



# **National Institutes of Health Rapid Access to Interventional Development (NIH-RAID) Pilot Program Needs Assessment Evaluation**

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# Chapter 1

## Introduction

This preliminary report is the product of a comprehensive “needs assessment” on the NIH-RAID Pilot Program. This is the first of the NIH Roadmap programs to undergo such an analysis. The purpose of this report is to compile, analyze and present the information necessary for the NIH-RAID Working Group to establish: 1) whether there is a critical need for NIH-RAID preclinical drug development resources within the drug development community; 2) whether the NIH-RAID program is achieving its goal to advance NIH’s translational medicine objectives; 3) how well the NIH-RAID program promotes and expedites promising new therapeutic candidates to advance to clinical development and commercialization.

Following the initial needs assessment, Tunnell Consulting examined the NIH-RAID program, both from within NIH and outside of NIH, to obtain feedback and suggestions about the program. We have interviewed scientists with experience in RAID-like programs, and have interviewed a variety of experts from the drug development community; biotech, pharma, medical schools, universities, non-profit institutes, foundations, the FDA, and IC leaders. Insights were collected from a diverse group of scientists and managers: medicinal chemists, immunologists, process engineers, molecular biologists, pharmacologists, microbiologists, gastroenterologists, pediatricians, and translational scientists, among others.

Within this report, Tunnell has conducted archival research to identify existing institutions offering RAID-Like services to the translational research community, allowing an assessment of whether NIH-RAID occupies a unique niche to advance pre-clinical drugs through development and into the clinic. We then examined the NIH-RAID program application requirements, procedures and statistics. In order to better understand the flow of applications and participation in the program, we have studied: 1) scope of the NIH-RAID program support; 2) application barriers, 3) program awareness, 4) Types, relevance, and completeness of services offered, 5) types of therapeutic products supported, 6) alternative funding or service support available to the pre-IND drug development community, 7) any perceived gaps in NIH-RAID supported activities, and 8) suggestions for possible improvements to the NIH-RAID program. We have endeavored to supply a comprehensive assessment with recommendations in these areas.

## Chapter 2

### Archival Research: RAID-like Support

**Overview:** There are many profit and non-profit institutions offering drug development fee-for-service contracts to develop manufacturing processes, conduct Tox/ADME tests and other analytical tests and assays, consult about and prepare IND filings, etc. Some specialize in biologics, which have very recently become eligible for consideration in the NIH-RAID pilot program. Several are utilized by both the private sector and the government (e.g. SRI International, BioReliance). The institutions described below do not constitute a comprehensive list, as there are numerous academic institutions with translational medicine initiatives. Examples are listed at the end of Section A.

The RAID pilot program is unique, and is differentiated from other translational research support functions primarily by providing comprehensive drug development services rather than direct funding to program recipients. Within some university consortiums, some drug development services may be provided to a limited group of member participants (e.g. PharmaSTART), whereas RAID is available to a much wider range of eligible investigators. RAID also provides access to a truly comprehensive range of drug development services. The types of services available within university consortiums are typically more limited by resource constraints (e.g. ITMAT).

The fee-for-service providers often do have a full range of services – indeed, NIH-RAID contracts with many of these service providers to support their awardees’ projects. The service fees, however, are virtually invisible to RAID awardees. This allows the spending of allotted funds to be managed by NIH-designated experts in drug development rather than by academic investigators who may lack in-depth knowledge and experience in drug development.

Responses from interviewees (see NIH-RAID Interview Data and Appendix A) regarding the need for the NIH-RAID program were mainly, and often enthusiastically positive. This group included, though not unanimously, investigators within university consortiums providing limited services to their faculty.

#### **A. Non-Profits with Drug Development Services:**

- **PharmaSTART (under SRI-International, Biosciences Division)**
  - CA-based Consortium
  - Funds up to 30 hours of consulting per project in addition to funding services
  - <http://www.pharmastart.org/>

PharmaSTART™ is a consortium of research organizations led by **SRI International** that offers translational drug development services to help **California-based** universities, research

institutes, and small biotech companies bridge the gap between identifying new drug discoveries and bringing them successfully through clinical development. The goal of PharmaSTART is to facilitate the translation and funding of discovery research from California based universities and their small cap companies, by offering drug development consulting, networking, and drug development services including lead development, GLP toxicology, analytical and regulatory services and cGMP manufacturing. Currently, four Universities: Stanford University, UC Berkeley, UCSF, and UCSD participate in PharmaSTART as the founding members, but the program is expanding. Participation is mediated solely through the respective Office of Technology Transfer at each University. For other companies not associated with these founding members, the same services may be available for a fee.

