

NIH-RAID Pilot Mid-Course Review Meeting

Meeting Summary

March 7, 2008

Held at
**Embassy Suites Hotel at the Chevy Chase Pavilion
Washington, D.C.**

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MEETING SUMMARY

INTRODUCTION

The purpose of this meeting was to convene a review panel to assess the NIH-RAID pilot program mid-course, brief the panel and answer its questions, and provide the panel with time to discuss the program and develop recommendations.

This report presents (1) the review panel's recommendations, (2) a summary of the panel's discussion leading to those recommendations, and (3) a set of appendices that include a brief list of attendees, a glossary of acronyms, and useful facts about the NIH-RAID pilot program provided to the review panel members to aid in their discussion.

SUMMARY OF REVIEW PANEL RECOMMENDATIONS

1. Continue and expand RAID: The review panel strongly recommends continuing the RAID program, expanding its scope of activities (see below), and considering increased funding. For non-profit/academic researchers, RAID provides potentially the only route toward clinical development of their discoveries. RAID thus is a critical component of translating the fruits of NIH-funded research into new medicines that benefit the public. RAID is also potentially the only route for development of therapeutics targeting many "orphan" diseases, which are only small market opportunities and thus not commercially attractive. Finally, the proof-of-concept data obtained through RAID support may advance candidate therapeutics to an inflection point that attracts private support from biotechnology and pharmaceutical companies, which without such data would never commit funds to the project. Thus, RAID is a catalyst for attracting private funding to advance into clinical development technologies arising from NIH-funded research, thereby spurring job creation and economic activity that far surpasses the RAID budget.

2. Speed reviews: NIH needs to find creative ways to make the "R" ("rapid") in NIH-RAID meaningful. Having a dedicated fund instead of waiting for institutes/centers to agree to sponsor projects would be very helpful. The review panel therefore recommends NIH change its traditional approval process that requires approval by an institute/center council on an ad hoc basis for each project. The panel recommends authority be delegated to approve these modest applications rapidly.

3. Create Pre-RAID: The scope of NIH-RAID should be expanded to provide support for earlier stage projects that are not yet ready for RAID support. The focus of such a pre-RAID program would allow candidate therapeutics to undergo early stages of preclinical evaluation leading to proof of concept in animal models of efficacy. In contrast, successful RAID applications typically already have evidence of efficacy in small animal models of disease.

For a candidate therapeutic to be rationally tested in small animal models, a dosing regimen and route of administration must be defined. The proper dosing requires knowledge for example of compound plasma stability, microsomal stability, pharmacokinetics in rodents. Many academic investigators do not have access to basic pharmacology and drug metabolism services and expertise. The goal would be to provide early preclinical support

to explore the merits of candidate therapeutics, including selecting lead compounds among various available analogs, identifying routes of administration, and establishing dosing schedules that would then allow investigators to design animal model studies towards proof of concept with respect to efficacy. Armed with sufficient compound and knowledge of how to deliver it, PIs could then test the agents in animal models, thus establishing whether efficacy is sufficiently promising to warrant seeking further downstream RAID support. With proof-of-concept data established, the PI could then apply to RAID for development support.

These smaller projects might also seek support from pre-RAID for only one or two steps in the pre-clinical development path for experimental therapeutics (such as formulation of a compound, pharmacokinetics studies, or in vivo biodistribution studies), rather than a full program encompassing the entire range of activities, thus reaching clear go/no go decision points in compound development. NIH should direct targeted funding to these earlier pre-clinical development (“pre-RAID”) steps that academic researchers are not typically set up to do, and create a budget annually for this program, so that rapid decisions are made and so that projects advance quickly. The pre-RAID program could be a bridge from other NIH-funded initiatives (such as Molecular Libraries Screening Centers Network [MLSCN] and NCI-Drug Discovery Groups) and RAID. The reviews of mini-RAID applications could be performed by a standing review panel that meets telephonically on a quarterly basis (approx every 12 weeks), thus ensuring rapid decisions.

