection process within the context of long-standing institutional culture at the NIH. The prevalent NIH emphasis on strong hypothesis driven science based on preliminary findings and arms length peer review is very different from an interactive selection process involving all stakeholders and focused on high risk, "out-of-the-box" proposals. This variance with standing process and practice made it difficult for the NDC program to win the "hearts and minds" of all applicants, ECG members, and extramural reviewers participating in the program. Other NIH program officials implementing comparable programs soliciting "out of the box" proposals that aim to establish nascent fields of research and development must spend time to anticipate barriers to process implementation at the outset.

3. Program origins and planning

The basis of any process evaluation is a solid understanding of both the origins and the preliminary plans and expectations of the program being evaluated.[11] Such an understanding provides a reference point from which to assess the process as it actually occurred. In this section, the origins of the National Institutes of Health (NIH) Nanomedicine Development Centers (NDC) program are described, as are Nanomedicine Implementation Project Team (NIPT) officials' preliminary plans and expectations for the program. Accordingly, this section is purely descriptive and does not constitute this report's evaluative analysis, which is detailed in the Executive Summary. The empirical basis for this chapter includes interviews with NIPT officials, senior National Institutes of Health (NIH) officials who were not part of the NIPT, and programmatic documentation.[12]

3.1. NIH Roadmap Initiative

The roots of the efforts that were to become the NDC program may be traced back to the summer of 2002, when NIH Director Elias Zerhouni organized a series of meetings to identify major issues in biomedical research that at the time were not being addressed across the NIH's many institutes and centers. The goal of the meetings was to develop a limited set of actionable priorities. During these meetings, the development of nanotechnologies for biomedical application was identified as an area of research to be addressed by the NIH in the future. The overarching result of the meetings was the NIH Roadmap for Medical Research.

In November 2002, a working group was assembled to develop ideas for what eventually was to lead to the establishment of the NDC program. The group was headed by Jeff Schloss of the National Human Genome Research Institute. The group included both intramural and extramural scientists who met regularly via telephone conference call to develop ideas for the program. At first, the group envisioned a "traditional" nanotechnology program similar to those managed and operated by the National Science Foundation (NSF) and developed initial plans or "blueprints" for the application of tools and materials from other fields to biomedicine. These plans were aligned with the suggestions generated during the summer 2002 meetings.

The plans developed by the working group were presented at the 2003 NIH Budget Retreat. At that time, Dr. Zerhouni communicated that the efforts should remain closely aligned with the NIH's overarching mission (i.e., clinical application of research) and be distinct from other NIH activities related to the multi-agency National Nanotechnology Initiative (NNI).[13] Accordingly, the working group restructured and redefined their plans to focus on understanding the quantitative physical and chemical properties and engineering principles underlying

[11] See: Rossi, P.H., M.W. Lipsey, and H.E. Freeman (2004) *Evaluation: A Systematic Approach, 7th Edition*. Thousand Oaks, CA: Sage; also see: Scheirer, M.A. (1994) "Designing and Using Process Evaluation" In J.S. Wholey, H.P. Hatry, and K.E. Newcomer (Eds.) *Handbook of Practical Program Evaluation*. San Francisco: Jossey-Bass, p. 40-68.
[12] For a full description of methodology, see Appendices B-D.
[13] The NIH includes the NDC Program in its reports to the NNI.

biological systems to facilitate the development of interventions for curing diseases or for repairing damaged tissues.

In March 2003, the group was assigned official staff, thereby establishing the NIPT – the Implementation Group for the Nanomedicine Initiative. By November, the NIPT designated the National Eye Institute as the administrative home for the program and by March 2004, the NIPT had recruited members for the Extramural Consultant Group (ECG). During this period and up until the initial public meeting in May 2004, the NIPT developed most of the program's structural features, including the decision to sponsor two rounds of funding. Specifically, the idea was to sponsor the conceptual development of selected center proposals using existing mechanisms (e.g., P20, P50).

3.2. Flexible Research Authority

In view of the novelty and complexity of the burgeoning NIH Roadmap for Medical Research, the US Congress granted the NIH Flexible Research Authority (FRA) to help stimulate new approaches and ideas considered central to roadmap activities. In February 2004, Director. Zerhouni decided to use FRA for the Nanomedicine Initiative. FRA allows for the support of research and development using funding mechanisms other than contracts, cooperative agreements, and grants (i.e., "other transactions"). It also explicitly removes requirements that standard review procedures be followed, allowing the use of alternative review procedures. It was believed that FRA would facilitate the development of an NDC program that was truly distinctive from extant NIH areas of activity as well as from the nanotechnology efforts of the NSF and other Federal departments and agencies also participating in the NNI.

The use of FRA was unique at the NIH, and the NIPT spent several months investigating the use of "other transactions," specified by Congress, by other agencies such as DARPA. As there was no NIH precedent, the program was designed using the philosophy that the NIPT would design the process and manage the awards in a way that could develop and evolve based on the scientific needs. After the transition to FRA, the NDC program launched in May 2004 with a public meeting outlining potential areas of scientific and technical foci for the first cohort of NDCs as well as plans and expectations of the NIPT regarding the solicitation and submission of NDC proposals.

One of the discrete outcomes of the NDC program's use of FRA was the establishment of new funding mechanisms, the PN1 (to fund the planning awards) and the PN2 (to fund the NDCs), which was used to fund the eight current NDCs. The mechanisms were developed specifically to allow flexibility not only in identifying initiative participants and in awarding funds, but in post-award management of the funds and directions of the centers.

3.3. Plans and expectations

The implementation plans for the first two rounds of competition underwent some changes due to the transition from conventional NIH mechanisms to FRA. But these changes were relatively minor. Before the transition to FRA, the implementation plan was to solicit "letters of intent" whereby applicants outlined in five pages or less their vision for an NDC. After vetting of the letters, applicants whose ideas demonstrated promise were to be selected to receive planning awards to develop further their plans for an NDC. Next, a series of workshops were to be held that included the NIPT, planning award recipients, and members of the ECG. The primary activity of the workshops was to be interactive discussion amongst the participants (as opposed to directives and instructions from the NIPT) to clarify what constituted "nanomedicine" (at least for the NDC program) as well as to discuss the RFA to be used to solicit full center proposals.

After the transition to FRA, the basic structure of the NDC selection processes remained intact. The plan was still to limit the competition to applicants with the most promising and relevant ideas, per a selection process based on the submission of initial letters of five pages or less. The plan to facilitate application development through planning awards and to facilitate RFA development through structured interactions amongst NIPT officials and applicants also remained in place. However, the specific structure of these interactions changed after the transition to FRA.

First, the new plans required that applicants in receipt of planning awards submit an interim document (i.e., post planning award, pre-NDC application) outlining in greater detail their vision for the scientific focus and organization of their proposed NDC. These Concept Development Plans (CDPs) or "long white papers" were to be 35-50 pages in length and resemble more closely a fully-articulated center proposal. Second, the series of workshops was supplanted by a single "planning meeting" to span multiple days. The intended outcomes of the planning meeting were the same as those for the initial workshops – to facilitate two-way discourse about what constituted nanomedicine as well as to discuss the yet-to-be written RFA for full center applications. The long white papers were to be submitted prior to the planning meeting to help the NIPT and ECG organize meeting sessions and panels.

From the outset, it was planned that the second round selection process would exclude planning awards and the attendant submission of CDPs and planning meeting. The rationale for these exclusions was that by the end of the first competition, NIPT officials would have much clearer ideas about what constituted nanomedicine and about what should be the language of the RFA soliciting full center proposals during the second round.

Although the structure for implementing the NDC selection processes was premeditated and clear, the preliminary expectations over what precisely was to occur during each phase of the selection processes (see Section 4 for a full description) were considerably more general. This was especially the case during the first round of competition, for instance with regard to the planning meeting to elicit discourse among the NIPT, applicants, and the ECG. The open-ended nature of the expectations was a function of uncertainty at the beginning of the program as to what scientific and technical foci were relevant to nanomedicine. From members of the NIPT,

> "Going into the process we had no prototype [for an NDC] in mind. Mostly we had ideas regarding associations in expertise, the mixture of disciplines that could form a center. We left it to the individual groups to set up the focus and structure."
>
> "It makes sense to think novel ideas through with planning awards and pre-applications. It is very useful. We knew that [the selection process] would evolve as we went."

The next section describes the actual implementation of the NDC selection processes.

4. Program implementation

After providing a clear understanding of programmatic origins and preliminary plans and expectations (see Section 3 above), the next step in process evaluation is to provide a thorough description of the process, as it occurred.[14] In this section, the events of the first and second rounds of competition for Nanomedicine Development Center (NDC) funding are outlined. Accordingly, this section is purely descriptive and does not constitute this report's evaluative analysis, which is detailed in the Executive Summary. The empirical basis for this chapter includes interviews with Nanomedicine Initiative Project Team (NIPT) officials, senior National Institutes of Health (NIH) officials who were not part of the NIPT, and programmatic documentation.[15]

4.1. Descriptive framework

This study uses two conceptual models to guide preliminary evaluation of the NDC selection process. The first model is a process diagram that identifies the activities and outputs for each "phase" of the selection process. The second model is a stakeholder map that identifies the participants involved during each phase. Taken together, the process diagram and stakeholder map structure the descriptive component of this evaluation of the NDC selection process by identifying who participated and interacted with whom, when, and in what capacity.

Two versions of the process model and stakeholder map are presented below, one for the first round of competition in 2004-2005 (Figures 1 and 2) and one for the second round of competition in 2006 (Figures 3 and 4). The two rounds are considered here as separate processes because the selection process for the second round of NDCs was itself an output of the first round selection process. Accordingly, the second round selection process warrants description and evaluation in its own right as a new, stand-alone process for selecting NDCs.

As shown in Figure 1, the first round selection process consisted of six phases, with each phase characterized by particular activities and outputs. For instance, the first phase of the Round 1 process, "RFA for Concept Development Memos (CDMs)," is characterized by the NIH advertising the Request for Applications and the scientific community preparing CDMs (i.e., the phase activities), which yielded 81 CDM submissions (the phase outputs). The second phase, "CDM review," consisted of both NIPT officials and ECG members reviewing these submissions (i.e., the phase activity) and deciding which 20 would receive planning awards (i.e., the phase output). The remaining phases are delineated in a similar fashion. Figure 3 presents the process model for Round 2.

[14] See: Rossi, P.H., M.W. Lipsey, and H.E. Freeman (2004) *Evaluation: A Systematic Approach, 7th Edition*. Thousand Oaks, CA: Sage; also see: Scheirer, M.A. (1994) "Designing and Using Process Evaluation" In J.S. Wholey, H.P. Hatry, and K.E. Newcomer (Eds.) *Handbook of Practical Program Evaluation*. San Francisco: Jossey-Bass, p. 40-68.

[15] For a full description of methodology, see Appendices B-D.

Figure 2 provides a stakeholder map that details "who did what" during each of the process phases outlined in Figure 1a. To illustrate, revisiting the first phase of the NDC selection process, Figure 2 demonstrates who within the NIH participated, including the NIPT. Figure 4 presents the stakeholder map for Round 2.

Throughout this report, we use the process diagrams and stakeholder maps to frame presentation of the details of the NDC selection processes. Following the figures below is further description of the Round 1 and Round 2 selection processes. The purpose is to provide sufficient background information and context for the remainder of this report.

Figure 1. Round 1 NDC selection process diagram

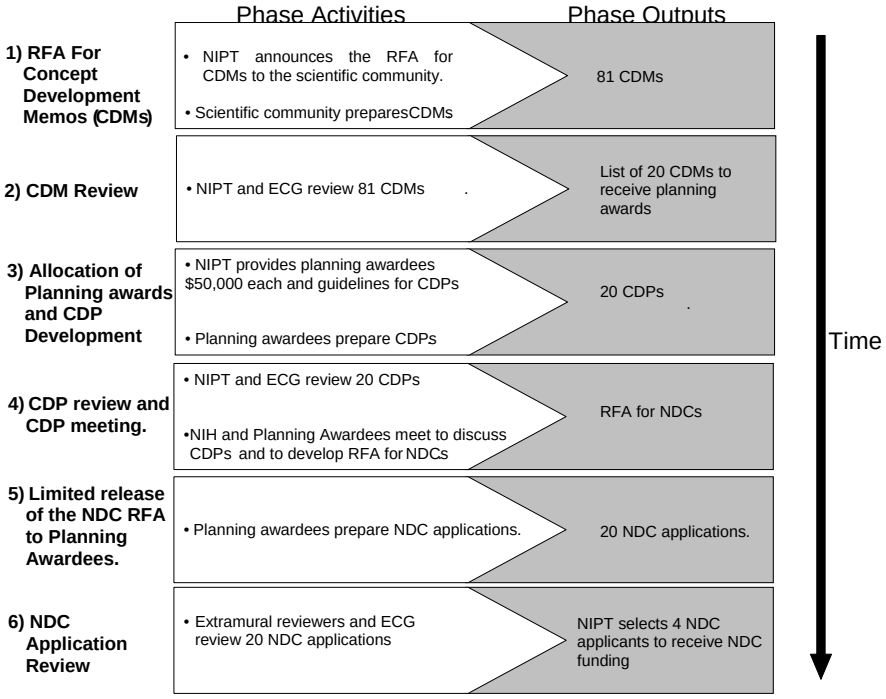


Figure 2. Round 1 NDC selection process participant and stakeholder map

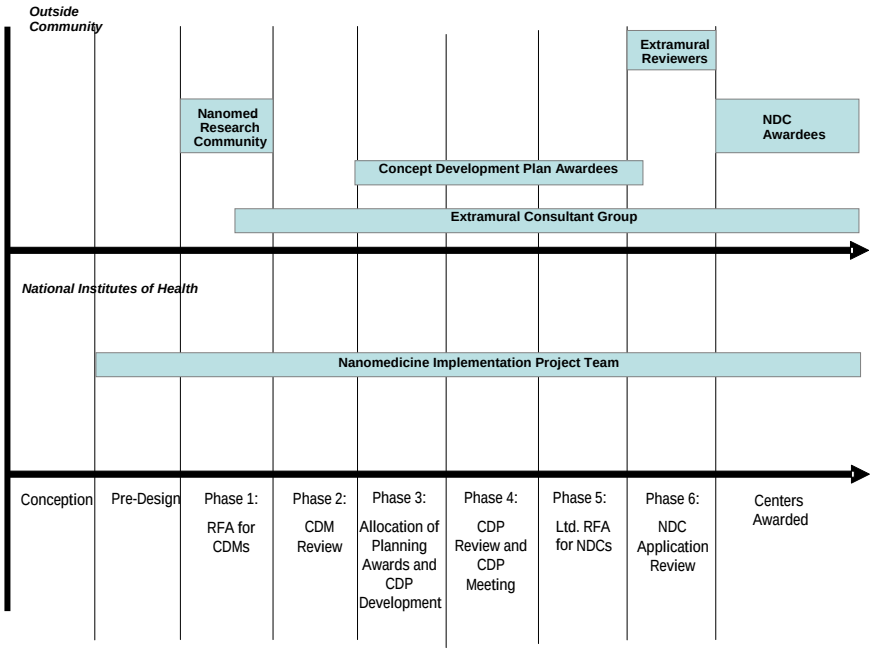


Figure 3. Round 2 NDC selection process diagram

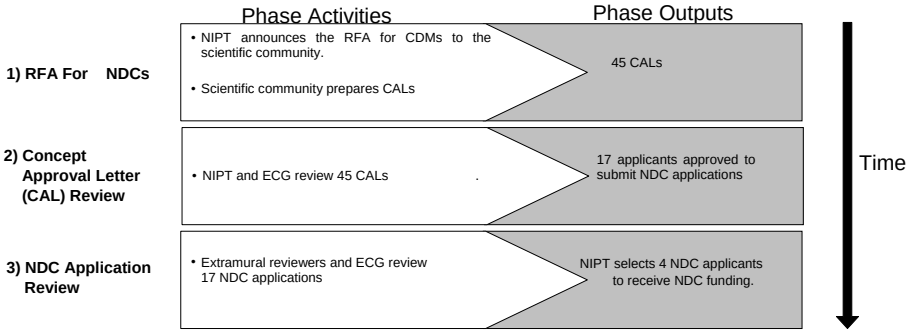
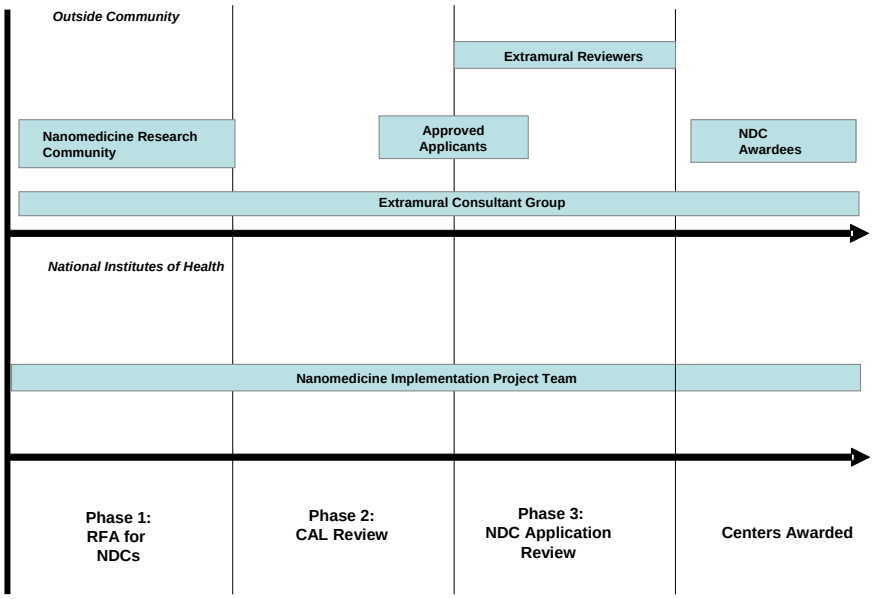


Figure 4. Round 2 NDC selection process participant and stakeholder map



4.2. Round 1 selection process, 2004-2005

4.2.1. Pre-competition activities and interactions

The first formal interactions between the external scientific community and the NIPT officials in charge of the selection process occurred at an informational meeting held on May 4, 2004. This public meeting was organized by the NIPT to receive early feedback from the scientific community regarding the NIH vision for the first generation of NDCs as well as to announce the details of the initial Request for Applications (RFA).