### **Key Objectives:**

- to facilitate development and translation of drug from within Universities and Medical Centers into industry
  - to provide a comprehensive and specific drug development plan that provides a road map for drug development to University faculty or faculty associated spin off companies
  - to support and foster inter-institutional collaborations in research, development and clinical testing
  - to educate consortium members in the process of drug development
  - to foster and connect pharmaceutical and venture capital investment to emerging drug candidates
  - to enhance collaborations and competitiveness for development-directed government grant support
  - to facilitate the development of new drugs that address orphan diseases
  - to spearhead new inter-institutional initiatives for support of drug development infrastructure and drug development
- **SRI International**
    - Based in Menlo Park, CA with facilities in Washington D.C. and about 20 other locations in the US and elsewhere
    - Biosciences Division provides complete range of services
    - <http://www.sri.com/biosciences/indexN.html>

SRI International is a non-profit, independent research institute whose Biosciences Division of about 200 people has the resources to take chemical and biological research programs from initial discovery to the IND stage to start human clinical trials. They work with government, industry and academic partners.

- **ITMAT - Institute for Translational Medicine and Therapeutics**
  - U. Penn Consortium
  - Garret FitzGerald, MD, Institute Director and Professor of Medicine at U. Penn School of Medicine
  - <http://www.itmat.upenn.edu/>

The Institute for the Translational Medicine and Therapeutics (ITMAT) supports research at the interface of basic and clinical research, with a particular focus on the development of new and safer therapeutic entities. ITMAT includes its own faculty and basic research space, the former General Clinical Research Center (GCRC) which has been integrated with that of Children's Hospital of Philadelphia to form the Clinical and Translational Research Center (CTRC) and an expanding repertoire of cores, programs, and centers designed to support research endeavors between proof of concept in cellular and animal model systems across the translational divide into proof of concept and dose selection in humans. Educational programs relating to translational research, including a newly founded Masters in Translational Research, are also housed within ITMAT. The objectives of ITMAT are (i) to provide an intellectual home and core critical mass for those who pursue translational research; (ii) to expand the number of faculty pursuing translational research at Penn through direct recruitment and enhancement of recruitment packages of any academic entity; (iii) to expand this critical mass by education of existing faculty in translational research and (iv) to develop as a single point of contact for Penn investigators seeking information and support to pursue translational research and for outside agencies wishing to engage with Penn in this area. ITMAT has expanded to include investigators focused on clinical and translational research in all schools at Penn, the Children's Hospital of Philadelphia, the Wistar Institute, and the University of Sciences in Philadelphia. These partner institutions competed successfully for the *Clinical and Translational Science Award (CTSA) funded under the NIH Roadmap, designating ITMAT as the academic home for the program.*

- **TEDCO – Technology Development Corporation**

- Maryland's leading source of funding for seed capital and entrepreneurial business assistance for technology transfer and development programs.
- Renée Winsky, President and Executive Director
- <http://www.marylandtedco.org/contactus/index.cfm>

TEDCO is bringing innovations from universities and federal labs into the State's economy by facilitating the transfer of technology to the private sector and by providing emerging technology companies and university researchers with vital seed funding and specialized technical assistance.

- **CTSI/SOS – Clinical and Translational Science Institute/Strategic Opportunities Support.**

- NIH sponsored translational medicine support in six scientific areas to the University of California San Francisco and consortium members.
- <http://ctsi.ucsf.edu/sos/index.php>
- [http://pub.ucsf.edu/today/news.php?news\\_id=200701111](http://pub.ucsf.edu/today/news.php?news_id=200701111)

UCSF was awarded a large grant from the National Institutes of Health in October 2006 to enhance and facilitate the process of clinical and translational research on campus.