Pre-RAID is inappropriate for large animal PK or biodistribution studies, formal in vivo toxicology, advanced formulation and in vitro stability, GMP manufacturing, process chemistry and large-scale synthesis of compounds (> 100 mg) or large-scale biological production (e.g. protein drugs, monoclonal antibodies). These activities should be reserved for RAID. Pre-RAID is for proof of concept studies. RAID is for supporting preclinical IND enabling studies. Application instructions should provide clarity about what types of support are appropriate for pre-RAID versus RAID.

4. Expand the scope of services to induce protein drugs and gene vectors: The review panel considered the current range of molecules for which RAID support is available (chemicals, natural products, peptides, oligonucleotides), and recommended adding protein-based drugs (especially monoclonal antibodies) and gene vectors. If NCI has access to contract laboratories that can produce biologics, these should be added to the types of compounds that NIH-RAID can develop. Biologics development candidates could be prioritized for support based on ease and cost of production, thus eliminating from consideration biological agents that are difficult to produce in scale and/or that are expensive to produce. Because the NIH no longer funds national gene vector laboratories, adding gene vectors to RAID is recommended.

5. Create a rapid funding mechanism for animal model testing of candidate therapeutics. Many academic laboratories and contract laboratories have established small animal (rodent) models of disease in which candidate therapeutics could be tested, but a funding mechanism to support this activity is not readily available. The review panel recommends creating a funding program modeled after the X01/RO3 grant mechanism recently developed in connection with the Molecular Libraries Screening Centers Network (MLSCN) initiative, whereby short applications (5-10 pages) are reviewed 3-times per year by a standing committee, awarding \$25,000 to support testing of candidate therapeutics in rodent

disease models. This animal models program will thus complement pre-RAID to encourage proof-of-concept testing of novel candidate therapeutics.

6. Add a letter of intent (prescreening): The program should require applicants to provide a letter-of-intent (LOI) for prescreening purposes, as this can allow the institutes/centers to begin their own planning earlier as to the kinds of NIH-RAID projects they will support (thereby speeding up the overall process). The LOI should require sufficient information from the applicant in a checklist fashion that indicates whether certain proof of concept studies or compound characterization criteria that are generally required for project funding have been met, prior to preparation of a complete application. The LOI process should be used to encourage dialog with NIH program staff and potential applicants to explore project suitability for RAID and clarify expectations. The goal of the LOI process should be to reduce the pool of inappropriate or premature projects, while also making it very clear what criteria must be satisfied for funding eligibility. It is important that the LOI process not slow the overall application process.

7. Allow for-profit businesses to apply: The review panel recommends that for-profit businesses be permitted to apply to pre-RAID and RAID for support on a trial basis. However, because it was noted that academics have a greater need for funds to access pre-clinical development services, compared to for-profit companies, an effort should be made to maintain a balanced portfolio of projects (non-profit versus for-profit) so as not to have the program cannibalized by companies. Preference should be given to small, under-capitalized companies.

8. Explore ways to optimize project management: The panel members expressed a strong desire for direct communication between the contractors doing the work and the PIs, rather than relying on NIH to play the role of “middle man.” The data (and reports) generated by contractors should be shared directly with the PIs. In addition, more frequent communication between PIs and RAID staff would likely improve the efficiency of the process of preclinical development, and ensure that the biological and clinical context for development of each agent is integrated into the development activities. Organizing 3-way teleconferences with the PI, RAID staff, and external contractors was also strongly suggested. Criteria for success versus failure will vary among disease indications and agents, requiring robust and frequent dialog to maximize chances for success. Setting clearer expectations for the timeline for performance of work would also help. The external contractors for RAID should make available to program staff and PIs a matrix showing the scheduling for each step of each project, creating a timeline for performance. Thus, the review panel recommends direct dialog of PIs with the external contractors doing the work, to ensure that the knowledge of the PI and domain-specific expertise is integrated into the work plan. In addition, the review panel advises that work plans with timelines for execution are developed, sharing scheduling matrices for the funded projects with the PIs and pre-scheduling times for teleconference reviews of data with PIs. This approach will ensure robust communication among the parties involved (PI, NIH-RAID staff, and external contractor).