The meeting lasted a full day. The initial presentations were by senior NIH officials, including Deputy Director Raynard Kington, the Director of the National Eye Institute (NEI), Paul Sieving, and Jeff Schloss of the National Human Genome Research Institute. In these presentations, the overarching scientific and clinical goals of the NDC program were articulated:

- Characterize quantitatively the physical and chemical properties of molecules and nano-machinery in living cells;
- Gain an understanding of the engineering principles used in living cells to "build" molecules, molecular complexes, organelles, cells, and tissues;
- Use this knowledge of properties and design principles to develop new technologies, and engineer devices and hybrid structures, for repairing tissues as well as preventing and curing disease

In addition, the NDC program was described in context of the broader mission of the NIH Nanomedicine Roadmap Initiative. Schloss characterized the program as the beginning of a ten

year process towards the clinical ability to manipulate biological systems within living cells for the improvement of health.

After a series of sessions on the multiple types of expertise that could contribute to nanomedicine development and on example development "targets" for centers, the afternoon sessions focused on strategies for creating cross-institutional and cross-disciplinary research teams. The final discussion was led by the NIPT Director, Richard Fisher, who detailed the application process and timeline for the first round of competition (see below).[16]

4.2.2. Phases 1 and 2: CDM submission and review

Scientists interested in applying for center funding were required to pass a preliminary competition phase before moving forward in the selection process. Interested parties submitted in response to the initial RFA a five-page white paper called a CDM. In the CDMs, applicants outlined in broad terms their respective visions for the scientific and technical focus and structure of their proposed NDC. In particular, CDMs contained descriptions of how preliminary planning funds would be used to further develop these visions and plans. These descriptions included the organizing of workshops and teleconferences (e.g., reserving conference rooms), identifying and soliciting experts in the field to participate in the workshops and teleconferences, providing these participants with video conferencing capabilities if they cannot attend in person, and providing participants with funds for travel, lodging, and per diem if they can participate in person. In some cases, funds were allocated for workshop participants to bring post-doctoral assistants and other junior colleagues. The deadline for submitting CDMs was July 26, 2004.

Eighty-one CDMs were received in response to the RFA. In accord with Flexible Research Authority (FRA), the NIPT used a group of extramural consultants – forming the program's Extramural Consultant Group (ECG) – to help review the CDMs. The two chief review criteria were the breadth of the scientific and technical foci and the responsiveness of these foci to the goals of the Nanomedicine Initiative as stated in the RFA. The NIPT and the ECG selected 20 CDMs to receive Concept Development Awards (CDA) of $50,000 each.

[16] In addition to the sources of data outlined in the Executive Summary, the observations in this section were drawn from viewing an online video of the informational meeting on October 20, 2007 at http://nihroadmap.nih.gov/nanomedicinelaunch/ .

Table 2. Timeline of events for the first round selection process

Activity	Date or deadline
Public informational meeting to describe the initial RFA and the overall Nanomedicine Initiative	May 4, 2004
Receipt of Concept Development Memos	July 26, 2004
Funding of Concept Development Awards	September 30, 2004
Receipt of Concept Development Plans	February 15, 2005
Meeting of submitters of Concept Development Plans	March 10, 2005
Publication of solicitation for Nanomedicine Development Centers	April 1, 2005
Receipt of applications for Nanomedicine Development Centers	July 12, 2005
Review of Nanomedicine Development Center applications	August 31 to September 2, 2005
Funding of Nanomedicine Development Centers	September 15, 2005

4.2.3. Phase 3: Planning awards and CDP development

The CDAs were announced on Sept 30, 2004. The intent of the CDAs was to aid recipients in assembling research teams and further refining their ideas for their proposed center. The primary output of this preparation was a longer white paper called a Concept Development Plan (CDP), for which NIPT officials prepared and disseminated detailed instructions for distribution to planning awardees.

The main message conveyed in the instructions was that the CDPs did not have to resemble closely the concepts proposed in the CDMs. This message was stated multiple times and in boldface font. Specifically, the instructions detailed numerous aspects of the initial RFA that many CDMs did not devote attention to, including:

- Elucidating new fundamental knowledge of the biological systems;
- Enumerating the specific knowledge gaps that would be filled;
- Stating explicitly what new quantitative measurement capabilities would be developed;
- Explaining how decisions to develop novel measurements will be driven by specific gaps in knowledge of biological design or by the need to determine key parameters of the mathematical models being developed;
- Revealing potential engineering principles associated with. or that could be applied to, nanomedicine; and
- Justifying how data quality and measurement uncertainties would be addressed and how that would affect quantitative modeling.[17]

[17] This bulleted list is reproduced verbatim from the referenced "CDP instructions."

In no uncertain terms, the CDP instructions constituted a reiteration of the NDC program's goals writ large and clearly stated the expectation that CDPs be more responsive to the initial RFA than were the CDMs. The instructions also included guidelines for formatting the CDP.

Recipients used the planning awards for organizing workshops to further develop their vision for an NDC. Generally, the money was used to pay for flights, meeting accommodations, lodging, as well as administrative support. The workshops lasted between two and four days for each of the 20 groups.

Twenty CDPs were submitted to the NIPT by February 15, 2005. In addition to helping applicants further develop their respective visions for an NDC, the CDPs also served as an interim indication to the NIPT and the ECG of the extent to which applicants remained focused on program goals as specified in the initial RFA. The CDP was not intended by NIPT officials to constitute a first draft of the full center application.

Specifically, the CDPs elaborated on the vision for the proposed NDC included in the CDM, describing in specific detail the scientific and technical approaches that the applicant team would propose in the subsequent center application. Additionally, the CDPs included a proposed structure for how each center should be structured and should operate individually as well as within a broader network of centers.

4.2.4. Phases 4 and 5: CDP meeting and Limited Competition RFA

A month after submission of CDPs, the NIPT and ECG met with the principal investigators and some key personnel from each of the 20 teams that received planning awards. During this meeting, the applicant teams presented information about their CDPs and participated in "breakout sessions" to discuss the extent to which their ideas corresponded with the NIH Nanomedicine vision as well as how their proposed NDC would operate within a broader network of centers dedicated to nanomedicine.

Table 3. Agenda for the Nanomedicine Concept Development Plan meeting

Date	Time	Activity
March 10, 2005	8:30 AM	Welcome and Introductions (Richard Fisher – NIPT)
		Meeting Goals and NIH Vision (Jeff Schloss, Paul Sieving – NIH)
	9:00 AM	CDP Presentations, Part 1 (Chaired by Denis Buxton – NIPT)
	11:00 AM	CDP Presentations, Part 2 (Chaired by Catherine Lewis – NIPT)
	1:15 PM	CDP Presentations, Part 3 (Chaired by Eleni Kousvelari – NIPT)
	3:15 PM	CDP Presentations, Part 4 (Chaired by Karen Peterson – NIPT)
	4:45 PM	Wrap-up, New Issues (John Bowers – NIPT)
	5:30 – 7:30 PM	Poster session, Drinks
March 11, 2005	7:30 AM	Objectives, New Issues (Dan Gallahan – NIPT)
		Breakout Group Assignments and Instructions (King Li – NIPT)
	8:30 – 11:30 AM	Breakout Groups Meet (Center Models, Network Organization, Post-Award Issues, NIH Nanomedicine Vision)
	1:00 PM	Breakout Group Presentations
	3:00 PM	Adjourn (Richard Fisher – NIPT)

The meeting lasted for two days and was intended to help applicant teams be as responsive as possible in their center applications to the RFA, which was released a month after the meeting on April 13, 2005. The RFA was written specifically for the planning awardees who participated in the CDP meeting.

The RFA for full applications was relatively unique in its call for "higher-risk" studies and the preclusion of the requirement to include preliminary data and findings. However, applicants were required to address the level and nature of risk for the proposed research and to present a rational scientific plan for achieving stated center goals. Additionally, the RFA was unique in the requirement that applicants describe how the proposed center would interact with other NDCs in a network of centers, though applicants were informed that proposed network interaction would not be used as a formal review criterion.

4.2.5. Phase 6: Application review and center awards

The full NDC applications were reviewed from August 31 to September 2, 2005. FRA empowered the NIPT to develop a review process that diverged from conventional NIH practice. The new process was motivated by the need to consider during review not just the ability of applicants to meet programmatic as well as scientific and technical goals, but also to consider the selection of high-risk proposals lacking preliminary data and results.

The review process was relatively interactive. Members of the NIPT and the ECG participated during the reviews by interacting freely with the extramural reviewers, who were identified and recruited by the NIPT. Prior to the review meeting, the NIPT and ECG hosted two conference calls to inform the reviewers about the new procedure.

Each NDC application was assigned six extramural reviewers, with each reviewer reading numerous applications in addition to those they were reviewing formally to facilitate discussion of potential collaborations among the proposed centers. The review teams also included members of the ECG. Reviewers submitted written reviews using Internet Assisted Review – the online system used across the NIH to manage the process of electronic submission of critiques by reviewers. In addition to the written critiques, reviewers indicated their enthusiasm for the application as high, medium, or low.

Final scores were determined by private voting, and applications were grouped into bins with priority scores of 100 (best), 200, or 300 (worst). Extramural reviewers and members of the ECG were not involved in the final decision process. The decision of which applications to fund was made solely by the NIPT.

4.3. Round 2 selection process, 2006

4.3.1. Phases 1 and 2: Concept Approval Letter submission and review

Unlike the first round of competition, in the second round a single RFA was used to solicit five-page Concept Approval Letters (CALs) and full applications. Substantively, there was no significant difference between the second round CAL and the first round CDM. Functionally, CALs were used by NIPT officials to determine who would be permitted to submit full center applications. However, unlike first round CDMs, second round CALs were not used to award planning funds to approved applicants.

Forty-five CALs were received in response to the RFA. In accord with FRA, the NIPT and ECG approved 17 to submit a full center application. As in the previous year, the chief review criteria were the breadth of the scientific and technical foci and the responsiveness of these foci to the goals of the Nanomedicine Initiative as stated in the RFA.

Similar to the first round, the second round solicitation called for “higher-risk” studies. However, the RFA did require applicants to address the level and nature of risk for the proposed research, to present a rational scientific plan for achieving stated center goals, and to describe how the proposed center would interact with existing NDCs in a network of centers.

Table 4. Timeline of events for the second round selection process

Activity	Date or deadline
Publication of solicitation for Nanomedicine Development Centers	January 26, 2006
Receipt of Concept Approval Letters	March 15, 2006
Approval to Apply	April 17, 2006
Receipt of applications for Nanomedicine Development Centers	June 23, 2006
Review of Nanomedicine Development Center applications	July 30 to 31, 2006
Funding of Nanomedicine Development Centers	September 20, 2006

4.3.2. Phase 3: Application review and center awards

Approved applicants submitted their full NDC applications by June 23, 2006. They were reviewed from July 30 to July 31, 2006. As during the first round of competition, FRA empowered the NIPT to use a review process that diverged from conventional NIH practice.

The review process for the center applications was nearly identical to that employed during the first round of competition, wherein members of the NIPT and the ECG participated directly in the reviews by interacting freely with the extramural reviewers. Among the characteristics of the review process that were the same in Round 2 as in Round 1:

- Extramural reviewers were identified and recruited by the NIPT.
- Prior to the review meeting, the NIPT and ECG hosted two conference calls to inform the reviewers about the new procedure.
- Each NDC application was assigned 6 extramural reviewers, with each reviewer reading numerous applications in addition to those they were reviewing formally to facilitate discussion of potential collaborations among the proposed centers.
- The review teams included members of the ECG in addition to extramural reviewers.
- Reviewers submitted written reviews using Internet Assisted Review – the online system used across the NIH to manage the process of electronic submission of critiques by reviewers.
- In addition to the written critiques, reviewers indicated their enthusiasm for the application as high, medium, or low. Final scores were determined by private voting, and applications were grouped into bins with priority scores of 100 (best), 200, or 300 (worst).
- Extramural reviewers and members of the ECG were not involved in the final decision process. The decision of which applications to fund was made solely by the NIPT.

4.4. Differences between the Round 1 and Round 2 selection processes

As the above descriptive framework and descriptions demonstrate, the second round process for selecting NDCs did not include planning awards, require the drafting of CDPs by approved applicants, nor did it include a meeting wherein applicants and members of the NIPT and ECG interacted to discuss proposed ideas and plans for a potential NDC. According to NIPT officials, the exclusion of these features during the second round process was "by design." During the first round, the planning awards, CDPs, and CDP meeting were required to facilitate consensus amongst participants as to the meaning of the concept of nanomedicine and how it should be pursued in a cross-disciplinary and inter-institutional university research center. Indeed, the Round 1 solicitation for full center applications was not drafted until after the CDP meeting had occurred. During the second round, according to NIPT officials these steps in the selection process were no longer required. While they were far from consensus over what constituted nanomedicine, they felt they had defined what an NDC should "look like" sufficiently to use an updated version of the previous round's solicitation for full center applications.

5. Effectiveness findings: Facilitating interactions

In addition to describing what happened during program implementation, another major component of process evaluation is assessing the extent to which the implementation process was "effective." There are a number of criteria along which an implementation process may be deemed effective or not, depending on the programmatic goals. These criteria may be generic across programs (e.g., Did the process reach the target population?) or specific to a particular program (e.g., Did the Concept Development Plan meeting facilitate interactions and the cross-pollination of ideas?).[18]

However, it is important to remember that process evaluations are not the same as output and outcome evaluations. While the Nanomedicine Development Center (NDC) selection processes certainly produced outputs and effected outcomes, it is not the purpose of this report to measure such outputs and outcomes. Rather, the purpose is to assess how effectively the Nanomedicine Implementation Project Team (NIPT), enabled by use of Flexible Research Authority (FRA), implemented a novel center selection process whereby scientists and engineers from a range of biomedical, engineering, and physical science disciplines engaged with one another through a highly interactive process involving applicants, extramural reviewers, NIPT program staff, and Extramural Consultant Group (ECG) members.

Accordingly, one of the primary measures of effectiveness employed in this evaluation is the extent or intensity of interactions that occurred at each phase of the NDC selection processes. Because not all interactions occurred in the ways intended by the NIPT and ECG, the nature and impact of the interactions that occurred at each phase of the selection processes are also evaluated.

This section, presents the perspectives of NDC awardees, unsuccessful applicants, extramural reviewers, and ECG members regarding the interactions they experienced during their participation in the NDC program. Taken together, the data indicate that the NDC selection processes were highly effective at facilitating interactions, but that these interactions did not always have the desired effects.[19] This section is empirical and draws on data collected during in-depth discussions.[20] No quantitative decision rules were used for inclusion or exclusion of the findings. Both unique and common perspectives are presented.[21]

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[18] General criteria for program effectiveness, such as "program coverage" and the novelty of the proposals submitted, are evaluated in subsequent sections of this report.

[19] For evaluative conclusions and recommendations regarding the interactions of the NDC selection processes, see the Executive Summary.

[20] For a full description of methodology, see Appendices B-D.

[21] It is important to note that in a qualitative case study, statistical inferences need not and cannot be made. For example, the perspective of one NIPT member could be of greater insight and value to the program than a common (and perhaps contrary) perspective shared across all extramural reviewers. Accordingly, the findings in this report are presented as-is. When they are interpreted in the Executive Summary, weight is given to the perceived evaluative value of the perspective and not to the number of interviewees supporting that perspective. However, some highly "valuable" perspectives may be shared across numerous interviewees. Moreover, the quantity of quotations to support one perspective versus another is a function of the data, not of the perceived importance of a particular perspective on the part of the Science and Technology Policy Institute (STPI) evaluation team.

5.1. Applicant perspectives

Most of the applicants interviewed agreed that the selection process was "very different" in terms of the interactions they had, no matter the degree of success the applicants experienced during the selection process. Applicants who were triaged after submission of their initial "short white paper" (i.e., the Concept Development Memo in Round 1, Concept Approval Letter in Round 2) as well as those who were ultimately awarded center funding described the interactions as "more frequent" and "unorthodox" when compared to conventional selection processes.