In one of its first moves to reach this goal, the recently established Clinical and Translational Science Institute (CTSI) announced that its Strategic Opportunities Support (SOS) Center is up and running. This program is co-directed by Kathy Giacomini, PhD, co-chair of the SOS Steering Committee and chair of the Department of Biopharmaceutical Sciences at the UCSF

School of Pharmacy, and by Paul Volberding, MD, co-chair of the SOS Steering Committee and vice chair of the Department of Medicine at the UCSF School of Medicine.

The SOS Center will provide a transparent, peer-reviewed process that awards funds to encourage and to enable research and career development in clinical and translational research. The goal of the program is to provide pilot grants and other forms of support to faculty involved in clinical and translational research. The SOS Center has been designed to be an incubator and a catalyst for young researchers and experienced principal investigators to explore novel areas and to test the limits of innovative technologies and methodologies. It is meant to accelerate translational science and the conversion of scientific discoveries from laboratories into practical medical advances for patients and communities that need them most. Mentoring resources will be provided and the Center will serve as a one-stop mechanism to identify pilot funding sources for clinical and translational research. The Center will also enhance the careers of investigators who are interested in obtaining expertise and skills required for modern clinical and translational research.

The committee is focusing on two areas of translational research. One is the process of applying discoveries generated during research in the laboratory and in the preclinical studies to the development of trials and studies in humans. The second area concerns research aimed at enhancing the adoption of best practices in the community.

### **Six Science Areas**

CTSI's SOS Center solicits proposals for research projects in six clinical and translational science areas:

1. Investigator-initiated Pilot Awards in Clinical and Translational Research;
2. Novel Clinical/Translational Methods Catalyst Awards;
3. Translational Technology Awards;
4. Multidisciplinary/Multicenter Research Project Planning Awards;
5. Underrepresented Faculty in Clinical and Translational Research Awards; and
6. Flexible Mini-Sabbatical/Leave Awards.

All eligible UCSF faculty and faculty in CTSI-associated institutions may apply for one or more grants in the six areas mentioned above.

- **CTSA – Clinical Translational Science Awards**

- <http://www.ctsaweb.org/index.cfm>
- <http://www.ctsaweb.org/partinst.cfm>

### **CTSAs**

Drawing from experience of the [NIH Roadmap for Medical Research](#) and extensive community input, the **Clinical and Translational Science Awards (CTSAs)** program creates a definable academic home for the discipline of clinical and translational science at institutions across the country.

This consortium includes 24 **academic health centers (AHCs)** located throughout the nation. When fully implemented in 2012, about 60 institutions will be linked together to energize the discipline of clinical and translational science. The CTSA consortium is funded by the **National Center for Research Resources (NCRR)**, a part of the National Institutes of Health (NIH).

### **NIH and CTSA Institutions: Working Together as a National CTSA Consortium**

A major goal of the CTSA initiative is to develop a national consortium of CTSA institutions that will work together to transform the discipline of clinical and translational research across the country. The Clinical and Translational Science Awards (CTSAs) is a consortium that is transforming how clinical and translational research is conducted, ultimately enabling researchers to provide new treatments more efficiently and quickly to patients. The consortium is designed to:

- Encourage the development of new methods and approaches to clinical and translational research
  - Improve training and mentoring to ensure that new investigators can navigate the increasingly complex research system
  - Design new and improved clinical research informatics tools
  - Assemble interdisciplinary teams that cover the complete spectrum of medical research
  - Forge new partnerships with private and public health care organization
- **BioCrossroadsLINX**
    - Indiana-based initiative to help Indiana's biopharma assets connect with biotech discovery centers such as San Diego, San Francisco, and Boston.
    - <http://news.uns.purdue.edu/x/2007b/071025BiocrossLinx.html>

BioCrossroadsLINX is a non-profit organization, established by BioCrossroads, Indiana's initiative to grow the life sciences, which will advance Indiana's strengths in drug development and manufacturing through educational and workforce development programs and regional collaborations. In addition, BioCrossroadsLINX will analyze, organize and publicize Indiana's research, industry and workforce strengths in biopharmaceutical development and manufacturing.

Recognizing an opportunity to advance Indiana's drug development and manufacturing strengths, BioCrossroads and leaders from Cook Medical, Indiana's Department of Workforce Development, the Indiana Economic Development Corporation, Ivy Tech Community College, and Purdue University, announced the launch of BioCrossroadsLINX, a non-profit organization building educational and workforce development programs and regional collaborations that will help Indiana's biopharma assets – its companies, its people, and its institutions connect with biotech discovery centers such as San Diego, San Francisco and Boston.