The panel also questioned whether the domain-specific expertise is available on the part of NIH staff to devise the most efficient and thoughtful development plan, given the broad range of disease indications and types of agents. External experts should be added to the review process regularly.

Another element of project management concerns the handling of failures. Most lead compounds will fail somewhere along the pre-clinical development path. The pre-RAID and RAID programs should consider mechanisms to rapidly substitute back-up compound series when the lead series fails, without necessitating a year-long process of reapplication, re-review, and re-approval for funding.

9. Clinical Development Plan support: The review panel recommended that RAID staff or other NIH staff provide strong assistance to PIs with generating clinical development plans for candidate therapeutics that receive RAID support. The goal should be to devise optimal clinical development plans early in the project, and tailor the preclinical activities accordingly. NIH should recognize that candidate therapeutics may come from Ph.D.-scientists rather than M.D. doctors, and thus providing clinical development and regulatory expertise early in the project is highly recommended to ensure that the appropriate preclinical studies are performed to support clinical development.

10. Outreach: The NIH should initiate strong outreach to encourage use of RAID and particularly to link RAID to other NIH initiatives, such as MLSCN, so that compounds progress towards clinical application. The observation that the small budget for the RAID program (\$16 MM) goes unspent typically is an indication that the academic community (and particularly the biotechnology community) is not adequately utilizing RAID as a partner in drug development. The various Institutes of NIH should educate the Program Officers about the program, and instruct them to proactively encourage NIH grant recipients to access the pre-RAID and RAID programs, rather than relying entirely on RAID staff for outreach. NIH's Program Officers must be advocates and facilitators. One suggestion is for Program Officers to utilize the annual Progress Reports submitted to NIH to identify promising projects for either pre-RAID or RAID support, and to proactively contact those PIs and encourage their participation.

11. Continue periodic evaluations: The review panel recommended continued monitoring of the RAID program and recommended expansions, suggesting that another review be convened in 2 yrs using the same panel members. The review panel requested an opportunity to see all application reviews (without attribution of course), both successful and unsuccessful, to determine the range of projects currently submitted to RAID, including disease indications, types of molecules (natural products, synthetic compounds, peptides, etc.), and drug presentation (formulations, routes of administration, etc.). For the present review, the panel was provided information only about the successful projects.

REVIEW PANEL DISCUSSION

- OPASI viewpoint. Dr. Wilder indicated that OPASI wants to know how the community perceives the program and whether the review panel believes that the current approach and resources provided are satisfactory or need to be changed. While the initial emphasis has been on assisting academic PIs, should attention and resources be focused (additionally or instead) further down the pipeline?

***Action:** The review panel will consider where to spend more NIH-RAID resources, keeping in mind how the program fits with other NIH programs (e.g., molecular libraries, screening networks).

- Promising compounds. While review panel members generally believe the onus is on the sponsor to develop sufficient data to show that a test drug has promise, nevertheless the NIH-RAID program is also needed to further unusual compounds and those (e.g., for rare diseases) for which the market is limited. In the latter cases, NIH-RAID will be developing the data to show whether these compounds have promise.

Still, there needs to be a balance because the program also ought to fund preclinical development steps after the first ones. OPASI staff would like to have the review panel's views as to what aspects of translation the NIH-RAID program should emphasize.

Scope (continued). OPASI staff stated that it is time to consider whether to expand the scope that was chosen four years ago. This could include funding both steps further down the pipeline and very early ("pre-RAID") steps. The review panel chair agreed that, given other NIH roadmap investments (e.g., the molecular libraries), the time is right for funding "pre-RAID" work that academic researchers are usually not set up to do; this could include compound scale-up synthesis, drug metabolism, pharmacology, and formulation work, so that investigators can design and conduct animal model experiments to establish proof of concept, prior to submitting an application to RAID for full support. While in theory R01 grants could fund this earlier work—and NIH views the R01 grants as the appropriate mechanism for proof-of-concept research—in reality such applications usually score poorly on R01 parameters.