5.1.1. Pre-competition and phases 1-2: Preliminary informational meeting and CDM submission and review

Applicant interactions with NIPT officials preceding the initial Request for Applications (RFA) soliciting the first round Concept Development Memos (CDMs) were fostered by the informational meeting held by NIPT officials on May 4, 2004. This public meeting was held to discuss the NIH vision for the NDC program, receive comments from the scientific community, and announce the details of the initial RFA.

The informational meeting was sufficient to preclude much interaction amongst NIPT officials and applicants during the span of time after the informational meeting but before submission of the CDMs by July 26, 2004. However, additional "pre-CDM" interactions did occur when applicants had personal contacts who were NIPT officials. In one case, the program official convinced an applicant to apply,

> "[My contact] told me about the RFA when it came out. I was confused by it, so she explained it to me. I was skeptical that my expertise would fit in well with the program vision and goals, but [my contact] thought otherwise. [The contact] translated the terms of the RFA into a language I could understand. We had a number of interactions to clarify what the program was looking for in an NDC."

In another instance, an applicant was made aware of the NDC program after the initial informational meeting had already occurred,

> "Before I was told about [the NDC program], I had no idea the program existed. I was usually looking in computational biology for funding opportunities. [My contact] sent me an email before the initial RFA deadline."

5.1.2. Phase 3: Planning awards and CDP development

Applicants during the first round of competition reported few interactions with NIPT officials or any other participants while drafting their Concept Development Plans (CDPs). What interactions did occur related to logistical elements of the selection process, for instance document formatting for the CDP. These interactions usually occurred as a brief email exchange between the program director, Richard Fisher, and the applicant.

5.1.3. Phase 4: CDP meeting

The CDP meeting was the pivotal phase of the NDC selection process, directly for the first round of competition and indirectly for the second round, because of the meeting's goal to determine what an NDC ultimately should "look like" in terms of scientific and technical foci, personnel and management, and as a node in a broader network of multiple NDCs. During this meeting, which occurred during the first round of competition on March 10, 2005, NIPT officials sought input from the 20 recipients of planning awards who had recently authored and submitted CDPs by February 15, 2005 and also from ECG members. Accordingly, applicants interacted with NIPT officials, ECG members, as well as with one another.

At the meeting each applicant team presented their ideas for a potential NDC to program officials and ECG members as well as to their fellow competitors. While many of the applicants described the meeting as "interesting," most reported that the requirement to present their plans made them feel uneasy about the selection process.

> "[The CDP meeting] was interesting. It was the first time I ever met my competitors in an application process. This is not something you normally do. On one hand we had to present to the program officials and advisors and also to our competitors what we are doing. This was unusual and unconventional. After [the presentations], we didn't interact with anybody other than our team."

> "The meeting was quite interesting. They put the competitors in a room together. It was very uncomfortable and high pressure during the presentation."

> "It was like *Survivor*. We had break out sessions and [the participating NIPT officials] told us we were writing the RFA. So each group wanted the RFA to reflect what each was doing. It was quite contentious. It was unusual to argue with competitors."

Applicants interacted less formally during a poster session and during breakout panels comprised of multiple applicant teams, NIPT officials, and ECG members. The poster sessions proved to facilitate little interaction beyond follow-up questions from NIPT officials and ECG members. Applicants did not report interacting with one another at the poster session. For the breakout panels, each applicant team distributed investigators across the different panels.

The breakout panels facilitated some interaction amongst applicants, ECG members, and NIPT officials regarding complementarities among some of the applicant teams. However, as with the presentations, the applicants felt uneasy about these interactions,

> "The message I heard from the program officials was 'maybe you guys can collapse into consortia and apply together.' But the prevailing attitude was 'I'm not going in with anybody.'"

> "There was very little real thinking about cross-center synergies. Everyone was thinking about competing."

> "It was part of the RFA to describe potential interactions with the other planning awardees' centers, if they were to be funded, that is. But I do not recall any such discussions at the CDP meeting."

Generally, the applicants did not view the CDP meeting as an opportunity to develop collaborations with one another. During the interviews, applicants were pressed about why they perceived so negatively the interactions and discussions of potential synergies with one another. Some responded that they were simply "being competitive,"

> "The important thing was to know who our competitors are. After [the meeting], we were cautiously optimistic."

Others disclosed that they did not believe that combining groups into a single NDC application to be plausible financially.

> "The problem was that the money was only a million [dollars] a year. I had 20 investigators. To combine with another center would be implausible."

In summary, the 20 applicant teams who participated in the CDP meeting found the interactions to be unorthodox and uncomfortable. Further, the applicant teams considered the meeting to be more instructional than interactive, with NIPT officials dictating what does and does not constitute "nanomedicine" in the context of the program rather than engaging with the applicants to conjointly develop a working definition. Accordingly, some reported growing skeptical about the program and its goals after the CDP meeting, rather than feeling encouraged about the input they received during the meeting regarding their respective plans for an NDC. However, others reported feeling "encouraged and confident" about their chances for receiving center funding – after learning about the center concepts they were competing against – which ultimately proved justified since these applicant teams were awarded center funding during the first round of competition.

5.1.4. Phases 5-6: Limited competition RFA and application review

During the first round of competition, there was little interaction involving applicants after they submitted full NDC applications, by July 12, 2005. When applicants were included in "post-NDC application submission" interactions, they were with NIPT officials and were initiated by applicants with personal contacts serving on the NIPT. From the same applicant who was convinced by a program official to apply for a planning award during the "pre-CDM" phase of the first selection process,

> "[My contact] told us how we should write our application, how to position the 'final pitch.' This input was extremely valuable."

5.1.5. Round 2 interactions

Compared to the first round of competition, the second round for selecting NDCs was relatively non-interactive. This is in large part owing to the fact that during the second round there were no planning awards and, subsequently, no interim CDPs before submission of the full applications. Moreover, a large proportion of the applicants approved to submit a full application for the second round participated during the first round. Accordingly, applicants reported few Round 2 interactions beyond the submission of document deliverables. However, Round 2 was still relatively interactive from the perspective of extramural reviewers, NIPT personnel, and ECG members.

5.2. Extramural reviewer perspectives

Extramural reviewers' participation in both rounds of competition was limited to the formal review of full center applications. They did not participate in the triage review of the CDMs at the outset of the first competition, to determine the recipients of planning awards. Furthermore, at no phase of the NDC selection processes did the extramural reviewers have official contact with the applicants.

Most of the extramural reviewers interviewed characterized the review board process as relatively interactive when compared to conventional review boards, notably per the explicit involvement of NIPT officials and ECG members. This characterization held no matter during which round of competition the reviewers participated. The interactions were characterized as "strange" but also as "helpful" in terms of keeping in mind the NDC program goals for centers pursuing "out of the box" and "near science fiction" concepts. However, others perceived the interactions in a less helpful and in one instance even a suspicious light, with some reviewers reporting that they felt NIPT officials to be advocating for specific center applications.

5.2.1. Pre-review: Teleconferences

The extramural reviewers for both rounds of competition had little contact with each other, NIPT officials, or ECG members prior to the formal reviews. However, for each round there was a preliminary conference call – lead by NIPT officials and including the extramural reviewers – to discuss how the review was to differ from "standard NIH practice." Generally, the conference calls were perceived as "different" yet "instructive." From an extramural reviewer who participated in both rounds of competition,

> "[The conference call] was new to me. I had not experienced that before. We were all on the call listening to the program officials' instructions. The emphasis was on getting the review criteria straight… they wanted less emphasis than usual on preliminary results."

Prior to the review meeting, some extramural reviewers additionally were contacted individually by NIPT officials to help determine which applications they felt competent to review.

5.2.2. Phase 6: Application review and center awards

For each round of competition, the review meeting was the pivotal phase of interaction for the extramural reviewers. For the first round, the review ran from August 31 to September 2, 2005. For the second round, the review ran from July 30 to July 31, 2006.

During the meetings, all applications were discussed. NIPT officials and ECG members were present and free to participate in the discussion, though only the extramural reviewers submitted scores for the applications (see below). In general, NIPT officials' and ECG members' participation consisted of questions and comments to clarify an aspect of the center application and/or the requirements of the RFA and the Nanomedicine Initiative more generally. These contributions were received well by most of the extramural reviewers, who understood what NIPT officials "were trying to do." From a reviewer from the first round of competition,

> "The NIH program staff was allowed to speak up and explain things. Clearly, they had worked hard up to that point and they wanted to make sure that the applications were reviewed to a different standard."

Another reviewer considered the interactions an improvement upon standard NIH practice,

> "It was actually kind of helpful. [NIPT officials and ECG members] shed light on some of the issues regarding the applications. We started asking program staff about specific investigators. It was helpful to get this perspective. In contrast, in CSR study sections, sometimes you feel like you don't have all of the information you need. This time this wasn't the case."

However, some reviewers perceived the participation of NIPT officials and ECG members to be disruptive.

> "The way the input was given [by NIPT officials and ECG members] was unusual. They had more to say about the goals of the program than they did about the applications."

> "It was an interesting panel. Some of the NIH staff had been involved for a longer time and had been following the applications. Others, reviewers like myself, were involved only in the end. My opinion did not appear to be weighted as highly as the comments of those that were involved long-term."

Other reviewers reported concern that NIPT officials made comments to advocate specific applications rather than to remind and inform the extramural reviewers about the program's relatively unique goals.

> "During the review, [NIPT officials] acted as cheerleaders… I had significant reservations about whether this was right. I have always been a staunch defender of the R01."

In the end, most extramural reviewers did not feel that the participation of NIPT and ECG members affected which applications were ranked highly and which ones received lower scores. However, many reported that they ranked "riskier" proposals higher than they would have in previous review experiences.

After scoring the applications, extramural reviewers had no formal interactions with each other, NIPT officials, or ECG members. Most were not aware of how their scores were to be used in the final decision to fund centers, though there was general understanding that the scores were to be used as recommendations to be considered by NIPT officials in their funding decisions rather than as final rankings used to distinguish the winning applications.

5.3. Extramural Consultant Group perspectives

Relative to applicants and extramural reviewers, members of the ECG had extensive interactions throughout both rounds of competition. ECG members interacted with NIPT officials during the initial triage reviews of the CDMs and CALs, with NIPT officials and planning awardees during the first round CDP meeting, and with reviewers and NIPT officials during the reviews for both rounds. Additionally, for both rounds ECG members were present at the meetings at which NIPT officials decided on the applications that would be awarded center funding.

Most of the ECG members interviewed characterized the selection process as relatively interactive when compared to conventional funding mechanisms. Many characterized the interactions as "unfamiliar" but also as "progressive" insofar that the NIPT officials they were advising were focused on stimulating ambitious center proposals that probably would not be funded by alternate programs implementing standard NIH practices. Unlike extramural reviewers and applicants, ECG members did not report having reservations or doubts about the program's goals or the use of FRA to pursue those goals.

5.3.1. Phases 1-2: CDM submission and review

Most members of the ECG became involved with the NDC selection process once the CDMs and CALs were submitted by applicants. In both rounds, the ECG members assisted NIPT officials in reviewing the five-page submissions in the course of a single day's meeting.

Some of the ECG members felt the side-by-side interactions with NIPT officials to be more interactive than previous experiences,

> "What was different was that the program managers were at the same table as us. It was more of a dialogue than I have ever experienced before, within the NIH."

ECG members also found these interactions to be helpful,

> "The program guys were asking questions that were clearly motivated towards what they wanted to achieve with the program and were asking questions like 'How is this different

> than [the applicant's] R01 program that is already funded?" and 'Where's the medicine part of the project?' It was very helpful."

Yet, some characterized the initial interactions with NIPT officials as relatively awkward,

> "[ECG members] didn't know how to behave at first. They were there as advisors, advising how money should be spent. There was a lot of unfamiliarity with the process… There were lots of questions about FRA."

However, one of the ECG members found the interactions with NIPT officials to be consistent with previous experience using conventional mechanisms,

> "It was normal at the CDM stage – similar to R01 procedures. Though the proposals and the program generally were very different, at the CDM stage we were working together [with NIPT officials] to see if there was promise for a viable program, which is a fairly normal thing to do."

Generally, the ECG members interviewed agreed that these preliminary interactions were productive, yet not necessarily persuasive,

> "I think the interactions colored my thoughts, but they did not change my mind. Most of us had unswayed opinions. Not much score-changing occurred despite all of the discussion, but it helped me to remember that this was a different process and was not a typical study-section type of process."

In both rounds, ECG members were not included in the final meetings to decide which applicants to invite to submit NDC applications.

5.3.2. Phase 4: CDP meeting

For the first round of competition, the CDP meeting was the next point at which ECG members interacted with other participants in the NDC selection process. At the CDP meeting, ECG members listened to applicants present their proposals for an NDC and participated in the breakout panels. Although the overarching goal of the meeting was to generate consensus about what constituted "nanomedicine" and what did not, most ECG members confirmed what the applicants reported – that the meeting was more instructional, with NIPT officials and ECG members advising applicants on how to alter their center proposals to better suit program needs.

Most of the ECG members interviewed characterized their interactions with applicants as adversarial,

> "As I recall, the implementation team and advisors were telling the applicants 'here's the big vision your application should have,' because the applicants were struggling with the out-of-the-box ideas the program wanted to promote. There was a lot of unnecessary complaining [by the applicants] and not enough focus on developing ideas in terms of the centers."

> "The program was out of the realm of what [the applicants] had usually done, so we needed to help them see that we really wanted to see futuristic, blue-sky ideas that were more than ten years out. We helped people understand what the process was and what was required. It created a lot of tension with the applicants."

The ECG members interviewed did not have many comments about their CDP meeting interactions with NIPT officials. The key interactions were with the applicants. Generally, at the CDP meeting as well as during the review of full applications (see below), the ECG members viewed themselves as extensions of the NIPT.

5.3.3. Phase 6: Application review and center awards

During the meetings for review of the full center applications in both rounds, ECG members interacted directly with extramural reviewers and NIPT officials. ECG members interacted with extramural reviewers as reviewers themselves,

> "I reviewed as a first, second, and third reader. Everyone showed up having read [the full center applications.] We developed a rank-order and then left it to the implementation team to determine which ones would be funded."

ECG members also functioned as advocates of program goals,

> "Some of the reviewers were working as if it was a standard R01. It was part of my role to help them understand that this was supposed to be different and that we needed to cut [the applicants] some more slack when reviewing their proposals."

> "One or two of the reviewers expressed confusion as to what was expected of the applications. What is the quality of the science or something more? We conveyed to them that there had to be more than the science, a 'center mode,' as well as clear application towards medicine."

Many of the ECG members noted that their interactions with NIPT officials were comparably guiding,

> "NIH people were really speaking out about what was expected. This kept us on track. People from various institutes provided a more global perspective of what the expected impact of the centers should be."

After scoring the applications, ECG members had no formal interactions with each other, NIPT officials, or reviewers. Most were not aware of how their scores were to be used in the final decision to fund centers, though there was general knowledge that the scores were to be used as recommendations to be considered by NIPT officials in their funding decisions rather than as final rankings used to distinguish the awardees from the losing applications.

6. Effectiveness findings: Impact on proposals

As the above section demonstrates, the Nanomedicine Development Center (NDC) selection processes involved substantial interaction among applicants, Nanomedicine Implementation Project Team (NIPT) officials, Extramural Consultant Group (ECG) members, and extramural reviewers. These interactions had some effects intended by NIPT officials, including interactions altering the scientific scope (i.e., broadening or narrowing) of proposals so that they better matched program goals. However, the interactions did not have the many of the intended effects, for instance those designed to foster collaborations among the applicants.[22]

The most interactive phase across both rounds of competition was phase 4 of Round 1 – the Concept Development Plan (CDP) meeting that included the NIPT, ECG, and principal investigators and some of the key personnel from each of the 20 applicant teams that received planning awards. The purpose of the meeting was to help applicant teams be as responsive as possible to the eventual limited competition solicitation for NDC applications.

This section focuses on the perceived and actual impacts of the interactions that occurred during the CDP meeting on the NDC applications. After presenting applicants' reports about the impact of the meeting on their ideas and approaches towards a potential NDC, findings from content analyses of the application documents submitted during the selection processes (e.g., Concept Development Memos [CDMs], CDPs, full center applications) are reported. Accordingly, this section is empirical.[23] No quantitative decision rules were used for inclusion or exclusion of the findings. Both unique and common perspectives are presented.[24]

6.1. Applicant perspectives

The primary goal of the CDP meeting was to ensure that the research proposed by the center applicants, including their scientific and technical goals, was aligned with the NIPT's vision of nanomedicine to be pursued by a network of NDCs (see Section 4 for a full description of the meeting). However, most of the applicants interviewed did not feel that their interactions during the CDP meeting had significant effects on their research plans or their scientific and technical approaches.

[22] For evaluative conclusions and recommendations regarding the impact of the NDC selection processes on center proposals, see the Executive Summary.

[23] For a full description of methodology, see Appendices B-D.