Outsourcing specific drug discovery and development services is a growing trend in both the biotech and pharmaceutical industries. As a result, there are opportunities for Indiana companies

to capitalize on rising demand and to build upon existing strengths. Indiana is one of only a few areas in the United States with a concentration of companies that excel in specialized and sophisticated drug development services such as contract research, contract manufacturing, and logistics. Through these 40+ companies and nearly 7,500 employees, Indiana is positioned to support both large pharma organizations and smaller biotech companies.

"Indiana is home to a fast-growing sector within the life sciences industry, and we're going to leverage our strengths to link our assets to complementary groups in other areas. Regional collaboration is a differentiating factor for us. We've been making the connections with important discovery centers like San Diego, and they're keenly interested in Indiana's drug development companies in order to move their discoveries from the laboratory to the marketplace," said David Johnson, President and CEO, BioCrossroads.

"We see this as an opportunity that will lead to growth in the development sector by encouraging academic and workforce development collaboration, as well as a way to identify gaps that can be filled by existing, local companies who can develop marketing strategies to promote their capabilities." Johnson continued.

"There are several complementary opportunities between BioCrossroadsLINX and Purdue," said Dr. Charles Rutledge, Vice President for Research at Purdue University, and the chairman of BioCrossroadsLINX. "Purdue's pharmacy, advanced manufacturing and engineering disciplines all have roles within drug development. In addition, the initiative goes hand in hand with some of our research and education efforts such as the Chao Center for Contract and Industrial Manufacturing and the National Institute for Pharmaceutical Technology and Education."

BioCrossroads will be hiring a consultant in San Diego to serve as a liaison between the West Coast discovery companies and this Indiana biopharma development sector, and will identify new collaborative opportunities for Indiana research institutions and companies. A BioCrossroadsLINX Web site is also in development. Through a robust search function, it will house information about Indiana's drug development capabilities, serving as a public resource and database.

The Vice President of Industry and Government Affairs, Cook Medical said "We talk to pharmaceutical and biotech companies across the U.S. and around the world, and they're turning to new partners and contract service providers out of a rising need to share risks, reduce costs and improve productivity. Much of what these companies need is already here in Indiana."

### **Some Additional Non-Profits with Translational Medicine Initiatives:**

**Scripps Florida (consortium)** - <http://www.scripps.edu/florida/tri/>

**Oregon Translational Research and Drug Development Institute (OTRADI)** - <http://www.oregoninc.org/events/inno/OTRADIfacts.pdf>

**Beckman Research Institute** - <http://www.cityofhope.org/bricoh>

**Johns Hopkins Institute for Clinical and Translational Research (ICTR) (consortium) -**  
<http://ictr.johnshopkins.edu/blog/index.cfm>

**NY State Center of Excellence (CoE), University at Buffalo (consortium) -**  
[http://www.bioinformatics.buffalo.edu/brochures/nysbi\\_bro\\_062606.pdf](http://www.bioinformatics.buffalo.edu/brochures/nysbi_bro_062606.pdf)

**Burroughs Wellcome FUND (\$150K/yr for 5 yrs)**  
[http://www.bwfund.org/programs/translational/clinical\\_scientists\\_background.html](http://www.bwfund.org/programs/translational/clinical_scientists_background.html)

**Weill Cornell Medical Center (WCMC): The Clinical and Translational Science Center (CTSC) (consortium) -** <http://www.med.cornell.edu/ctsc/>

**Duke Translational Medicine Institute**  
<http://www.dukemedicine.org/Initiatives/ClinicalAndTranslationalScience>

**Clinical and Translational Science Institute (CTSI), U. Rochester Medical Center -**  
<http://www.urmc.rochester.edu/ctsi/>

**RTRN – Translation Research Network in Minority Institutions -**  
<http://www.rtrn.net/subpage.htm>

## **B. For-Profit Companies offering Drug Development Services:**

- **RTI International**
  - Based in RTP, North Carolina
  - Has an office in Rockville, MD
  - <http://www.rti.org/page.cfm?nav=6>

Drug discovery and development is a core research activity at RTI International. For more than 40 years, RTI has worked with pharmaceutical companies and government agencies to bring new medicines to market. RTI offers a combination of in-depth experience, regulatory compliance, and state-of-the-art equipment and facilities. Drug discovery activities are supported by a broad range of specialized development services as listed below, with links.