OPASI staff also asked whether the review panel will recommend any parameters if it decides to recommend including biologics. One review panel member cautioned about taking into consideration the additional expense involved in manufacturing biologics. Further, NIH-RAID "simply can't do it all." Nevertheless, the panel argued that ease and cost of production of a biological agent could be considered in reviewing applications and that those biological agents with suitable production properties should be considered for RAID support.

Reviewing applications. The review panel expressed concerns whether the appropriate expertise exists on the study-section that reviews RAID applications to cover the wide diversity of therapeutic indications represented by the various divisions of NIH. Though NIH staff indicated that expertise is brought into the review process as needed, this is a subject that merits thoughtful evaluation.

- Should the review process be more rapid? Considering that the pharmaceutical industry's experience is that only 1 in 12 test drugs is successful, NIH-RAID needs to be

able to process more compounds more rapidly. Review panel members discussed how it ought to be possible to more quickly identify and fund smaller projects that do not require much funding—in less than a year—instead of having a one-size-fits-all application review process.

This faster process could involve prior approval of the modest grants involved, such as through a dedicated fund. The panel proposed that each institute pre-approve a specific amount of funding for RAID projects each fiscal year, limiting special reviews for funding only to those projects that surpass the annual budget, and thus allowing for more rapid decision-making.

Furthermore, NIH staff could narrow the number of final applications by triaging the proposed preliminary letters-of-intent and recommending that some applicants not proceed to the application stage. This would reduce barriers to application submission, by avoiding fear of unfruitful preparation of lengthy application that are unlike to meet the criteria for funding.

- Reevaluation. As the program responds to the review panel's recommendations by implementing some changes, it should plan to have a reevaluation in about two years to determine the success of the changes. Regular reevaluations could also assess whether the balance of project types is satisfactory or needs changing.
- A business track. NIH should consider opening the RAID program to pharmaceutical and biotechnology companies. The program has budgeted funds that go unused each year. Possibly a different application track should be developed for these businesses.
- Co-funding RAID projects by NIH institutes/centers. A review panel member remarked on the value and strength of having more than one institute/center co-fund NIH-RAID projects. When the pilot phase is concluded and the institutes/centers completely take over the funding, it will be important to have the co-funding continue. OPASI staff assume that NIH will still provide infrastructure that will maintain consistency among the institutes and centers in the funding mechanism and the nature of the projects funded.
- Communications. Communication between PIs and RAID staff could be improved, in terms of both frequency of communication and in terms of providing greater clarity about work performance plans and timelines for execution.
- Review panel. Members of the review panel reached a consensus that they needed more time to solidify their recommendations, and agreed to schedule a teleconference to finalize recommendations. They also recommended that the NIH-RAID program continue to use their services for future evaluations as the RAID program evolves.

APPENDIX A ATTENDEES BY ORGANIZATION

Review panel members: Gunda Georg (University of Minnesota), Patrick Griffin (Scripps Research Institute, Florida), Charles Grudzinskas (NDA Partners), David Jacobson-Kram (FDA), Mary-Jeanne Kallman (Lilly Research Laboratories), Langdon Miller (PTC Therapeutics), Bruce Pratt (Genzyme Corporation), John Reed (chair) (Burnham Institute for Medical Research), George Thomas (University of Cincinnati), Daniel Wright (NIDDK)

NINDS staff: David Badman (contractor), Jill Heemsker, Anthony Jackson, Story Landis, Thomas Miller (project team leader), Lydia Munger

NIMH staff: Jamie Driscoll

Additional project team members: Nanwei Cao (NIAAA), Robert Goldman (NIAID), David McCann (NIDA), June Lee (NICHD), Traci Heath Mondoro (NHLBI), Beth Spinelli (NIAID), Myrlene Staten (NIDDK), Jerome Wujek (NEI)