[24] It is important to note that in a qualitative case study, statistical inferences need not and cannot be made. For example, the perspective of one NIPT member could be of greater insight and value to the program than a common (and perhaps contrary) perspective shared across all extramural reviewers. Accordingly, the findings in this report are presented as-is. When they are interpreted in the Executive Summary, weight is given to the perceived evaluative value of the perspective and not to the number of interviewees supporting that perspective. However, some highly "valuable" perspectives may be shared across numerous interviewees. Moreover, the quantity of quotations to support one perspective versus another is a function of the data, not of the perceived importance of a particular perspective on the part of the Science and Technology Policy Institute (STPI) evaluation team.

Some applicants indicated that their proposals "did not change much" from CDP to full center application, while others reported that their proposals did not change at all beyond the additional formatting and substantive requirements for the full NDC application. However, a few applicants reported that their encounters with NIPT and ECG personnel resulted in mild shifts in the scientific and technical scopes of their proposals. For example, some broadened their proposals,

> "My ideas didn't change much, but they did somewhat in the sense that the breadth of goals expanded. After the meeting, I was focused on a broader set of biological principles. We added a few more individuals to the team."

While other applicants narrowed their approach,

> "Not much changed. At first, I wrote a proposal with a very broad, ambitious, 10 year plan. I proposed to study multiple biological systems. After, I focused and proposed to study one system."

No applicants reported allying with other applicant teams on a joint proposal or even any serious discussion about collaboration. However, two applicant teams who met at the CDP meeting but who did not receive center funding (in either round of competition) are currently collaborating today,

> "I did make some real connections. I am setting up collaboration with them right now. In the end, none of us got money, but I made new contacts and am now embarking on new projects. I probably would not have met them without the meeting."

In addition, applicants reported numerous other unintended consequences of the CDP meeting. Some complained that the meeting generally did not provide adequate guidance for preparing the full center applications,

> "I think the outcome [of the meeting] was unclear to me. It wasn't really providing guidance. I thought the purpose [of the meeting] was intended for the NIH to get guidance from the group of planning awardees to help define their nanomedicine vision. But this didn't happen."

Another applicant left the meeting somewhat confused regarding what the NIPT was looking for,

> "[After the meeting] I still didn't understand what the risk level should be. They asked us to be bold for long term plans and to focus on basic science, debating what would be the right balance for the risk and the viability of ideas. I was not really sure what the balance should be and decided to go with a more ambitious plan."

6.2. Content analysis of application documents

In addition to discussing with applicants the impact of the CDP meeting and other interactions on their center proposals, the content of the application documents (e.g., CDP, Round 1 NDC application) were analyzed across numerous dimensions, including:

- Scientific, technical, and clinical foci, goals, and experimental approaches
- Interaction within a broader network of NDCs
- Structures for facilitating intra-NDC interactions

Each of these dimensions is operationalized in a variety of ways. For instance, analysis of proposed interaction within a broader network of NDCs relies on discrete indicators such as other NDCs an application listed for potential collaboration as well as on qualitative assessments of the content of the NDC documents for suggested mechanisms for inter-NDC interaction. See Table 5 for a summary of the operationalization of key concepts for the content analysis.

Table 5. Qualitative and discrete indicators used in the content analysis[25]

Concept	Operationalization
A. Scientific, technical, and clinical foci, goals, and experimental approaches	i. *Qualitative content assessment:* Application documents were read and analyzed to assess the character of the sample and same-applicant changes in scientific, technical, and clinical focus, as well as in goals and experimental approaches, as they progressed through the NDC selection process (e.g., in Round 1, from CDP to NDC application).
B. Networking and inter-NDC interactions	i. *Qualitative content assessment:* Application documents were read and analyzed to assess the mechanisms proposed to facilitate inter-NDC interactions. ii. *Discrete assessment of listed NDCs:* Assessment of specific mention of other NDC applicants in application documents.
C. Structure and intra-NDC interactions	i. *Qualitative content assessment:* Application documents were read and analyzed to assess the mechanisms proposed to facilitate collaboration amongst investigators within the same NDC. ii. *Discrete assessment of investigator-co-location:* Both scientific and management co-location are assessed.

Like with the interview data presented in the previous section, the emphasis of the content analysis is on change facilitated by the NDC selection processes. To what extent did applicants approved to apply in Round 1 alter their scientific, technical, and/or clinical foci, goals, and experimental approaches as they progressed from CDP to NDC application? How were Round 2 applications from participants who were approved to apply in Round 1 (but who

[25] No metrics are included for measurement of the extent to which NDC proposals adhered to an "ideal" envisioned by NIPT officials because the NDC program selection process during Round 1 began with no such reference point but rather used the process to develop a vision for the NDCs in conjunction with applicants and ECG members (see Executive Summary).

did not succeed in attaining NDC funding in Round 1) different than those submitted by applicants who did not participate in Round 1?

Though the interview data suggest that the NDC selection processes did not result in substantial change across the three dimensions listed in Table 5, content analysis may reveal more nuanced changes not reflected by self-reported data (i.e., from interviews). The dimensions were selected to guide the content analysis because they are aligned with several of the key elements of the NDC program as presented in the RFA and as described to us by the NIPT. Further, an explicit goal of the process, and specifically of the CDP meeting during Round 1, was to encourage applicants to better align their teams and centers with the aims and objectives of the NDC program.

The entirety of the documents submitted by applicants during the NDC selection process was not included in the content analysis. Rather, the documents delivered by a stratified sample of applicants were analyzed. Applicants were stratified based on their involvement and relative success within the NDC selection processes and a sample of 18 applicants from across the two rounds of competition was chosen for the content analysis. The applicant strata include:

- Round 1 NDC Awardees
- Round 1 Planning Awardees who did not apply in Round 2
- Round 1 Planning Awardees who became Round 2 NDC Awardees
- Round 2 NDC Awardees who did not apply in Round 1
- Round 1 Planning Awardees who applied in Round 2 without success
- Round 2 applicants who were not Round 1 Planning Awardees

The sample included the population of NDC Awardees (i.e., document deliverables from the eight awardees across Round 1 and Round 2). Of the remaining strata of applicants, half from each stratum were randomly chosen to comprise the remainder of the sample.

Each successive document submitted by the applicants in the sample was analyzed per the "measures" discussed in Table 5. Alterations across the same-applicant documents (e.g., from CDP to Round 1 NDC application) with regard to scientific, technical, and clinical foci, goals and/or experimental approaches were considered "changes" only if they represented a substantial change in the nature and/or scope of the research planned for the proposed NDC. The re-wording of ideas to enhance the clarity of the proposed work, minor additions or deletions of specific experiments, or "repositioning" of essentially the same experiments were not considered to constitute change *per se*. Further, scientific and technical elaboration of previously proposed concepts was not considered "changes."

In addition to assessing change, we also characterized the sample of applicant document deliverables.

6.2.1. Characterization of the sample

Of the 18 applicants included in the sample, all discussed, to some extent, the conduct of experiments that would further understanding of cellular processes as nanomachines. A clear

majority used language in their application documents (e.g., CDP, Round 1 NDC application) suggesting that this was their primary goal and enumerated specific experiments to study the nanomachinery responsible for in vivo functioning of one or more cellular processes. These applications usually proposed the application and optimization of existing approaches and techniques to address new problems.

In contrast, a minority of the applications included in the sample used language suggesting that the predominant focus was on the development of nanodevices (e.g., nanoconductors, nanosensors, optical on/off switches) designed to mimic, manipulate and/or interrogate one or more cellular processes or on the optimization of nanodevices for biomedical application. These applications, generally, proposed the creation of new technologies for cellular analysis and/or manipulation.

A vast majority of applications characterized here as "nanomachinery" (i.e., focused on understanding in vivo cellular processes) proposed an observational and reductionist approach in which a variety of analytical and computational technologies are used to study in vitro and/or live cell systems. A large fraction of these "nanomachinery" applications stressed specifically elucidation of the engineering design principles underlying those processes. The remainder proposed more generalized data gathering to gain knowledge about the processes without a clear focus on the engineering aspects. In addition, nearly half of these applications proposed to study a variety of different cellular processes rather than focusing on a single cellular pathway or process.

While there are differences between the proposals characterized here as either having their goals primarily focused on understanding the cells "nanomachinery" versus proposals with their primary goals focused on developing or engineering a "nanodevice," these categories are used heuristically and should not be considered exclusive or definitive demarcations between the proposals included in the sample.

6.2.2. Substantive changes in scientific, technical, and clinical foci, goals, and experimental approaches

The applicant documents included in the sample were analyzed qualitatively for substantative changes in the scientific, technical, and clinical foci, goals, and experimental approaches of each proposed NDC. This analysis was focused on tracking changes across these parameters as applicants progressed through the NDC selection process – in Round 1, from CDP to NDC application; in Round 2, from CAL to NDC application. Cross-competition (i.e., from Round 1 to Round 2) changes were also tracked for members of the sample who were approved to apply in both rounds.

The findings for this component of the content analysis are presented in two ways. First, *when* changes occurred is considered (e.g., within Round 1, from Round 1 to Round 2). Second, the *substantive nature* of changes is considered. Discrete alterations in the composition of the investigators participating in the proposed NDCs are considered last, due to the limitation of the findings from this line of inquiry.

6.2.2.1. Changes within a single application round

For each applicant included in the sample, the stated goals and experimental approaches of the proposed NDC were refined as the selection process progressed. However, in no instance did an applicant alter substantially the scientific, technical, and/or clinical focus or goals of the proposed NDC during a singular round of competition (i.e., during Round 1 only, during Round 2 only). The general nature of "within round" changes were usually re-wordings for clarity, additions or deletions of specific experiments, scientific and technical elaboration of previously proposed experiments, or "repositioning" of essentially the same experimental lines of inquiry. In addition, the Round 1 applications in the sample showed little substantive change in any of the "characterization" parameters discussed above (e.g., "nanomachinery" versus "nanodevice" focused).

Presentation of the goals and objectives of the NDC were often refined, elaborated, and made more specific with each subsequent application document though without a major shift in substantive foci. In some instances, the goals and objectives were re-organized such that activities previously aimed at different goals were merged into a singular goal. In other cases, the positioning of the goals changed. For instance, while the goal statement in the CAL of one applicant was focused on engineering a particular cellular system, in the subsequent NDC application the research was described in terms of systems biology and positioned using an engineering problem. By including the specific engineering problem, the applicant made more explicit the potential practical application of the research. However, the scientific and technical focus of the proposed NDC did not change. Finally, some of the documents submitted later in the process included changes in the particular model systems proposed – such as particular pathogenic bacteria, specific signaling pathways, or cell systems to be used during the investigations.

These types of "within round" changes are observed for all applicants included in the sample, for each stage of the Round 1 and Round 2 selection processes. There is no apparent stage of the NDC selection processes (e.g., the CDP in Round 1) that facilitated particularly novel alterations in the applications. Nor were unique changes observed for any particular strata of applicants.

6.2.2.2. Changes from Round 1 to Round 2

The content analysis found more substantive alterations in "cross competition" NDC proposals (i.e., same applicant, from Round 1 NDC application to Round 2 NDC application) than were found across "within round" application documents. For applicants in the sample who were planning awardees in Round 1 and re-applied in Round 2 (after not receiving NDC funding in Round 1), there were relatively substantive shifts in focus when compared to the clarifications and elaborations characteristic of "within round" alterations. Round 2 applicants in the sample who were unsuccessful in Round 1 took one of three approaches to their Round 2 proposals: (a) focusing their Round 2 proposals on more extensive investigation of one aspect of the research program proposed in Round 1, (b) proposing a totally different but more focused program, or (c) repositioning the goals of the same set of experiments.

> "[Our round 1 NDC application] was purposely diffuse and grand in its scope, because that was what was interpreted as desired by the RFP. The reviewers disliked it because it was broad and diffuse in its science and focused on a single institution without seeking out the best collaborators to pursue the science."

For applicants in the sample who participated only in Round 2, the NDC applications submitted were not substantially different in character from those submitted by the applicants in Round 1. As in Round 1, the proposals sharpened focus and added or elaborated on experimental approaches in proceeding from the CAL to the NDC application, but made no substantive "within round" changes.

6.2.2.3. Changes in the discussion of clinical relevance

All of the proposals identified one or more disease states or medical problems that were relevant to the cellular process or nanodevice proposed for investigation. The specific relevance of the proposed work to solving a defined medical problem or controlling a cellular process in a particular way to improve health was often quite general and/or speculative. The "nanodevice" proposals were aimed at devices of a general category (e.g. nanoconductors) with several potential medical applications suggested, and each proposed late-stage experiments in specific disease models. The "nanomachinery" characterization proposals in the sample all discussed the potential to treat diseases resulting from defects in the process(es) examined, with half proposing specific experiments aimed at manipulating the process to impact a particular disease.

Beyond the mention of specific diseases and experiments, the applicants in the sample did not introduce substantively new information concerning the clinical relevance of their proposed NDCs as they progressed through the selection processes. Generally, the discussion of clinical applications was rather broad and diffuse at the beginning (e.g., in the CDMs in Round 1, CALs in Round 2). The Round 1 CDPs discussed more explicitly the potential clinical applications, and the NDC applications in both rounds included more direct and elaborate discussion of the relationship between the proposed NDCs' scientific and technical goals and applications in the clinic. In a few cases, applicants added experiments using a more clinically relevant cellular pathway or system to explore a basic biological process. However, in no case among the sample did applicants add at the NDC application stage substantially new research approaches aimed at solving a specific clinical problem.

The limited detail provided in the medical focus of the applications is not surprising. If the goal of the program is to gain fundamental new understanding about the engineering principles guiding cellular processes that affect health, then any specific application of that new understanding to solving a particular medical problem would, at this early stage, be largely speculative. Only when improved understanding of the cellular process has been achieved can new engineering-level approaches be hypothesized and tested for addressing a disease or condition associated with that process.

6.2.2.4. Investigator "multi-disciplinarity"

The original RFA made explicit the need for proposed NDCs to be comprised of investigators from numerous disciplinary backgrounds:

> "These Centers will require collaboration by scientists from disciplines that may not typically interact with each other. For example, Centers might be populated with cell biologists, mathematicians, biochemists, engineers, molecular biologists, statisticians, etc. A key to progress in nanomedicine is the development of multi- and interdisciplinary teams of scientists who together will define the properties, knowledge, and concepts required by this initiative."[26]

To assess the multi-disciplinary nature of the investigators participating in the proposed NDCs included in the sample, several parameters were evaluated. Defining "multi-disciplinarity" based upon the departments of participants, the assembled teams typically contained investigators whose primary appointments lie in a range of academic departments, including engineering, chemistry, and a variety of biology departments. Since departmental affiliation is not a perfect measure of "disciplinarity," the publication records of key investigators as described in their biosketches were also assessed. The most recent five years' worth of publications whereby the key personnel member acted as either the first or last author were analyzed; "discipline" was defined based both on publication titles and the journals in which the articles were published. As a final measure of one's "disciplinarity," the titles of research programs listed under "Research Support" were analyzed for each investigator.

The "disciplinarity" of each key investigator was then assessed based upon the consolidated picture presented by these different parameters. From this perspective, few teams (less than one-fifth) represented in the application set analyzed had broad representation across all disciplines enumerated in the RFA. These proposals (all of which involved five or more institutions) were all awarded NDC funding. One application involved primarily one discipline (computer modeling) with some representation of nanomaterials research and biochemistry and it was awarded funding as well. However, a majority of the applications were multi-disciplinary in that they involved a variable subset of the relevant disciplines.

With regard to involvement of medical disciplines, most teams included one or more key investigators with an MD or MD/PhD. But only two applications included an MD whose role was primarily clinical guidance and input as opposed to providing research expertise in a particular cellular process or in biomedical device development. One of these applications was awarded funding and the other was not.

6.2.2.5. Changes in key personnel during the NDC selection process

A majority of the proposals changed their key personnel listings over the course of the NDC selection process. However, closer inspection of the teams suggest that although a fair

[26] RFA-RM-04-018. The 2006 RFA was more specific in its clinical focus, with corresponding language including, "Each multidisciplinary center will consist of a team of clinicians, biologists, engineers, physical scientists, and mathematicians that work together."

number of applicants altered (i.e., added and/or deleted) personnel during the process, a core set of investigators, on the order of five to eight, was fairly stable. This analysis indicates that the NDC program experienced a considerable amount of personnel change during the selection process relative to other centers programs (e.g., at the National Science Foundation).[27] Though the meaning of this finding is somewhat unclear, from an evaluation perspective it constitutes another vantage to identify and describe the changes that may have occurred in correspondence with specific steps within the NDC selection process.

The name and affiliation of every PI, co-PI, collaborator, or otherwise attributed "key personnel" was extracted from all applicant document deliverables. This includes approximately 1,500 individuals. By tracking the association of each individual with the various application documents, the timing and quantity of personnel changes made throughout the selection processes were identified. Although extreme care was given to the extraction of personnel lists from application documents, it should be acknowledged that the nature, format, and contents of key personnel within each application document varied widely both between stages of the selection process and between applicants. Some applicants included listings of non-funded principals and collaborators in their NDC applications, while others did not. Within the CDMs, CALs and CDPs, the listing of personnel was even more varied.