[Drug design and synthesis](#) - Applying expertise in modern drug design, modeling, synthesis, analytics, and identification techniques

[Drug development services](#) - Offering comprehensive services that include formulation development; synthesis of radio labeled compounds; developmental and reproductive toxicology (DART); general toxicology; bioanalysis; drug metabolism and pharmacokinetics (DMPK); and chemistry, manufacturing, and controls (CMC) capabilities

[Clinical through post-approval research](#) - Providing scientifically rigorous research and consulting services in health economics, health outcomes, psychometrics, pricing and reimbursement, health preference assessment, epidemiology, pharmacovigilance, clinical

development, and biostatistics to help biopharmaceutical companies successfully develop and gain market approval for their products

[Natural products laboratory](#) - Screening a diverse library of bioactive compounds derived from plants, bacteria, and fungi to identify new disease-fighting, chemically active agents

RTI's research portfolio of products and services include:

[Analytical chemistry services](#) - Employing state-of-the-art analytical tools for chemical detection and analysis

[Certification and testing services](#) - Specialized tests and analyses that support pharmaceutical development, high-tech manufacturing, and environmental research

[Microanalysis and microscopy](#) - Applying expertise in microscopy, x-ray diffraction, and gravimetry to help clients determine the source of problems with products or processes

[Technology commercialization support](#) - Helping clients commercialize technical innovations by connecting them to entrepreneurial partners and business opportunities

- **Cambrex/Lonza**

- Comprehensive global services
- <http://www.cambrex.com/content/pharma/article.id.458>
- <http://www.lonza.com/group/en.html>

Cambrex sold their Research Products and Microbial Biopharmaceutical business to Lonza.

Cambrex now specializes in small molecule development, while Lonza does both small molecule and biologics in addition to cell therapy products. Cambrex and Lonza have R&D and cGMP manufacturing facilities in the US and Europe. They both offer a broad range of process development, analytical development, process scale-up, safety assessments and optimization services.

- **Covance**

- Comprehensive global services
- Offices in PA, NJ, MD plus many others
- <http://www.covance.com/>

Covance is a comprehensive drug development services company. They provide preclinical and clinical development and commercial service offerings.

Nonclinical, or preclinical, services encompass toxicology, pharmacology, metabolism, bioanalysis, pharmaceutical analysis and biosafety testing in support of nonclinical drug development.

- **BioReliance**

- *Focused on Biologics*
- [http://www.bioreliance.com/services\\_intro.html](http://www.bioreliance.com/services_intro.html)
- [http://www.bioreliance.com/services\\_intro.html](http://www.bioreliance.com/services_intro.html)

All assays are performed under full compliance with Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) standards. Many biologicals now licensed by the FDA, EMEA and other international agencies have been tested and validated by BioReliance.

### **Biologics Safety Testing**

BioReliance safety testing includes a broad spectrum of cGMP- and GLP-compliant biosafety, virology, immunochemistry, molecular biology and microbiology testing services.

### **Viral/TSE Clearance -**

BioReliance has been conducting viral clearance studies for European, Asian and US clients since 1984.

### **Manufacturing Services**

BioReliance manufacturing capabilities include production of viral therapeutics, cell therapeutics and microbially expressed protein products.

### **Toxicology Services**

BioReliance provides GLP compliant genetic, *in vivo* and molecular toxicology testing on pharmaceutical, biopharmaceutical, medical device or pesticide products.

### **Analytical Services**

At BioReliance, Analytical Services involve the testing of biotechnology products to show that their molecular structure meets predefined criteria and that the macro-molecules remain safe, stable and efficacious in the final product formulation. In these studies, the product is physiochemically characterized using a variety of standard and state-of-the-art analytical methods.

### **Laboratory Animal Diagnostic Services (LADS)**

BioReliance's Laboratory Animal Diagnostic Services (LADS) department provides diagnostic services for a complete spectrum of animal diagnostic and analytical services.