OPASI staff: Scott Jackson, Elizabeth Wilder

NCI staff: Jim Cradock, Raj Misra, Nicola Smith, Pramod Terse

NIAMS staff: Stephen Katz

APPENDIX B
GLOSSARY OF ACRONYMS & ABBREVIATIONS

ADME – Absorption, distribution, metabolism, and excretion
CAT – Clinical Applications and Translations (Program), an NCI program
FDA – Food and Drug Administration
FTE – Full-time employee (equivalent)
IND – Investigational new drug (development)
IP – intellectual property rights
NCI – National Cancer Institute
NIAAA – National Institute of Alcohol Abuse and Alcoholism
NIAID – National Institute of Allergy and Infectious Diseases
NIAMS – National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICHD – National Institute of Child Health and Human Development
NIDDK – National Institute of Diabetes and Digestive and Kidney Diseases
NIMH – National Institute of Mental Health
NINDS – National Institute of Neurological Disorders and Stroke
OPASI – Office of Portfolio Analysis and Strategic Initiatives
(within the Office of the Director, NIH)
RAID – Rapid Access to Interventional Development
SBIR – Small business innovation research (grants)

APPENDIX C THE NIH-RAID PROGRAM

KEY FEATURES

- Aim. This program facilitates the preclinical development of candidate therapeutics.
- Resources. Rather than providing the applicants with funding, NIH-RAID provides access, at no cost, to contractors who perform preclinical development tasks. Experienced NCI staff serves as intermediaries between the principal investigators and the NCI contractors who perform the work.
- Applicants. Currently only academic institutions and nonprofit organizations are eligible. Many applicant organizations are collaborating with businesses.
- ***Action:** Dr. T. Miller, project team leader, requested that the review panel consider whether businesses should be eligible for the program.
- Sharing costs. The NIH Roadmap pays 100% of administrative costs and 50% of project costs. One or more of the NIH institutes and centers contributes the other 50%.
- Review Process. The review process involves peer review of applications, followed by a meeting with the PIs of meritorious projects to review the technology submitted for development support. A funding decision is then made in collaboration with a sponsoring institute or institutes (collaborative funding) of NIH. The applicant is not required to know how to do the proposed pre-clinical development or work or how to initiate clinical trials, but they should have plans for how clinical development will proceed if the project is successful. An acceptable plan is to propose that the technology will be licensed to a company for Phase I testing.
- Scope of services. Services include synthesis in bulk of small molecules, synthesis of oligonucleotides, chemical synthesis of peptides, scale-up production; development of analytical methods; isolation and purification of natural products; pharmacokinetic/ADME studies including bioanalytical method development; development of suitable formulations; manufacture of clinical trial drug supplies; range-finding initial toxicology; IND-directed toxicology; and product development planning and advice in IND preparation. The program does not currently manufacture antibodies, recombinant proteins or gene vectors, but does conduct pharmacokinetic and toxicology studies on these biologics.
 - ***Action:** Dr. T. Miller asked the review panel to consider whether the program should be expanded to include the manufacture of larger and more complex products—including gene vectors, antibodies, and recombinant proteins.

QUESTIONS AND ANSWERS: REVIEW PANEL AND PILOT STAFF

- Reviewers. If the reviewers lack specific expertise needed to evaluate an application, ad-hoc reviewers with appropriate expertise are identified.

- Improvements. During the review process, there is an opportunity for the reviewers to point out to applicants how they could add to or change their plans.
- Types of resources. NIH resources can include safety/toxicology, pharmacology, and assistance with drafting an IND. The NIH assistance is usually preclinical—to help the applicant towards an eventual IND. No large-animal toxicology has been funded yet, but it could be.
- Process and timing. The program announcement specifies the application format and components. Applications are accepted three times per year. All applications are reviewed approximately four months after being submitted. After peer review, the NCI creates a preliminary cost-estimate for the applications which received a score of 200 or less. Program staffs at the institutes and centers are shown all applications (regardless of their review score) and decide whether there is enough interest to schedule further exploration via a meeting with NIH-RAID staff and the investigators. Sometimes it can take two months to arrange such meetings.