Every applicant team made a significant number of changes to their rosters of key personnel. On average, rosters changed 60 percent of the listed personnel and contained an average of 13 key personnel. However, on average six people were consistently listed throughout the application process. These data suggest that a core-set of scientists consistently constituted the senior scientific leadership for the center throughout the NDC selection process. As such, the large number of personnel changes observed within these applications does not tend to correspond with significant shifts in the applications' scientific or technical foci or clinical application though they may be indicative of providing the center with additional expertise facilitating the use or development of a new technology or biological system.

One of the premeditated goals for the CDP meeting was to enable teams to identify other teams with which they could potentially merge or reassemble to better accommodate the vision of the NDC. This analysis revealed only two instances of an exchange of personnel across applicant teams from the CDP to the final NDC application. Excluded from this calculation are two additional personnel exchanges between applicant teams from the same university. Below, further analysis of the extent to which the NDC applications addressed operating within a broader network of NDCs is discussed.

6.2.3. Proposed interaction within a network of NDCs

Each NDC applicant was instructed to address how their proposed NDC would operate within a broader network of NDCs. This section of the content analysis addresses the extent to which applicant documents reference such a network. Each applicant document (i.e., CDP, Round 1 NDC application, CAL, Round 2 NDC application) was analyzed for specific mention of other NDC proposals and, for Round 2 documents, for mention of extant NDCs.

[27] This statement is the perspective of centers experts at the STPI. No control group of non-NDC centers were considered to support this statement empirically, in the current report.

This section also qualitatively assesses in each applicant document the nature of the "NDC network" discussed. While some applicants emphasized the scientific and technical complementarities that exist between their proposed NDC and other NDC proposals, other applicants emphasized the mechanisms with which they would facilitate inter-NDC collaboration, such as workshops and Internet portals for data and resource sharing.

Because the factors of force, movement, assembly/disassembly, spatial organization, dynamics, etc. are present in many cellular processes, all of the proposed Centers were focused on gaining knowledge or developing, optimizing, and applying tools and technologies that should be generalizable to the understanding of other cellular processes, suggesting that they could have, were they to be funded, developed insights usable by other NDC applicants.

The analysis in this section finds no correlation between mentioning specific NDCs to include in an "ideal" NDC network and being awarded NDC funding. Many of the winning proposals in both rounds of competition failed to mention any specific cross-NDC synergies or any mechanisms for generating collaboration. Further, there is a considerable mix of changes across each applicants' documents, with some enhancing their discussion of network interactions and others eliminating such discussion altogether. Taken together, the findings for this component of the content analysis reinforce findings from interviews with external reviewers, who maintained that network structure was not a real consideration during the review process.

6.2.3.1. Identification of specific NDCs with which to "network"

For each applicant included in the sample, the document deliverables (e.g., CDP, NDC application) were analyzed for, in Round 1, specific mention of other NDC proposals and, in Round 2, for specific mention of extant NDCs (i.e., the first cohort of four NDCs funded in Round 1). The results are presented by round.

Round 1 NDC applications

In the first round of competition, the 20 recipients of Planning Awards were instructed at the CDP meeting to consider complementarities with one another and to address such complementarities in their NDC applications. However, the extent to which these instructions were fulfilled is variable.

The sample includes 12 applicants who submitted documents during the first round of competition. Of these, seven applicants referenced other NDC proposals in their NDC applications; the range for specific references to other NDC proposals was one to five. There are no apparent differences within the sample strata. For instance, the four recipients of NDC funding in Round 1 did not demonstrate a higher "rate" of referencing other proposals in their NDC applications than did applicants who were not awarded NDC funding.

Round 2 NDC applications

In the second round of competition, 17 applicants were approved to submit full NDC applications. Because of the previous Round 1 competition, applicants had opportunity to reference the operation of their proposed NDCs within a broader NDC network at the letter of intent (i.e., CAL) phase as well as in their Round 2 NDC applications.

The sample includes ten applicants who submitted documents during the second round of competition.[28] Of these, four applicants referenced other NDC proposals in their CALs with a range of one to three proposals. For the ten Round 2 NDC applications included in the sample, five referenced specific NDCs – the same "rate" demonstrated by the Round 1 NDC applications in the sample. The range for specific references to other NDCs was one to four. The references were limited to NDCs awarded during the Round 1 competition due to the fact that the Round 2 competition included no opportunities for applicants to interact.

Similar to the results for the Round 1 component of the sample, there are no major differences within the Round 2 sample strata. The four recipients of NDC funding in Round 2 demonstrated a lower "rate" of referencing other NDCs in their CALs than did applicants who were not awarded NDC funding after the Round 2 competition. However, the four recipients of NDC funding in Round 2 did demonstrate a higher "rate" of referencing other proposals in their NDC applications than did applicants in the sample who were not awarded NDC funding in Round 2.

6.2.3.2. Qualitative differences in the NDC network-related text

For each applicant included in the sample, the document deliverables (e.g., CDP, NDC application) were analyzed for the "nature" or "content" of the proposed NDC network. Generally, the results demonstrate two types of NDC network-related discussion – that concerning the scientific and technical complementarities across the NDCs identified in each NDC application and that concerning the mechanisms with which to facilitate inter-NDC collaboration. The NDC applications that failed to mention specific complementarities with other NDC proposals and, for Round 2 applicants, with extant NDCs awarded during the first competition were limited to discussion of collaborative mechanisms.

Proposed mechanisms

There were numerous mechanisms proposed in NDC applications, from both rounds of competition, with which to facilitate interaction amongst funded NDCs. No specific type of mechanism was related to the degree of success of the NDC applications. Further, no mechanism was specific to either Round 1 or Round 2. Last, having listed specific NDCs with which to collaborate (see above) did not correlate with the discussion of networking mechanisms, generally or for a specific type. Accordingly, the discussion in this section is focused on describing the types of mechanisms and not on particular correlations evident within the sample (since none exist).

[28] The sum of applicants submitting documents in Round 1 and Round 2 (22) exceeds the sample size (18) because the sample includes applicants who participated in both competitions.

The mechanisms for facilitating interaction across NDCs may be divided into four categories: meetings, transfer (e.g., sharing tools and resources, cross-training), joint research, and electronic media (remote interaction by way of Web-based interfaces). For the sample of 18 applicants, the most frequently mentioned mechanisms were meetings including conferences (with formal presentations), workshops, and symposia. Many of the NDC applications proposing meetings as an interactive mechanism also proposed including directors of other NDCs on their external advisory committees.

Another mechanism for facilitating NDC-NDC interaction was joint research. While none of the NDC applications in the sample mentioned specific research projects, one proposed that the joint research be amongst scientists with common backgrounds and training. Importantly, this applicant noted the difficulty of inter-organizational research collaboration by not confounding potential collaborations with interdisciplinarity. Another application noted the difficulty of inter-organizational research collaboration and chose to refrain from getting too specific:

> "Our experience has demonstrated that successful interdisciplinary collaborations across universities, schools, and departments are not measured at the administration level. We have found that successful collaborations are seeded at the *grass roots* level, i.e. a casual conversation between investigators or students followed by laboratory visits where a productive working relationship can then bloom. We believe that the true collaboration among other NIH [NDCs] should also start at this grass roots level" (emphasis original).

Both the applicant emphasizing same-discipline research collaborations and the one emphasizing "grass roots" collaborations were awarded NDC funding.

Other NDC applications emphasize various forms of transfer between NDCs. Some noted that the tools to be developed by their proposed NDCs could be of use to numerous other NDCs. Others proposed to set aside travel funds for PhD students and post-doctoral fellows to foster "cross training" at other NDCs in the network. Next to meetings, the most frequently mentioned mechanism for inter-NDC interaction was electronic media, including viral communication environments, chat rooms, Web conferencing, and password-protected internet portals for data sharing. Notably, the NDC application proposing the portal emphasized that data would be shared only after intellectual property protection measures had been taken.

<u>Proposed complementarities</u>

Practically all of the NDC applications in the sample proposed their research and development activities to be complementary to the activities of other NDCs. Most of these propositions were general – either mentioning every other NDC or mentioning none of them. The notable characteristic demarcating one Round 2 NDC application is that the applicant included written confirmation from the directors of each of the NDCs funded in Round 1 which indicated that they would collaborate with the NDC if it was funded.

6.2.3.3. Changes from Round 1 to Round 2

For the four applicants in the sample who applied in both Round 1 and Round 2, the two who made specific references to other NDC proposals in their Round 1 NDC applications also made specific references in their Round 2 applications.

From the Round 1 to Round 2 NDC applications included in the sample, there were minimal changes in the discussion of the scientific and technical complementarities and the proposed mechanisms for inter-NDC interactions. In three cases, the discussion was practically identical in content. In a fourth case, the discussion became less detailed.

6.2.4. Proposed structure and management of NDCs

Each NDC applicant was instructed to address how their proposed NDC would be structured and managed internally. This section of the content analysis addresses the structural and management propositions included in applicant documents. Each applicant document (i.e., CDP, Round 1 NDC application, CAL, Round 2 NDC application) was analyzed for the co-location of principal investigators and key personnel, management structure, mechanisms for intra-NDC interaction, and the inclusion of administrative staff and professionals.

The analysis in this section finds no correlation between particular structural and/or management characteristics and being awarded NDC funding. For instance, many of the winning proposals in both rounds of competition included principal investigators who were not co-located and mentioned no specific mechanisms for facilitating intra-NDC interactions. A majority of the applicants included in the sample made some mention of an internal organizing committee – often referred to as the "executive committee" or a "steering committee." Many also mentioned establishing an external advisory board comprised of experts in the field (but outside the proposed NDC) and of directors of other NDCs (though none were mentioned specifically).

Unlike with applicants' discussion of the operation of their proposed NDCs within a broader network of NDCs, there was not much change regarding center management and structure across each applicants' documents as they progressed through the center selection process (e.g., in Round 1, from CDP to NDC application). Taken together, the findings for this component of the content analysis demonstrate applicants' consideration of the structure and management of their proposed NDCs to be unexceptional. This finding is not surprising, since new strategies for internal organization and management was not an explicit goal of the NDC program.

6.2.4.1. Co-location, size, and origins

A majority of the applicants in the sample propose NDCs that are not "co-located" – meaning that the proposed center investigators reside at different institutions and that there is no proposed "bricks and mortar" infrastructure (e.g., laboratories, meeting facilities) for common use among all center investigators. The applicants use numerous terms to describe this type of center structure, such as "virtual center," "collaboratory," and "center without walls."

That a majority of the proposals in the sample are not co-located is not surprising given the ambitious scientific, technical, and clinical goals of the NDC program – which require specialized expertise available at only a handful of universities and research institutions (e.g., government laboratories) in the U.S. and sometimes abroad.[29] Numerous applicants echoed this theme in their NDC applications:

> "It is our experience and belief that productive collaboration does not necessarily need to be physically close."

> "Our philosophy is that it is unacceptable to assume that the talents necessary for such an ambitious undertaking reside at a single or even a few institutions."

The numeric range of institutions – mostly US universities, with some US government laboratories, European universities, and European university research centers (e.g., Fraunhofer Institutes, Max Planck Institutes) – represented by the proposed investigator memberships in the NDC applications included in the sample was one to eleven institutions. All but one of the applications in the sample included two or more institutions. More than half of the sample listed investigators from five or more institutions.

The quantity of institutions did not necessarily correlate positively with larger investigator memberships. The NDC application in the sample that was co-located (i.e., listing investigators from but a single university), for example, listed more investigators than numerous applications listing investigators from three to four institutions. However, the largest investigator list (31 scientists) was proposed in the NDC application with the greatest institutional span (11 universities and research organizations).

It is important to distinguish between different types of co-location. Thus far, we have been discussing *scientific capacity* co-location (e.g., of all investigators), not *management* co-location (e.g., of principal investigators and co-principal investigators). While the former is perhaps unrealistic due to the scientific and technical goals of the proposed NDCs and more broadly of the NDC program, the latter can be important for a cohesive center that is distinguishable from a series of loosely-related R01 projects. For the sub-sample of applications that included two or more principal investigators (PIs), half were co-located at the same university or at universities in the same city.[30] The ramifications of NDC management co-location (or the lack thereof) will not be clear until the NDC program has progressed to the point where an output (versus process) evaluation is in order.

Another important distinction to make is whether the proposed NDC is to constitute a new university research center or a new facet of an existing university research center. While there is not extensive detail in this regard across the applicant document deliverables analyzed, one application did indicate that the structure and management of the proposed NDC to be

[29] Multiple proposals included scientists working in British and German universities and research centers.

[30] This measure used geography (i.e., city) versus institution (i.e., university) to determine co-location. For example, PIs at Georgia Tech (in Atlanta) and Emory University (also in Atlanta) are considered to be co-located. This relatively flexible operationalization of co-location is acceptable since the subject is management, not research collaboration.

already in place in that the NDC funding would be used by an extant university research center focused on nanotechnology.

6.2.4.2. Internal management structure

Every application in the sample that devoted substantive text to internal management structure (two did not) proposed that an "executive committee" or "steering committee" would be formed to oversee center administration. In all instances, the proposed committee was to be comprised of the PI and Co-PIs (if any). For the NDC applications with a single PI, the proposed committees included additional investigators. In some instances, the committees included administrative professionals with advanced degrees in business administration and/or finance. These professionals retain full responsibility for administrative tasks that have no scientific and/or technical component. This specialized approach to center management has proven effective in other federal-level centers programs.[31]

The descriptions of the functions to be fulfilled by the internal executive committees were diffuse and superficial across the applications in the sample. Practically all descriptions mentioned that the committee would "set research priorities," "establish milestones," "allocate funds," and engage in "strategic planning" – without providing further detail. Some NDC applications included further functional description, including the evaluation of projects, determining whether projects are completed, and reviewing proposals for new projects. Applications that proposed the employ of administrative professionals additionally listed tasks such as the hiring and firing of personnel, fulfillment of reporting requirements, and acting as liaison between the NDC and outside entities including the home university and the NIH.

Though a small minority of the applications in the sample discussed the employ of administrative professionals, numerous others mentioned that they would hire administrative staff (versus professionals) to aid the center director in workaday operations. These "non-professional" positions were not proposed as integral parts of the proposed executive committees, but rather as assistant-level positions in charge of setting up tele- and video-conferences, making travel arrangements, handling travel reimbursements, and so on.

6.2.4.3. Synergies across proposed projects

Synergies across the lines of research proposed (e.g., the intended use of one project's data or developed approaches by a second project or the development and shared use of common-pool resources) showed a wide degree of variation. Approximately one third of the applications proposed "strongly integrated" experimental programs aimed at understanding all aspects of a specific cellular process or achieving a device development goal through a complementary and synergistic set of research projects. Another one-third proposed multiple, parallel, lines of inquiry and data gathering relevant to a cellular process but provided limited descriptive evidence of an integrated approach to achieving a comprehensive understanding. The final one-third discussed integration of some aspects of the program and not others. The

[31] See Bozeman, B. and C. Boardman (2003) *Managing the New Multipurpose, Multidiscipline University Research Center: Institutional Innovation in the Academic Community*. IBM Center for the Business of Government: http://www.businessofgovernment.org/pdfs/Bozeman_Boardman_report.pdf.

level of integration was slightly higher in awardees than unsuccessful applicants for both rounds and also more prevalent in the "nanodevice" proposals than in the "nanomachinery" proposals. Although the actual integration of the experimental program may be greater or less than discussed in the proposals, there was a clear difference in the degree to which the applicants explicitly stressed how they would integrate the program or not.

6.2.4.4. Mechanisms for intra-NDC interaction

Many (though not all) of the applications in the sample discuss in the context of center structure and management the mechanisms with which to facilitate internal collaboration amongst NDC investigators. As with the descriptions of the functions of the executive committees, the descriptions of the mechanisms for facilitating intra-NDC interactions are superficial.

Each of the applications in the sample that list as investigators scientists who are not co-located emphasizes the use of tele-conferencing and video-conferencing to hold regular meetings. The one NDC application comprised of investigators from the same university includes no such emphasis, since investigators listed in this proposal are co-located. Many also proposed to use Web-based portals for data sharing and for conducting "virtual simulations" based on results.

Another common mechanism across the applications was "annual meetings," "symposia," "seminars," "workshops," and "retreats" wherein investigators present and discuss the findings of the research conducted using NDC funds. None of the applications provided specific detail about the proposed meetings – whether facilitated via multimedia or by travel funds for participants – beyond the proposition that they would occur on a regular basis (e.g., monthly, annually). Notably, one NDC application mentioned that they would hold monthly meetings for "leadership skills development," though without explaining exactly what that would entail.

In the section of the NDC applications on center structure and management, many applications also proposed to fund graduate students and post-doctoral fellows. One application went so far as to propose that the entirety of NDC funding would be used to support graduate students and post-docs. This proposal was made by an existing university research center focused on nanotechnology.

6.2.4.5. External advice and oversight

A majority of the applications in the sample proposed to establish and external advisory committee comprised of experts in their field of research who were not directly affiliated with the proposed NDC. Two of the twelve applications in the sample indicating such suggested that they may seek to appoint directors of other NDCs to act as external advisors.