## Support Services

Quality Systems

Project Management and Client Services

Regulatory and Technical Support

- **Diosynth**

- *Focused on Biologics*

- <http://www.diosynthbiotechnology.com/>

- [http://www.diosynthbiotechnology.com/modules/mastop\\_publish/?tac=Process\\_Development](http://www.diosynthbiotechnology.com/modules/mastop_publish/?tac=Process_Development)

### Process Development Links - Analytical, Stability and Formulation | Purification & Technology Transfer | Fermentation | Cell Culture

The process development group designs and assembles processes for recombinant protein or peptide products. Processes are developed using both mammalian and microbial expression systems. A comprehensive range of analytical development services as well as formulation development and stability studies are offered.

Diosynth Biotechnology develops "upstream" processes using both mammalian and insect and microbial expression systems. Diosynth has experience with a wide range of expression systems and the development of processes using batch, fed-batch, continuous and perfusion production technologies.

Mammalian cell experience includes:

- CHO, NS0, BHK
- Hybridomas
- Murine myelomas
- Human cell lines

They also provide cGMP production using baculovirus expression in insect cell systems (*Sf9* and *Sf21* cells). Once a process is developed at "bench scale" (typically using 10-L fermenters/bioreactors), it will be scaled-up to 110-L scale (mammalian processes) or 140-L scale (microbial processes).

- **Charles River**

- Based in Wilmington, MA

- Comprehensive services

- <http://www.criver.com/>

Charles River Laboratories provides research models and laboratory animal support services, preclinical services, and clinical services to the biomedical market. Links to their services are below:

**Discovery Services**

**Toxicology Services**

**Laboratory Sciences  
Pathology Services  
Drug Metabolism and Pharmacokinetics  
Consulting and Program Management**

- **Aptuit**

- Comprehensive global development services
- Based in Greenwich, CT with a local office in Mt Laurel, NJ
- <http://www.apuit.com/default.aspx>

Aptuit provides a comprehensive suite of drug development services. They offer centralized project management is working to establish the industry's first seamless IT system, which will allow access to data anywhere in the world, in real time.

- **Quintiles**

- Comprehensive services
- Based in RTP, NC with local offices including Rockville, MD
- <http://www.quintiles.com/AboutUs/Overview.htm>

Quintiles offers a range of integrated product development services from early development through late-phase trials.

- **Quest Pharmaceutical Services**

- Global company with focused development services
- Office contacts by region; specific locations not on website
- <http://www.questpharm.com/drug.htm>
- <http://www.questpharm.com/Pre-Clinical/Preclinical.html>

The key components of an IND data package are the Pharmacology, Toxicology and Safety Pharmacology; Adsorption, Disposition, Metabolism, and Excretion ([ADME](#)); and Chemistry, Manufacturing and Control (CMC) sections of the submission.

QPS' comprehensive preclinical capabilities allow completion of all the Drug Metabolism and Pharmacokinetics ([DMPK](#)) studies necessary to support an IND filing.

## Chapter 3

### The Need for NIH-RAID

In order to test the hypothesis that there is a real need for the NIH-RAID program, we asked the translational research community the question. The overwhelming response to this question was “yes”. We also asked the question, “Are you interested in learning more about NIH-RAID, and would you consider applying for services?” The majority also answered this question with a “yes”; however those from biotech and pharma companies did not feel that they were in a position to currently benefit from the RAID services. Nonetheless, several said that they would like to pass information along to friends and colleagues. If scientists are interested in receiving more information; applying to RAID, or recommending the program to a colleague, all these responses show affirmation of a developmental need. The table below verifies the need for the NIH-RAID program, and details the responses from the varied scientists that were interviewed.

**Table # 1 --- Non-User Response to the Need for RAID**

<b>Scientist Interviewed:</b>	<b>Yes</b>	<b>Interested in Learning More; or Would Refer a Colleague</b>	<b>No</b>	<b>No Opinion</b>
<b>1</b>	<b>X</b>			
<b>2</b>	<b>X</b>	<b>X</b>		
<b>3</b>	<b>X</b>	<b>X</b>		
<b>4</b>	<b>X</b>	<b>X</b>		
<b>5</b>	<b>X</b>	<b>X</b>		
<b>6</b>	<b>X</b>	<b>X</b>		
<b>7</b>	<b>X</b>	<b>X</b>		
<b>8</b>	<b>X</b>	<b>X</b>		
<b>9</b>	<b>X</b>	<b>X</b>		
<b>10</b>	<b>X</b>	<b>X</b>		
<b>11</b>			<b>X</b>	
<b>12</b>	<b>X</b>	<b>X</b>		
<b>13</b>	<b>X</b>	<b>X</b>		
<b>14</b>	<b>X</b>	<b>X</b>		
<b>15</b>		<b>X</b>		<b>X</b>
<b>16</b>	<b>X</b>			
<b>17</b>	<b>X</b>	<b>X</b>		
<b>18</b>	<b>X</b>	<b>X</b>		