After the investigator seminar, the NCI prepares a firm cost-estimate and timeline; then the institutes/centers decide whether to fund the project [this can be the longest step in the process]. The NIH-RAID staff involves the institutes/centers as early as possible.

As of the March 7 midcourse review meeting, 12 of 55 applications have been approved; 14 are pending. Three of the funded projects are completed, and 6 are active. The program has lists of disease areas addressed and institutes/centers that have funded projects or participated but not yet funded any. The projects vary in specificity: some have backup molecules, and some do not. A Gantt chart is prepared for each project.

- Rapidity of review. NIH staff would like to have faster reviews. The current time to approval is 8 to 12. 26 months was the longest time to approval due to extenuating circumstances. Length is mostly dependent on the amount of time taken for institute/center reviews for funding meritorious applications, which currently require obtaining approval by the institute's or center's director on an ad hoc basis. Currently, funds are not earmarked for NIH-RAID projects within the budgets of most institutes of NIH.

NCI has sufficient FTEs (five approved and three filled, with the fourth potentially being filled this year) and has 30 relevant contracts (in the U.S., small business, able to use good laboratory practices, which NIH does not regularly have). NINDS has one full-time FTE (Mr. A. Jackson) and a half-time contractor (Dr. D. Badman, a former staff member who retired).

One panel member wondered if the institutes/centers could be part of the initial review team as a way to speed up the review process; as part of this, the representatives of the institutes/centers ought to be empowered to make the funding decisions (which current NIH processes do not allow). Given that the budget for NIH-RAID projects is currently small, amounting to \$8 MM total contributed by NIH institutes (\$8 MM from Roadmap), and thus the amount funded by each institute is a tiny portion of its annual budget, the review panel argued that staff should be delegated authority to fund meritorious projects up to some specified amount, only above which would require approval from the institute director.

- Funding. The annual NIH-RAID budget is \$8M, with a total of \$16M through equal matching by NIH institutes/centers. However, the pilot program has not come close to using this amount, possibly because investigators have been slow to learn about it. The program is scheduled for to accept applications through 2011, with approved projects funded through 2013. NIH envisions a transition at that time to full funding by institutes and centers.
- Outreach efforts.

Action: Program staff invited the reviewers' advice on outreach to increase awareness of NIH-RAID.

- Staff questions for review panel.

- To what extent does the vision and direction of the NIH-RAID Pilot Program promote translation of findings by the biomedical research community?
- What does the NIH-RAID Pilot Program add to existing private, academic, and public resources available to investigators?
- Is progress being made toward achieving the original objectives?
- Is the Program meeting a critical, unmet need for the community, and should it continue after the current funding period ends?
- What changes, if any, could make the program more effective in the future?

- Review panel chair: some topics to address. Dr. Reed and other panel members developed the following topics: (1) the review process and how it works (including whether the applicant has demonstrated a proof of concept before applying); (2) the scope of services offered; (3) project management issues, (4) resource allocation, and the communications process; (5) how failures are handled and whether backup compounds can be substituted; (6) whether a role for corporate sponsors should be encouraged or inhibited; (7) outreach; (8) timelines and turn-around times; (9) integration of new NIH programs (e.g., earlier preclinical or closer to INDs) into NIH-RAID and exploration of how NIH-RAID interfaces with other NIH programs.

Data that applicants provide. The program does not specify to its peer reviewers the types of data needed and allows peer reviewers to advise program staff on the need for additional data through the summary statement and score.

Action: Per today's advice from a panel member, the program will make sure that recipients understand this process when reissuing the program announcement in October 2008.

Panel members also asked if would be realistic for applicants to have an opportunity to discuss the variables and other ramifications with NIH staff prior to submitting an application.

- Scope of services. One panel member proposed that since obtaining in-vivo efficacy data in an academic environment can be a bottleneck, providing some limited funding for industrial sources to test experimental agents in animal models could be a useful addition to NIH-RAID services. Dr. Miller noted that the program has funded some academic PIs to do this, but it would not be feasible to offer efficacy services for the entire range of diseases.