6.2.5. Adherence of proposed NDCs to the "ideal" NDC envisioned by NIPT officials

Typically, process evaluations of research centers programs address the extent to which the proposals adhered to a premeditated, "ideal" center, in terms of focus and function, as envisioned by program officials. As discussed at the outset of this report (see the Executive Summary), the current study constitutes an evaluation of an atypical process wherein the initial plans and expectations of program officials were, while established, relatively flexible. Accordingly, comparing the NDC applications in the sample to a premeditated "ideal" is not a possibility. NIPT members interviewed, including the program director, maintained that a major purpose of the selection process was to work with applicants and ECG members to develop the NDC "concept" as the Round 1 selection process progressed. In other words, there was no premeditated prototype or "ideal" for the NDC program.

However, it is still possible to evaluate, at a general level, the extent to which the language used in the NDC applications in the sample address the two goals emphasized in all three NDC program RFAs (i.e., for Planning Awards in Round 1, for NDC funding in Round 1, and for NDC funding in Round 2). The first goal was to fund centers that characterize quantitatively the nanomachinery of cellular processes to elucidate engineering design principles. The second goal was to fund centers that develop tools to control and manipulate the nanomachinery of a cellular process for tissue repair and/or interference with disease processes.

A majority of the 18 applications examined used language that suggested the proposed NDCs would elucidate the engineering design principles of a cellular process and then use that information to create a way to manipulate the process to improve health. The remainder of the sample used language that proposed the creation or optimization of nanodevices to manipulate cellular processes to improve health, though not necessarily by basing those devices on an engineering-level understanding of the cellular process.

7. Effectiveness findings: Impact on reviews

In this section, extramural reviewers' perspectives regarding their interactions with the Nanomedicine Implementation Project Team (NIPT) officials and Extramural Consultant Group (ECG) members are presented. Particular emphasis is given to the impact that these interactions had on the reviews and on the review process. Taken together, the data indicate that the NIPT and ECG provided extramural reviewers with additional information during the reviews, but did not alter the review scoring.[32] This section is empirical and draws on data collected during in-depth discussions.[33] No quantitative decision rules were used for inclusion or exclusion of the findings. Both unique and common perspectives are presented.[34]

7.1. Extramural reviewer perspectives

Extramural reviewers' participation in both rounds of competition was limited to the formal review of full center applications. As described above, most of the extramural reviewers interviewed characterized the review process as relatively interactive when compared to conventional reviews. Also described above, some of the extramural reviewers found their interactions with NIPT officials and ECG members to be informative and helpful, while others found the interactions somewhat intrusive, if not inappropriate. The effects of these interactions – like the effects of interactions during the Concept Development Plan (CDP) meeting – were somewhat mixed.

The interactions did not seem to alter the application rankings of the extramural reviewers. When asked whether the NIPT and ECG affected the rankings, practically all reviewers interviewed responded with a simple "no." Some provided additional detail,

> "We did not let the NIH folks affect our reviews. We put science first."

> "There was bristling among us reviewers. We were saying 'no, no, no – go with science first.'"

In contrast, other extramural reviewers indicated that the interactions had the constructive effect intended by NIPT officials,

[32] For evaluative conclusions and recommendations regarding the impact of the NIPT and ECG on the reviews and the review process, see the Executive Summary.
[33] For a full description of methodology, see Appendices B-D.
[34] It is important to note that in a qualitative case study, statistical inferences need not and cannot be made. For example, the perspective of one NIPT member could be of greater insight and value to the program than a common (and perhaps contrary) perspective shared across all extramural reviewers. Accordingly, the findings in this report are presented as-is. When they are interpreted in the Executive Summary, weight is given to the perceived evaluative value of the perspective and not to the number of interviewees supporting that perspective. However, some highly "valuable" perspectives may be shared across numerous interviewees. Moreover, the quantity of quotations to support one perspective versus another is a function of the data, not of the perceived importance of a particular perspective on the part of the Science and Technology Policy Institute (STPI) evaluation team.

> "Following the advice of [the NIPT], I was able to accept riskier proposals."

> "[The NIPT] focused on the review process. They ensured that the criteria we used were consistent with the program goals. If we got off track, they reminded us about the criteria and what they envisioned for the centers."

The interactions during the review meetings do not seem to have been conducive to extensive consideration of a network of complementary Nanomedicine Development Centers (NDCs). Most of the reviewers interviewed said that the network concept was not a major consideration in review. For instance,

> "Consideration of the network of centers was contrived. It was clear that most of the centers would have enormous difficulty arranging collaborations just within their own centers, much less between geographically distant centers in other areas of the country."

> "It was not a major consideration. There were conflicting goals in a way. On one hand there was the criterion for interaction across centers, on the other the centers were to be non-duplicative."

In the end, the reviewers were split on the effectiveness of NIPT and ECG active participation in the review meetings. Negative comments included,

> "[The NIPT] could have made the same funding decisions without any input from the scientific committee. I don't think my reviews were necessary."

> "I'm rather skeptical that the best science was funded."

But these sentiments are balanced by positive reviewer comments about the overall effect of keeping the reviews focused on the program goals,

> "The review process was fair and helpful. The NIH folks provided valuable information."

8. Effectiveness findings: Program coverage and proposal novelty

A measure of effectiveness employed that is generic across process evaluations is "coverage" – the extent to which the program reached the target audience. The interview data indicate that the selection processes did not exclude systematically facets of the scientific community capable of contributing to nanomedicine.[35]

The final measure of effectiveness employed in this report is "novelty." While it is beyond the purview of this report to second-guess peer review, it is appropriate to ascertain whether center proposals solicited through use of FRA differed significantly from the proposals typically solicited by conventional National Institutes of Health (NIH) processes and practices. Though Nanomedicine Implementation Project Team (NIPT) officials and Extramural Consultant Group (ECG) members perceived the application pools from both rounds of competition to be comprised of "unique" proposals, many of the extramural reviewers interviewed felt that a large proportion of the proposals, including those awarded Nanomedicine Development Center (NDC) funding, could have been funded via conventional mechanisms without the use of FRA.[36]

In this section, the perspectives of NIPT officials, ECG members, and extramural reviewers are presented. This section is empirical and draws on data collected during in-depth discussions. No quantitative decision rules were used for inclusion or exclusion of the findings. Both unique and common perspectives are presented.[37]

8.1. Program coverage

8.1.1. Perspectives of NIPT officials, ECG members, and extramural reviewers

Program "coverage" – the extent to which participation by the target population is achieved – is not often a concern for scientific programs, for instance when solicitations are open and conventional (and therefore familiar) mechanisms are used to fund researchers. However, the use of FRA to fund research in a relatively new area of science and engineering begs the question of whether some subgroups of the scientific community participated more than others and whether other subgroups were systematically excluded from participation.

[35] For evaluative conclusions and recommendations regarding program coverage, see the Executive Summary.
[36] For evaluative conclusions and recommendations regarding proposal novelty, see the Executive Summary.
[37] It is important to note that in a qualitative case study, statistical inferences need not and cannot be made. For example, the perspective of one NIPT member could be of greater insight and value to the program than a common (and perhaps contrary) perspective shared across all extramural reviewers. Accordingly, the findings in this report are presented as-is. When they are interpreted in the Executive Summary, weight is given to the perceived evaluative value of the perspective and not to the number of interviewees supporting that perspective. However, some highly "valuable" perspectives may be shared across numerous interviewees. Moreover, the quantity of quotations to support one perspective versus another is a function of the data, not of the perceived importance of a particular perspective on the part of the Science and Technology Policy Institute (STPI) evaluation team.

Measuring program coverage almost always relies on a reliable idea of who does and who does not comprise the target population. Due to the breadth and newness of the concept of "nanomedicine," however, the target population is sufficiently broad to defy definition along discrete disciplinary boundaries. Accordingly, the opinions of those involved in the management and operations of NDC selection processes (i.e., the NIPT, the ECG, and extramural reviewers) are used here to assess program coverage.

A majority of those interviewed felt NDC program coverage to be adequate, for both rounds of competition. When asked whether in the application pools they did not see areas of science and engineering that they thought promising areas of inquiry for nanomedicine, most responded negatively. Responses from reviewers included,

> "I was not surprised by the applications I saw. There was nothing I expected to see but didn't."
>
> "The distribution of concepts across the applications seemed reasonable. There were no glaring omissions."
>
> "The applications covered a lot of different areas. I'm sure I could think of missing areas, but I was impressed by the breadth of the applications."

From NIPT officials and ECG members,

> "I was comfortable with the applications, though a lot of groups didn't involve clinicians."
>
> "I think the coverage was good. I don't remember thinking there was an area not covered that should be."

However, some reviewers and ECG members identified discrete scientific foci they felt were missing from the application pools, including proposals focused on particular viral models and the nucleic acid aspects of biosystems. While no NIPT officials identified underrepresented areas, some acknowledged that particular areas did not fare well in the selection process, for example,

> "There were areas that were underrepresented. Or, there were certain areas that didn't do as well. A lot of signaling and imaging proposals didn't make the cut. They just weren't as focused. We were looking for more structured approaches."

8.1.2. Controlling for potential selection bias

Generally, the coverage of the NDC selection processes is viewed as adequate by the NIH and extramural personnel who implemented the process. But this does not account for potential bias in the responses due to exclusion of particular scientific and/or engineering backgrounds from the composition of the NIPT, ECG, and the extramural reviewers. Accordingly, the disciplinary "spread" of each group was analyzed in terms of scale and scope.

The background and expertise of each member of the NIPT, ECG, and review board was discerned by inspection of documentation provided by NIH biographical sketch forms or of documentation on institutional Web pages, including curriculum vitae, publication listings, and research summaries. The vast majority of these participants were interdisciplinary scientists with specialties that could not be coded into specific disciplines. For instance, several of the ECG members were chemists or biochemists, but had publication records in biophysics and molecular biology. Accordingly, analysis of individuals' departmental affiliation or formal degree title would be misleading.

Characterizing the participants based on their current areas of research, few non-biomedical scientists were identified amongst the NIPT, ECG, or extramural review board members. Accordingly, the perceived coverage of the NDC program generally excludes the perceptions of non-biomedical scientists with experience and expertise relevant to the goals of the NDC program. For instance, material scientists, computer scientists, or engineers that are not engrained within the life sciences may perceive NDC program coverage as less complete than indicated above. However, given the clear biomedical focus of the NDC program, that there were some non-biomedical scientists included in the program is beneficial.

8.2. Novelty of the proposals

While it is beyond the purview of this report to second-guess peer review, it is appropriate to ascertain whether the use of FRA resulted in center proposals that were significantly different from proposals solicited through conventional NIH processes and practices. Each NIPT official, ECG member, and extramural reviewer interviewed was asked about whether they perceived the NDC applications to which they had access to constitute "out of the box" research that would probably not be funded by conventional NIH mechanisms (e.g., R01, P20, P50).

While the NIPT officials and some of the ECG personnel interviewed reported perceiving the proposals to be novel in comparison to their prior experiences, all six of the extramural reviewers interviewed disagreed by reporting that they felt the proposals to be "fundable" via conventional NIH mechanisms. However, the reasons communicated by the reviewers spoke more to the feasibility of the management and operations of the proposed centers than with the novelty of their respective scientific and technical foci. Accordingly, the responses from the NIPT and ECG members interviewed have higher validity than those from the reviewers interviewed.

Across the board, the NIPT officials and ECG members interviewed believed many of the NDC proposals to be novel. Specifically, all of the NIPT officials interviewed and all but two of the ECG members interviewed felt the proposals to be novel.[38]

[38] Because most of the responses from interviewees within these strata were simple (e.g., "Yes") with little to no elaboration, the inclusion of direct quotations would not enhance this description of the findings. However, the absence of quotations should not be interpreted as evidence that the finding is less important than findings for which quotations are included.

Several of the extramural reviewers interviewed felt differently. When asked about the novelty of the proposals, most of the reviewers took issue with the "center mode" proposed in the applications,

> "I am skeptical that this process was any better than investigator-initiated grants. For nearly all of the proposals we reviewed, no one seemed to believe that any synergies would be born. The applications seemed to be just a group of people in seek of support for their individual research efforts. There was no emphasis on building a strong center."

> "I thought there was nothing in those grants that couldn't have been reviewed by the R01 mechanism. There was nothing special about the proposals. The new mechanism [(FRA)] was unnecessary."

> "It wasn't obvious the [NDC] program was needed [to fund the applications]. The rationale that this type of work wouldn't be funded otherwise does not seem accurate. It seemed the applicants could get money from already existing mechanisms. The nano centers weren't clearly as necessary as promoted."

These criticisms are not entirely valid. They have less to do with the progressiveness or novelty of the scientific and technical foci of the NDC proposals than with the feasibility of the management and operations of the centers proposed. This point is borne out by the fact that, during both rounds of competition, the review meetings were somewhat contentious regarding the extent to which the center applications made use of preliminary data and results. Many reviewers felt they were being asked by the NIPT to fund "science fiction not science,"

> "I had specific concerns regarding the scientific merit of the applications, which apparently was not the basis for the evaluation. My impression was that imagination was weighted much more heavily. "Science fiction" and "way-out-there research" were terms repeated by the program officials often. I was told not to worry about feasibility."

This was a challenge for the NIPT and ECG. ECG members assisted the NIPT in guiding reviewers during the review meetings,

> "Some of the reviewers were working as if it was a standard R01. It was my role to help them understand that this was supposed to be different and that we needed to cut [the applicants] some slack."

Therefore, it is a fair assessment to conclude that at least a proportion of the center proposals, though they may not have been convincing to the reviewers interviewed either from the scientific or management perspectives, indeed were novel when compared to conventional applications in the sense that they did not make extensive (or any) use of preliminary data and research findings.

Appendix A: Summary tables

A.1. Round 1

Table 6. Participants and stakeholders for the first round selection process

Participant	Description
National Implementation Project Team (NIPT)	NIH personnel charged with developing and implementing the NDC program.
External Consultant Group (ECG)	University-based scientists recruited by the NIPT to facilitate program implementation as consultants on all aspects of the process and to provide "high level" scientific and technical perspective.
Applicants, planning awardees	Members of the scientific community approved to submit applications for full NDC funding.
Extramural reviewers	University-based scientists recruited by the NIPT to review full applications for NDC funding.

Table 7. Application documents for the first round selection process

Document	Description
Concept Development Memo (CDM)	An openly solicited "short white paper" of 5 pages or less proposing an area for research and development for an NDC. These documents were used by NIPT officials to determine recipients of twenty planning awards.
Concept Development Plan (CDP)	A "long white paper" of 30-50 pages describing in greater detail planning awardees' respective propositions for an NDC. The NIPT and ECG used these documents to identify topics for discussion at the CDP planning meeting.
Center Application	A final, full application for center funding submitted by planning awardees for review by the NIPT, ECG, and extramural reviewers.

A.2. Round 2

Table 8. Participants and stakeholders for the second round selection process

Participant	Description
National Implementation Project Team (NIPT)	NIH personnel charged with developing and implementing the NDC program.
External Consultant Group (ECG)	University-based scientists recruited by the NIPT to facilitate program implementation as consultants on all aspects of the process and to provide “high level” scientific and technical perspective.
Applicants	Members of the scientific community approved to submit applications for full NDC funding.
Extramural reviewers	University-based scientists recruited by the NIPT review full applications for NDC funding.

Table 9. Application documents for the second round selection process

Document	Description
Concept Approval Letter (CAL)	An openly solicited “short white paper” of 5 pages or less proposing an area for research and development for an NDC.
Center Application	A final, full application for center funding submitted by planning awardees for review by the NIPT, ECG, and extramural reviewers.

Appendix B: Methods

B.1. Discussions

The predominant empirical basis of this study is comprised of data that was collected during a series of semi-structured interviews with NDC program participants. The interviews were designed to elicit information sufficient to generate a detailed description of both rounds of the NDC selection process and also to answer the descriptive and evaluative study questions (see Appendix C).

The purpose of this section is fourfold, to:

- Explain how interviewees were selected and contacted
- Describe the interview process
- Detail how the interview data were coded and analyzed
- Introduce the bank of interview questions from which customized interview protocols were generated for each interviewee, depending on the nature of his or her participation in the NDC selection process.

B.1.1. Interviewee selection

Interviewees were randomly selected within each of the major strata of NDC participants, including:

- Program leadership (NIPT members)
- ECG members
- Unsuccessful applicants*
- NDC directors (winning applicants)*
- Extramural reviewers

The category for unsuccessful applicants is denoted by an asterisk because this stratum of NDC participants was further stratified based on the degree of success experienced during the NDC selection process. For instance, in each round, some applicants were approved to submit a final NDC application while others were not. Interviewees within these sub-strata were selected at random.

The category for NDC directors is denoted by an asterisk because all eight of the potential candidates were interviewed. Therefore, the entire population (versus a random sample) of winning NDC applicants was selected for interview.

Despite the overt attempt at randomness in selecting interviewees, it is important to note that the sample of NDC participants interviewed does not constitute a random sample in the statistical sense.