Some researchers were very enthusiastic about the critical need that the NIH-RAID program fulfills; while others were positive yet not as enthusiastic. In order to give the reader a realistic sense of the responses (with regard to need), we have listed some of the quotes: “absolutely critical”, “very worthwhile”, “most definitely needed”, “absolutely, the need is there for biotech start-ups”, “yes, there aren’t many avenues available for developing therapies”, “the need is huge”, “the need for RAID is critical”.

## Chapter 4

# Awareness of the NIH-RAID Program

### Data Collection Methodology:

Tunnell Consulting conducted 23 interviews to collect data about the NIH-RAID Pilot program. All those that were interviewed were experienced in an aspect of drug development. Scientists interviewed spanned a wide variety of disciplines such as, neurology, cardiology, immunology, virology, toxicology, etc. Interviews were conducted on a wide variety of scientific experts residing at both non-profit and profit institutes; and from both large and small institutions. Data was collected from academic institutions, research foundations, biotech and pharmaceutical companies. The interviewees were subdivided into 4 major categories and an interview form for each group was developed to uniformly capture data with regard to the nature and need for the NIH-RAID program. The interview forms utilized for the groups were: 1) RAID users, 2) RAID non-users, 3) NIH ICs, and 4) NIH-RAID-like Services. A “user” designates someone involved in drug development that has been approved for NIH-RAID support, or is in the process of re-applying for RAID support. The “non-user” category is the group of people that are involved in drug development, but have not yet applied for NIH-RAID support. The NIH ICs group was interviewed to examine the internal awareness of the NIH-RAID program. The final group of RAID-like services was primarily to examine the “competitor” awareness of NIH-RAID. These four interview forms can be found in Appendix A.

## Awareness of the NIH-RAID Program:

### 1. Awareness Among Non-Users of RAID

Table #2 -- Awareness Outside of NIH

Non-Users Outside of NIH Interview #	No Awareness of RAID	Low Awareness of RAID	Medium to High Awareness of RAID	How Interviewee Became Aware
1		X		Through NIAID's VRC
2	X			--
3	X			--
4		X		Colleague Applying
5			X	Colleague Applying
6	X			--
7			X	Served as RAID Reviewer
8	X			
9		X		Ask to do Mid-Course Review
10		X		Served on NIH Roadmap Committee
11		X		Through Past NIH Roadmap Association
12			X	Reviewer for NIA
13	X			--
14	X			--

There were a total of 18 non-users of the NIH –RAID program that were interviewed. Fifteen of these non-users were from outside of the NIH community; four of these interviews were from inside of the NIH IC Extramural Research programs. Table #2 above, depicts the level of awareness within the non-users (i.e. those that have not yet applied to the RAID program for support). Eleven out of fourteen interviewed, ~ 78%, had low or no awareness of the NIH-RAID program. Even those that had heard of the NIH-RAID program were not aware of the details of application or types of support services provided by the RAID program. The remaining 22% had

a reasonably good knowledge of the RAID program and its services. It was this 78% low awareness score that spurred us to investigate the internal NIH awareness of the RAID program. There is no doubt a great awareness of the RAID program by those that have served upon the NIH-RAID Working Group Committee. (The interviews of the Working Group can be found within Appendix B).