Expand RAID: Staff asked the review panel also to consider whether the scope of the NIH-RAID program should be expanded or the emphasis should be shifted.

Biologics. Biologics development was originally excluded from NIH-RAID due to the greater expense and length of development time involved in comparison with small molecules. In November 2007, the program issued a Notice allowing applicants to request the completion of animal studies for certain biological classes. Dr. Joseph Tomaszewski, deputy director, Division Cancer Treatment and Diagnosis, NCI, has indicated that NIH-RAID has the capacity now to add the manufacture of gene vectors to its list of services if this is approved by Dr. Stephen Creekmore, chief, Biological Resources Branch, DCTD, NCI. Potentially NIH-RAID could help move gene vectors forward to a therapeutic stage. A review panel member suggested that protein therapeutics ought to be added as well. Others noted that “cell therapy” is not far enough along to be included.

Optimizing small molecules. An NCI staff member suggested that it could be useful to add optimizing small molecules as a service.

- Expertise. Given the broad range of diseases that the NIH-RAID program can address, decisions are made by seeking input from NIH program directors with scientific expertise in a given projects disease areas.
- Intellectual property rights. NIH does fund preclinical projects for which there is a roadblock regarding intellectual property rights that could prevent future completion of the drug therapy approval process. Consequently, the application process includes a question about ownership and patents for the compound and one application review criterion asking reviewers to assess if there is an IP roadblock.
- Letter of intent/preapplication proposal. A panel member wondered if a process requiring a letter of intent or other preapplication information could be useful to stop applications early that should not be funded. Currently, letters of intent are optional within the NIH-RAID program. Originally, NIH-RAID required a pre-application proposal but dropped this process to shorten the length of time for application reviews.
- Role(s) for business. The review panel may wish to consider whether it would be appropriate for pharmaceutical firms to apply for NIH-RAID services, and, if so, whether access should be restricted to small businesses. (Note: Three of the approved projects have had Phase 2 followup using SBIR funding.)

SBIR. A review panel member wondered if there should be a proactive approach to channel SBIR projects into NIH-RAID and/or vice versa. Another review panel member observed that there has been no outreach yet by the NIH-RAID program to the NIH CAT program, in which SBIR support of phase 2 trials is possible. A staff member responded that NIH is reluctant to do that when businesses are not currently eligible to apply to NIH-RAID. However, the NIH-RAID staff is looking into possible links to the SBIR program.

While Dr. Badman sees no conflict in involving small businesses when many of them already have a close association with an academic investigator, Dr. Miller indicated that the NIH-RAID program would prefer to be open to all business and not just those eligible for SBIR funding.

Negatives for business. Possible negatives for small businesses include the length of time (8 to 12 months) between application and funding award and having NCI as an intermediary instead of having direct contact with the contractors doing the work. Review panel members noted that having a preapplication process could provide the small company with a quick “no go” decision that would allow it to move on. Dr. T. Miller pointed out that NIH currently does not allow “pre-reviews” of scientific merit by NIH-RAID staff, only a determination of whether the application fits the program’s priorities.

A review panel member voiced the view that companies should not be funded unless they show serious interest in making sure that the project is accomplished, whether with their own funding or that of NIH. Another observed, however, that what NIH-RAID funds is the “non-sexy” part of drug development that others do not want to fund.

- Communications. NCI staff spoke of flexibility in post-award monitoring, with some PIs wanting a lot of interaction and others not. NCI holds a monthly progress meeting to inform NIH staff of project developments. Principal investigators are communicated with regularly and receive a project-tracking document bimonthly.
- Resource allocation. A review panel member raised a question about how well NIH-RAID resources are spread across the spectrum of drug development services. For example, since academic researchers have trouble doing early steps and triaging compounds, perhaps more resources should go into these steps of compound evaluation. Answering this question needs to take into account other programs besides NIH-RAID that contribute to drug development.