B.1.2. Soliciting the interviews

The interviews were solicited via email between April 23 and August 27, 2007. The template used for the email solicitations:

> Dear …,
>
> At the request of the NIH, the Science and Technology Policy Institute (STPI) is conducting a study examining the strengths and weaknesses of the process through which the NIH selected its Nanomedicine Development Centers in 2005 and 2006. The study will focus on the use of Flexible Research Authority to solicit and review center applications and to award applicants with centers funding.
>
> Because of your participation in the center selection process, we are writing to ask for your participation in this study, which entails a 30-45 minute discussion to occur sometime in the next two to three weeks. With your help, the study will inform the future use of Flexible Research Authority for award processes at the NIH.
>
> Below, please indicate your top two time preferences for the interview. In addition, be sure to include a contact phone number.
>
> Know that your input is invaluable for us providing recommendations in our final report. All information from the interview will be kept anonymous and confidential, analyzed within the STPI and only shared with the NIH in summary form.
>
> We look forward to speaking with you.
>
> Regards,
>
> Craig Boardman, Ph.D.
>
> Science and Technology Policy Institute
> 1899 Pennsylvania Ave. N.W., Ste. 520
> Washington D.C. 20006-3602
> 202-419-5480
> pboardma@ida.org
>
> Chris Hart, Ph.D.
>
> Science and Technology Policy Institute
> 1899 Pennsylvania Ave. N.W., Ste. 520
> Washington D.C. 20006-3602
> 202-419-3731
> chart@ida.org

In the case of non-response, subsequent emails of a more personalized nature were sent. Usually, the second email was sufficient to elicit a response, either agreeing to or declining the interview request.

B.1.3. Constructing the interview protocols

The STPI team developed numerous interview protocols, the questions contained in each dependent upon which round of the NDC selection process interviewees participated in (i.e., round 1 and/or round 2) and also on the nature of their participation (e.g., applicant, reviewer, ECG member). The interviewee-specific protocols were constructed using a master cache of interview questions developed to address the overarching study questions discussed in the introduction to this report (see Appendix C).

To facilitate cross-sectional analysis of the interview responses, interviewees in the same stratum were interviewed using the same or a very similar interview protocol. Applicants were all asked the same or similar questions, as were NIPT members, ECG members, and extramural reviewers. Many of the interview questions were used in interviews with participants across strata. For example, applicants (successful and unsuccessful), reviewers, NIPT members, and ECG members were all asked about the extent to which the NDC selection process was more

"interactive" than other application experiences they have endured, since the facilitation of such interaction was a major reason for using Flexible Research Authority.

Each interview protocol was designed to facilitate "semi-structured" discussions comprised of open-ended questions and responses. See Appendix D for the full cache of interview questions.

B.1.4. Implementing the interviews

The interviews occurred between May 1 and September 10, 2007, each lasting from 30 to 45 minutes. The interviews were conducted over the telephone.

Two members of the STPI team participated in each interview – one to conduct or lead the interview and the other to type notes. The interviews were not recorded.

Table 10. Quantity of interviews conducted, by interviewee stratum

Interviewee stratum	Number of interviews planned	Number conducted
Implementation Team	4	5
External Consultant Group	4	4
Reviewers during Round 1 only	2	2
Reviewers during Round 2 only	2	2
Reviewers during both Rounds	2	2
Round 1 NDC Awardees	4	4
Round 1 Planning Awardees who did not apply in Round 2	2-3	2
Round 1 Planning Awardees who became Round 2 NDC Awardees	2-3	3
Round 2 NDC Awardee who did not apply in Round 1	1	1
Round 1 Planning Awardees who applied in Round 2 without success	2-3	5
Round 2 applicants who were not Round 1 Planning Awardees	2-3	2
Totals	**26-30**	**32**

The total quantity of interviews conducted (32) is higher than the planned quantity of interviews due to the high rate of response for Round 1 Planning Awardees who applied in Round 2 without success and due to the interviewing of one additional Implementation Team member (we interviewed 5 instead of 4).

B.1.5. Collating and coding the interviews

After each interview, the notes were cross checked by the primary interviewer to ensure accuracy. Once all of the interviews were completed, the responses were collated by interview guide question to facilitate interview data coding and analysis. After collation, the responses to each question were coded, or separated into "bins," to facilitate the analysis.

B.2. Content analysis

As part of the feasibility study for the NDC selection process evaluation, research staff at STPI conducted content analysis of a sample of the application documents. This section describes the applicant documents that were analyzed, the specific attributes and indicators that were measured, and the content analysis methodology.

B.2.1. Documents for content analysis

B.2.1.1. Round 1 documents

The first round of the NDC selection process required applicants to submit a series of documents describing their respective plans for an NDC. Round 1 deliverables include:

- Concept Development Memo (CDM) – an openly solicited "short white paper" of five pages or less proposing an area for research and development for an NDC. These documents were used by NIPT officials to determine recipients of twenty planning awards.
- Concept Development Plan (CDP) – a "long white paper" of 30-50 pages describing in greater detail planning awardees' respective propositions for an NDC. NIPT officials used these documents to identify topics for discussion at the CDP meeting between NIPT officials, planning awardees, and ECG members.
- Center Application – a final, full application for center funding submitted by planning awardees for review by NIPT officials and extramural reviewers.

The open request for CDMs in round 1 solicited 81 submissions, 20 of which were selected to receive planning awards of $50,000 for the development of the CDP. Only recipients of planning awards were allowed to submit CDPs and full center applications. (For further description of the first round of the NDC selection process, see Section 4).

B.2.1.2. Round 2 documents

The applicant deliverables submitted during the second round of the NDC selection process differed from the first round in two respects. First, excluded was the CDP, requiring approved applicants to submit two instead of three documents.[39] Moreover, a Concept Approval Letter (CAL) was requested in lieu of the CDM. Functionally, there are no significant differences between the second round CAL and the first round CDM. Round 2 deliverables include:

- Concept Approval Letter (CAL) – a "short white paper" of five pages or less proposing an area for research and development for an NDC. These documents were used by NIPT officials to determine who would be permitted to submit full center applications.
- Center Application – a full application for center funding submitted by selected applicants for review by NIPT officials and extramural reviewers.

[39] Since the Round 2 selection process did not include planning awards, no CDPs were developed by the applicants.

The open request for CALs solicited 45 submissions, 17 of which were selected to submit full center applications. (For further description of the second round of the NDC selection process, see Section 4.)

Table 11. Application documents submitted

Round (year)	Applicant deliverable	Number
Round 1 (2004-2005)	Concept Development Memos (CDMs)	81
	Concept Development Plans (CDPs)	20
	NDC Applications	20
Round 2 (2006)	Concept Approval Letters (CALs)	45
	NDC Applications	17

B.2.2. Content analysis indicators and method

Application documents from the 20 planning awardees in the first round and from the 17 approved applicants in Round 2 were analyzed to address specific questions related to the process evaluation. The analysis focuses on indicators that could be observed and measured reliably and accurately. Two categories of content that meet this requirement are to be assessed: that related to the responsiveness of document deliverables to universal criteria that all proposed NDCs were expected to meet and that related to changes in the scientific, technical and clinical foci, goals, and experimental approaches of the proposed NDCs made by applicants as they traversed the NDC selection process.

B.2.2.1. Change

Each application document was analyzed with respect to three questions. These questions address three central yet unique goals of the NDC program that can be reliably and validly identified and scored within and across application documents.

- Did the scientific, technical, and/or clinical foci, goals, and experimental approaches of the proposals change as applicants progressed through the NDC selection process?
- Did the center applications address the formation of a network of NDCs and, if so, how and to what extent? Did this change as applicants progressed through the NDC selection process?
- How were the proposed NDCs structured? Did this change as applicants progressed through the NDC selection process?
- To what extent did the proposed NDCs adhere to an “ideal” NDC as envisioned by NDC NIPT officials?

Each of these dimensions is operationalized in a variety of ways. For instance, analysis of proposed interaction within a broader network of NDCs relies on discrete indicators such as other NDCs an application may list for potential collaboration as well as on qualitative assessments of the content of the NDC documents for suggested mechanisms for inter-NDC interaction. See Table 13 for a summary of the operationalization of key concepts for the content analysis.

Table 12. Qualitative and discrete indicators used in the content analysis[40]

Concept	Operationalization
A. Scientific, technical, and clinical foci, goals, and experimental approaches	i. *Qualitative content assessment:* Application documents were read and analyzed to assess the character of the sample and same-applicant changes in scientific, technical, and clinical focus, as well as in goals and experimental approaches, as they progressed through the NDC selection process (e.g., in Round 1, from CDP to NDC application).
B. Networking and inter-NDC interactions	i. *Qualitative content assessment:* Application documents were read and analyzed to assess the mechanisms proposed to facilitate inter-NDC interactions. ii. *Discrete assessment of listed NDCs:* Assessment of specific mention of other NDC applicants in application documents.
C. Structure and intra-NDC interactions	i. *Qualitative content assessment:* Application documents were read and analyzed to assess the mechanisms proposed to facilitate collaboration amongst investigators within the same NDC. ii. *Discrete assessment of investigator-co-location:* Both scientific and management co-location are assessed.

B.2.3. Sample selection

The entirety of the documents submitted by applicants during the NDC selection process was not included in the content analysis. Rather, the documents delivered by a stratified sample of applicants were analyzed. Applicants were stratified based on their involvement and relative success within the NDC selection processes and a sample of 18 applicants from across the two rounds of competition was chosen for the content analysis. The applicant strata include:

- Round 1 NDC Awardees
- Round 1 Planning Awardees who did not apply in Round 2
- Round 1 Planning Awardees who became Round 2 NDC Awardees
- Round 2 NDC Awardees who did not apply in Round 1
- Round 1 Planning Awardees who applied in Round 2 without success
- Round 2 applicants who were not Round 1 Planning Awardees

The sample included the population of NDC Awardees (i.e., document deliverables from the eight awardees across Round 1 and Round 2). Of the remaining strata of applicants, half were randomly chosen to comprise the remainder of the sample.

[40] No metrics are included for measurement of the extent to which NDC proposals adhered to an "ideal" envisioned by NIPT officials insofar that the NDC program selection process during Round 1 began with no such reference point but rather used the process to develop a vision for the NDCs in conjunction with applicants and ECG members (see Executive Summary).

B.2.4. Caveat

The content evaluation purposively does not include assessment of center applications in aggregate for scientific merit and general responsiveness to the program goals, as the peer-review process already evaluated the applications for exactly these measures. It is outside the purview of this study to assess or evaluate the effectiveness of the peer-review process.[41]

[41] However, during interviews we were able to capture the perceptions of reviewers, Advisory Committee members, and NIPT team members with regard to the quality and responsiveness of the applications. The NDC program's unique review process did not separate program and scientific review staff, so these data provide an aggregate assessment of scientific merit and responsiveness.

Appendix C: Original study questions

At the outset of the feasibility study, evaluation experts at the STPI outlined seven study questions to guide preliminary assessment of the NDC selection process. The first question (Q1 below) is aimed at understanding the background of the NDC program. The next four questions (Q2-Q5) apply to both the round 1 (2004-2005) and round 2 (2005-2006) selection processes. The second and third study questions are designed to identify any explicit or implicit plans or expectations that guided the NDC selection process. The fourth and fifth study questions are designed to characterize how the selection process actually occurred, to facilitate comparison of process plans and expectations with process implementation and outcomes. Question 6 (Q6) compares round 1 to round 2 activities and outputs. The last study question (Q7) is more interpretive, comparing the relative "effectiveness" of round 1 versus round 2. Each study question has numerous sub-questions.

C.1. NDC Program background information

An understanding of the origins of the NDC program is essential to identify all stakeholders and participants involved, directly or indirectly, with the conception of the NDC selection process. The following questions apply to events occurring before the first round NDC selection process.

Q1: What were the origins of the program?

Sub-questions include:

- What was the impetus for establishing the NDC program?
- What or who were the drivers that led to the establishment of the NDC program? Did it originate solely from within NIH or from both within and without (e.g., as part of the National Nanotechnology Initiative)?

C.2. Documenting the plan for the NDC selection process

One of the primary questions process evaluations are intended to answer is whether program implementation went according to plan and if the goals of the process were accomplished. Unless otherwise noted, the following questions apply to both rounds of the NDC selection process.

Q2: What were the goals of the selection process?

The goals of the NDC selection process appear to have been scientific (e.g., creating the capacity to address a particular scientific or technical problem), institutional (e.g., arranging personnel and resources and infrastructure) and administrative (e.g. development of the NDC selection process itself). Clarification of these goals is important to assess whether and to what degree the center selection process "worked."

Sub-questions:

- How was the prototypical NDC envisioned (e.g., its scientific foci, participants, cross-discipline collaboration, infrastructure and equipment, funding portfolio)?

- How was the initial network of NDCs envisioned (e.g., collaborative projects across the NDCs, transfer across the NDCs, informal networking and collaboration across the NDCs)?

- Was the vision for NDCs and for the network thereof preconceived, or did it develop as the selection process occurred?

- Was development of the NDC selection process itself intended to provide a new model that could be replicated and/or generalized for other initiatives?

Q3: What was the (explicit or implicit) plan or set of expectations driving the selection process?

Though implementation plans may be implicit rather than explicit, or just a common set of expectations among key stakeholders and participants, a reference point must be established from which to judge the appropriateness of the activities that constitute program implementation.

Sub-questions:

- Why was the selection process conceived in terms of Flexible Research Authority (FRA) rather than in terms of conventional mechanisms (e.g., P20, P50)? What led to the FRA being used (e.g. was it perceived as being more efficient, faster, more productive)?

- Which (or what aspects), if any, of the program goals necessitated the use of FRA versus the use of conventional mechanisms to select the NDCs?

- How were the phases (and therefore outcomes) of the NDC selection process conceived (e.g., Concept Development Memos, Planning Awards, the meeting between planning awardees and the Implementation Team, final applications)? Was there precedent for these phases and attendant outcomes (e.g., from another program)? Or were they original to the NDC program?

- Were there informal or codified guidelines or procedures guiding each phase of the process (e.g., directions for applicants, for reviewers, for the meeting between the Implementation Team and planning awardees)? Or was the process (or particular phases thereof) more “ad hoc?”

- Why were the selection processes different for round 1 and round 2? Was round 2 always intended to be different?

C.3. Documenting the actual NDC selection process

Comparing the activities of the NDC selection process as it was implemented to the (implicit or explicit) implementation plan, or at least to the expectations of participants and stakeholders about what should have happened during implementation, is central to process evaluation. In the case of the NDC selection process, this question is especially important given the novelty of the use of FRA to make center awards to the scientific community. Unless otherwise noted, the following questions apply to both rounds of the NDC selection process.

Q4: To what extent did the selection process occur according to plan or "as expected?"

Sub-questions:

- At each phase of the NDC selection process (e.g., CDP review and CDP meeting), what activities were performed by each of the participant and stakeholder groups (e.g., applicants, reviewers, Implementation Team members, other staff)?
    - Were these activities planned or at least expected or foreseen?
    - To what extent were these activities different from conventional procedures (e.g., P20, P50)?

- What were the characteristics of the outputs of these activities (e.g., Planning Awards, Concept Development Plans, reviews of NDC applications)?
    - Were these outputs what was expected (e.g., in terms of quality) by Implementation Team members, reviewers, applicants? For instance, in round 1 did the CDPs facilitate the development of the RFA for NDCs as expected?
    - Were there misunderstandings by applicants about what the various outputs should focus on, include, etc.? If so, at what stages did misunderstandings occur and what were the consequences?

- By whom and how were critical decisions made? (e.g., for round 1, to which CDMs to provide Planning Awards; for both rounds, which NDC applications to fund as centers)
    - Which participants had a role in the final decision? Which did not?
    - What was the process and decision rule(s) guiding these decisions?
    - Were decision processes different from conventional procedures (e.g. P20, P50)?

- What barriers or delays were encountered, when and by whom?
    - What were the causes (e.g., a lack of formal planning, the newness of the NDC selection procedures, a misunderstanding of expectations on the part of participants)?
    - How were these barriers or delays overcome?
    - What effect did they have on the activities of other participants and stakeholders?
    - To what extent did the barriers or delays compromise the integrity of the NDC selection process (e.g., the pool of applicants, the time allotted for peer review of center applications, decision rules for selecting NDC awardees)?

Q5: To what extent did the selection process meet program goals and expectations?

- To what extent did the concept of the centers change during round 1?
  - For planning awardees/applicants, what changes occurred from Concept Development Memo to Concept Development Plan to NDC application?
  - What role did the CDP meeting play? Did it go as expected?
  - Were the changes related to the scientific focus of the proposed center, its organization and structure, and/or its personnel and management?
  - To what extent can these changes be attributed to applicant interactions with the Implementation Team? To any other aspect of the NDC selection process? To any particular phase of the process (e.g., the CDP meeting)?
  - To what extent are these changes associated with successful versus unsuccessful NDC applications? What types of changes, if any, are associated with successful versus unsuccessful applications?

- To what extent did the NDC selection process elicit the intended or ideal center applications?
  - Did the NDC applications match the envisioned prototype (e.g. scientific focus, participants, cross-discipline collaboration, infrastructure and equipment, funding portfolio, network collaboration, etc.)?
  - Did the unconventional process deter any relevant members of the scientific community from applying? Did it encourage new participation or collaborations from the scientific community?

- To what extent did the NDC selection process yield a network of centers?
  - Does the network seem well aligned with the original scientific goals of the program? What are the scientific complementarities?
  - What are the mechanisms or plans indicated at the program level for cross-center collaboration? At the center level?

- What were the benefits of the process when compared to conventional processes (e.g., P20/P50)?
  - Was it faster (e.g., by helping to identify and fund centers faster)?
  - More efficient (e.g., by helping to identify and fund the “right” centers with less effort and paperwork)?
  - More “open” (e.g., by encouraging applications that would not have been submitted otherwise)?
  - More productive (e.g., by helping to identify and fund centers and a network thereof that would not have been possible via conventional mechanisms)?

C.4. Comparing round 1 to round 2

Question 6 is aimed at a basic comparison of the two rounds of NDC selection. Question 7 is more interpretive and aimed at assessing "improvements" (or the lack thereof) from round 1 to round 2.

Q6: What changes occurred in the selection process from round 1 to round 2?

- How did the goals change?
- How did the plans or expectations change?
- How did the implementation change?

Q7: How do the round 2 center applications compare to the round 1 applications?

- Were round 2 applications "better"? Were round 2 applications from round 1 "unsuccessful applicants" "better" than round 2 applications from first time applicants?
- What caused any "improvements" that occurred? Changes to the selection process between round 2 and round 1? If so, which changes and how?

Appendix D: Original discussion guide

This section includes the master cache of interview questions used to develop interview guides. The questions were designed to help answer the study questions outlined at the outset of this study (see Appendix C). For each interview, questions were selected and modified based on the nature (e.g., NIPT, applicant) and timing (i.e., round 1, round 2, both) of the interviewee's participation in the NDC program. Accordingly, not all questions were used in all interviews. Further, these questions evolved as the study progressed. For transparency, the interview questions are reproduced here as originally drafted.

The interview questions are in regular font. Instructions for the interviewer are capitalized.

1. Did the NDC program originate solely within the NIH?

PROBES:

- Whose idea was it?
- When was it first articulated? In what forum?
- How did it eventuate into the NDC program?
- Why was it decided to fund nanomedicine research using the "centers mechanism" instead of funding PIs?
  - What characteristics of the NDC program's scientific goals suggested the need to fund a centers program?

2. What impact, if any, did the National Nanotechnology Initiative have on the conception of the NDC program?

3. Why was the Round 1 selection process conceived in terms of Flexible Research Authority (FRA)?

PROBES:

- At the start, what were the perceived benefits of FRA?
  - Faster? More efficient?
  - Conventional mechanisms don't have these benefits?

- Were there "special needs" of the NDC program that conventional mechanisms could not meet?
  - PROBE USING ABOVE CITED BENEFITS OF FRA. If so, explain.

- Were there perceived shortcomings of conventional mechanisms?
  - PROBE USING ABOVE CITED SHORTCOMINGS OF CONVENTIONAL MECHANISMS. If so, explain.

- At the early stages, was there any resistance to using FRA over conventional mechanisms?
  - From whom or what sources? On what grounds?

- Was the decision to use FRA tied to demands of NIH, or even from without (NNI)?
  - PROBE USING INFO FROM Q2 ABOUT ORIGINS OF NDC PROGRAM. If so, explain.

4. How was the NDC selection process for Round 1 developed?

PROBES:

- Who developed it?
  - IF NOT APPARENT, ASK: What NDC program "groups" did these people belong to (e.g., Implementation Team, ECG, none).
  - Were any "outsiders" consulted? If so, how were they qualified to inform the development of the NDC selection process?

- In what fora was the NDC selection process developed?
  - Formal meetings. Informal meetings? Over beers?
  - Something else?

- When was it developed?
  - Before the initial RFA for CDMs? After?

- How were the Round 1 "stages" arrived at? – CDM and Planning Award, CDP and CDP Meeting, THEN the request for center applications?
  - What was the rationale for each of these "steps" in the process?
  - Were the stages based on a precedent, on another center selection process used elsewhere and emulated by the NDC program?
    - If so, which aspects?
    - If not, were any precedents considered before deciding to develop the process anew? Which ones? Why were they rejected as models for the NDC selection process?

- Once the process was developed, was it "set in stone" or considered open to change even after implementation began?

- How long did it take to develop the process?
  - Was this the expected timeframe?
  - SEGUE TO QUESTION 5.

5. What disagreement or barriers (if any) were encountered when developing the NDC selection process for Round 1?

PROBES:

- Was there disagreement over the use of FRA?
  - What was the nature of the disagreement?
  - Who was in disagreement?
  - How, if at all, was the disagreement resolved?

- Was there disagreement over the any of the "steps" of the process?
  - What was the nature of the disagreement?
  - Who was in disagreement?
  - How, if at all, was the disagreement resolved?

- Were any bureaucratic (e.g., NIH) barriers encountered?
  - What was the nature of the barrier?
    - Did it have to do with the use of FRA?
    - Did it have to do with any of the "steps?"
  - From where did it emanate?
  - How, if at all, was the barrier overcome?

6. When planning Round 1, was there an NDC "prototype?" How were the centers envisioned before the selection process occurred?

PROBES:

- What attributes were the centers expected to possess?
  - Scientific foci?
  - Participants?
  - "Fit" into a network of centers?
  - Infrastructure and equipment?
  - Location?

- Were the attributes preconceived or did they develop and change during the NDC selection process?
  - PROBE USING ABOVE IDENTIFIED ATTRIBUTES. Please explain.

- Which attributes were static, which changed, which "went away," and what new ones were added?
  - PROBE USING ABOVE IDENTIFIED ATTRIBUTES. Please explain.

7. At the start, was there any expected "complementarity" among the first group of centers?

PROBES:

- PROBE USING ABOVE IDENTIFIED ATTRIBUTES. How were the centers expected to "network?"
  - Collaborative projects across NDCs?
  - Transfer across the NDCs?

- Less formal networking and cooperation across the NDCS?

- PROBE USING ABOVE IDENTIFIED ATTRIBUTES. Were these attributes preconceived or did they develop and change during the NDC selection process?

- Which attributes were static, which changed, which "went away," and what new ones were added?
  - PROBE USING ABOVE IDENTIFIED ATTRIBUTES. Please explain.

8. Was part of the plan to use the Round 1 selection process to adjust and hone the NDC selection process for future years' use or even for replication by other programs?

PROBES:

- Was the plan for Round 1 for the first NDC selection process to be a "pilot" selection process, to be adjusted after?

- Was the Round 2 selection process always intended to be "shorter" than the Round 1 process?

- Was the process intended to provide a model or framework for a more generalized FRA process?
  - For centers programs?
  - For non centers programs?

9. Please describe your participation in the NDC selection process.

PROBES:

- PROBE BASED ON THE INTERVIEWEE'S 'STATUS' (E.G., REVIEWER, PLANNING AWARDEE, CENTER AWARDEE, IT MEMBER, ECG MEMBER) Which "steps" of the process did you participate in?

- Did you participate in more or in different ways than you expected?
  - If so, how?

- IF THEY PARTICIPATED IN ROUND 1. Did you participate in the CDP meeting?
  - Please describe.
  - How did you plan or prepare for the CDP meeting?

10. At each step of the NDC selection process, with whom did you interact?

PROBES: PROBE BASED ON THE INTERVIEWEE'S 'STATUS.' FOR EXAMPLE, DID APPLICANTS HAVE DIRECT CONTACT W REVIEWERS?

- How regularly?

- Why?
- Were the interactions planned?
- Over what medium?
- Were they helpful?
- With whom did you interact the most?
- Which interactions were most valuable?
  - With whom?
  - At what step of the process? The CDP meeting?
  - How, why were these "valuable?"

11. How did your participation in the NDC selection process differ from conventional application and award experiences you have had?

PROBES:

- Was it less formal?
- Was it more interactive?
- Was it relatively confusing?
- What aspect of the process was "most different?" The CDP meeting?
  - How?

12. (For Round 1 only) Did you feel that you had constructive input into the development of the NDC selection process?

PROBES:

- What was the nature of this input?
- At what steps of the process did it occur?
  - CDP meeting?
- Do you feel your input was heeded?
- Do you feel your providing input in this way was beneficial to the program?

13. Did you feel that you had constructive input from the NDC program officials and participants during the process?

PROBES:

- What was the nature of this input?
  - Were the expectations for the center applications clear?
- At what steps of the process did it occur?
  - CDP meeting?
- Did you heed this input?
- Do you feel you benefited from this input? How?
  - Improved center application?

14. Did any of the (above) interactions and/or input cause you to make changes to your center application?

PROBES:

- PROBE ABOUT WHATEVER INTERACTIONS AND INPUT THE INTERVIEWEE MENTIONED ABOVE. Please explain.
- Do you feel the interactions/input improved the application, its chances for success?
- Did you disagree with any of the input?

15. Did any of the interactions and/or input cause you to make changes to your reviews? FOR REVIEWERS ONLY

PROBES:

- PROBE ABOUT WHATEVER INTERACTIONS AND INPUT THE INTERVIEWEE MENTIONED ABOVE. Please explain.
- Do you feel the interactions/input improved the reviews? How?
- Did you disagree with any of the input?

16. Did you feel the applications you reviewed were responsive to the RFA, to the expectations of the program? FOR ALL EXCEPT APPLICANTS

PROBES:

- WE SHOULD KNOW THIS FROM THE REVIEW SCHEDULE, BUT ASK TO VERIFY. How many application reviews did you participate in?

- Did you see any applications, from a scientific standpoint, that you didn't expect to see? Please explain.

- Were there scientific foci you expected or would have liked to have seen but did not? Please explain.

- Do you think any aspect of the use of FRA contributed to <REFER TO JUST-CITED APPLICATIONS HERE>?

17. Were you aware of how critical decisions (e.g., Planning Awards, Center Awards) were made?

PROBES:

- What did you know?
  - Who made the final decisions?
  - Were there objective "decision rules?"

- How did you know?
- How did the decision processes differ from your past experiences in other programs?
- What level of influence do you feel your reviews had?
- Do you think this "good" or "bad?"

18. Why was the Round 2 process different than the Round 1 process?

PROBES:

- THIS PROBE MAY HAVE BEEN ADDRESSED ABOVE. Was this always "the plan?"
  - Were the CDP and CDP meeting always intended to be "just Round 1?"
- Or was the change owing to a shift in the expectations and goals of the NDC program?
  - Why were the CDP and CDP meetings not included as part of the Round 2 process?
- Generally, were the Round 2 applications "better" than the Round 1 applications?
  - How?
  - Why?
    - If worse, would another CDP/CDP meeting stage in the process have helped?
    - If there was a CDP and attendant meeting in Round 2, do you think that the Round 2 awardees would have been the same? Would 3 of 4 of the awardees still have been Planning Awardees from Round 1? Did this group have an advantage? Given the unorthodox nature of the selection process, should this advantage have been nullified by another CDP and CDP meeting?

19. In hindsight, were the perceived benefits of FRA "real?"

PROBES:

- PROBE USING CITED BENEFITS ABOVE. Faster? More efficient? More "open?" Better applications? Better how?
- Could conventional mechanisms have been as effective?
  - If you could start again, would you recommend the use of FRA over conventional mechanisms?

20. What would you change about the NDC selection process?

- What "worked?"
- What didn't?
- Would you recommend the process for other programs?
  - Round 1 or Round 2 process?
  - What "steps" would you keep, change, do away with?
- For another round of NDC selection?
  - Round 1 or Round 2 process?
    - Add the CDP and CDP meeting back in?
  - What "steps" would you keep, change, do away with?

Appendix E: Brief literature review

This document is intended to accompany the Science and Technology Policy Institute's (STPI) evaluation of the selection process for Nanomedicine Development Centers (NDC) in 2004-2005 and again in 2006. It is comprised of three sub-sections.

The first sub-section defines the scope of process evaluations generally and addresses the reasons for implementing such evaluations. The second reviews the methods and indicators employed during process evaluations. The third presents the potential benefits of process evaluations, including but not limited to laying the foundation for subsequent outcome evaluations.

This document is organized in this way (rather than per multiple and potentially divergent methodological foci and findings regarding the process of process evaluation) because most extant "study" of process evaluation does not constitute research and analysis per se but rather practitioner level explanation and direction.

E.1. Defining and rationalizing process evaluation

Process evaluations are focused on programs as they are enacted rather than on programs' ultimate outputs and outcomes. The foci of process evaluations can vary as much as programs vary, but usually emphasize a program's initial framework or plans, its functions and goals within that framework, the formal operations and attendant activities implemented to fulfill program functions and goals, the resources and the personnel allocated to conduct operations and activities (Rossi et al. 2004). In short, process evaluation is defined by the goal of providing a full understanding of how a program worked and whether it worked according to program design and plans, but not by the goal of understanding whether a program worked to produce intended outcomes.

Process evaluations are employed if programs are long standing but have changed, if there is perceived or real malfunction in a program, if there exist perceived or real inefficiencies in program implementation, and/or to portray the implementation process for replication elsewhere (Scheirer 1994). New programs employing novel approaches for implementation (e.g., the use of Flexible Research Authority for NDC selection) also may be subject to process evaluation (Rossi et al. 2004, Ruegg & Feller 2003). In short, the rationale for process evaluation is to ensure that a program was implemented as intended, per the standards established for the program.

E.2. Process evaluation methods

The methods employed during process evaluations can depend on the timing of the evaluation (e.g., real time monitoring versus ex post evaluation) and on the nature of the evaluation questions (e.g., whether the process occurred as planned, whether the process was efficient). But generally the methods employed are qualitative (Yin 1994).

Descriptive case study is the most common approach for evaluations of the nascent phases of programs (Shadish et al. 1991) and may include interviews with program managers and other stakeholders, surveys of these same individuals, and analyses of extant program documentation. If the process evaluation occurs simultaneously with program implementation, these methods may be accompanied by direct observation of planning and stakeholder meetings and of specified implementation processes (Ruegg & Feller 2003).

E.3. Process evaluation results

The results of process evaluation may be viewed as a means to better outcomes and impacts evaluation and also as an end informing the development of new approaches to program implementation.

By determining precisely how a program was implemented, whether the implementation occurred according to plans, and the merit of those plans in light of program goals, process evaluation can be essential to subsequent evaluation of program outcomes and impacts. Without such process knowledge, any hypothesizing about why a program succeeded or failed to have the outcomes and impact(s) intended by program managers and stakeholders becomes tenuous (Rossi et al. 2004).

The process knowledge that results from process evaluation also may inform the development and potential improvement of new processes for program implementation. Even when programs are well planned, when there is little or no precedent for the implementation process there are unexpected barriers to and unintended consequences of program implementation (Shadish et al. 1991).

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Appendix F: About the authors

Craig Boardman is a Research Staff Member at the Science and Technology Policy Institute (STPI). His research agenda is focused on the organization of multi-discipline and multi-sector research collaborations. His study has resulted in articles in science and technology policy journals as well as in book chapters and in an IBM Endowment for the Business of Government report on university-industry research centers. He has advised both the US and Canadian governments on center design and management. Before joining the research staff at STPI, Dr. Boardman was a senior research associate of the Research Value Mapping Program at Georgia Tech. He received his doctorate in science and technology policy analysis from Georgia Tech in 2006.

Christopher Hart is a Research Staff Member at the STPI. Before joining STPI, Dr. Hart was a postdoctoral fellow at Yale University and earned a Ph.D. from Caltech with a dual major in developmental biology and computer science applications in biotechnology. His past research has focused on understanding how cells make decisions through the development of experimental, computational and bioinformatic techniques to collect and analyze genome-scale data. Dr. Hart was also an affiliate scientist with the machine learning systems group at NASA's Jet Propulsion Laboratories. His work has lead to the development of several novel algorithms which can enrich our understanding of genomic data. These techniques are also readily applicable to other data mining problems.

Judith A. Hautala is a Core Research Staff Member at the STPI in charge of Life Sciences. Prior to joining STPI in 2005, Dr. Hautala was Vice President, Research and Development, American Red Cross Biomedical Services and Director of the Jerome H. Holland Laboratory for the Biomedical Sciences. At the Red Cross she directed a research and development program in support of blood services and a grant funded discovery research program in areas related to transfusion medicine and novel cellular therapies. Prior to assuming the position of Vice President in January, 2002, Dr. Hautala was Senior Director, Administration for the Holland Laboratory with responsibility for intellectual property matters, negotiation of license and sponsored research agreements, and administrative services including facilities, financial management, regulatory compliance, R&D communications and core laboratory services.

Prior to joining the Red Cross in 1995, Dr. Hautala was Vice President, Business Development and then Vice President, Corporate Communications and Planning for Univax Biologics from 1993 to 1995 and Vice President, Corporate Development at Alpha-1 Biomedicals during 1992. From 1980 to 1992 she was with Genex Corporation, advancing from a Principal Research Scientist to Director of Technology Assessment to Vice President of Technology Development. In these positions, Dr. Hautala’s responsibilities included strategic and business planning, R&D management, technology assessment and licensing, business development, intellectual property management and investor and public relations.

Dr. Hautala received a B.A. in chemistry from Colorado College in 1967 and a Ph.D. in organic chemistry from Northwestern University in 1970. She conducted postdoctoral research in biochemistry at Memorial Sloan Kettering Cancer Center and held a research and teaching

molecular biology appointment in the Interdepartmental Genetics Program at the University of Georgia.