## 2. Awareness Among NIH Extramural Community

**Table #3 -- Awareness Within NIH Extramural Research Programs**

<b>Non-Users Outside of NIH Interview #</b>	<b>No Awareness of RAID</b>	<b>Low Awareness of RAID</b>	<b>Medium to High Awareness of RAID</b>	<b>How Interviewee Became Aware</b>
<b>1</b>			<b>X</b>	<b>Heard Dr. Badman Speak Last Week</b>
<b>2</b>	<b>X</b>			<b>--</b>
<b>3</b>			<b>X</b>	<b>NIH Roadmap Committee &amp; X01 Grant Mechanism</b>
<b>4</b>		<b>X</b>		<b>--</b>

We interviewed four IC Extramural Research Directors to detect the awareness of those that have not served on the RAID Working Group. We found that two had “low” or no awareness of RAID; while two had very good comprehension of the RAID program. The results of these interviews are contained in Table #3, above. In all cases, awareness of the RAID program was most often communicated by word of mouth; and direct or indirect contact with a reviewer or applicant of the RAID program.

## 3. Awareness Among Users of RAID

An additional 5 users of RAID, i.e. those that either have gained RAID support or are re-applying for RAID support, were interviewed for awareness. When RAID applicants were asked how they became aware of RAID, they offered the following contact history: 1) through a contact at Edison Pharmaceutical who knew Dr Baughman, who in turn contacted Dr. Tom Miller of NINDS, 2) through Dr. Rosseau who introduced applicant to Dr. Badman, 3) through their association with a biotech, Attenuon, and 4) through Dr. Mary Wolpert of NCI, and Dr Schaeffer of NIAID. 5) through NIA an introduction with NIH-RAID was made. Contact Again, in all cases the awareness of RAID developed from word of mouth; more specifically, the efforts of RAID’s Dr. Badman or through an NIH contact that was familiar with the RAID program, or its personnel.

# Chapter 5

## Ranking of Pre-Clinical Services

In the interview form we asked participants to give their general impressions of the pre-clinical services required; and to rank these services by their relevance to supporting drug development. The following list was developed for our survey. The following outline was not meant to be an all-inclusive list of every conceivable pre-clinical service; rather, it was to provide examples of potential services that could be offered:

### **A. Small Scale Synthesis**

### **B. Process Development:**

1. Streamline and scale-up synthesis
2. Bulk product purification
3. Analytical methods development (purity, identity, stability, potency, specifications)
4. Perform analytical methods for agent characterization
5. Formulation studies
6. Consistency runs to demonstrate process control
7. Technology transfer of processes to cGMP manufacturing
8. Demonstration of reproducibility and process control (multiple lots)
9. Stability on representative product lot(s)
10. Other

### **C. Tox/ADME for IND (GLP or non-GLP):**

1. Metabolic Stability
2. Metabolite ID
3. Protein Binding
4. Cyp Inhibition and Induction
5. Cell-based Toxicity
6. *In vivo* studies
  - i. MTD
  - ii. Dose range
  - iii. Other
7. Caco-2 permeability
8. Cardiotoxicity (hERG) testing
9. Other

### **D. Assistance & Guidance**

1. Provide primer to steps in preclinical plan
2. Provide specific product development plan
3. IND filing
4. Other

**Table #4 --- Ranking of Top 5 Service Priorities for NIH-RAID Support**

<b>Non-Users #</b>	<b>Service #1</b>	<b>Service #2</b>	<b>Service #3</b>	<b>Service #4</b>	<b>Service #5</b>
1	B1 Scale-Up Synthesis	D. Assistance & Guidance	---	---	---
2	B1 Scale-Up Synthesis	C. Tox/ADME	C9 Inflammation & Immunogenicity	D3 IND filing	----
3	B5 Formulations	B3 Analytic Methods	B7 cGMP	B9 Stability in GLP Lab	C9 Immunogenicity
4	All Listed	--	---	---	---
5	A. Small Scale Syn.	D2 Product Develop. Plan	---	---	---
6	C6 In Vivo Tox/ADME	D2 Product Develop. Plan	---	---	---
7	D. Assistance & Guidance	B7 cGMP Manufacture	B3 Analytic Methods	---	---
8	B1 Scale-Up	B3 Analytic Methods	B6 Consistency	C7 CACO-2 Tox	B7 cGMP Manufacture
9	B1 Scale-Up Synthesis	C. Tox/ADME	D. Assistance & Guidance	---	---
10	B1 Scale-Up Synthesis	B5 Formulations	B7 cGMP Manufacture	C6 In Vivo Tox	---
11	Disagrees	---	---	---	---
12	C9 Bioavailability	D4 FDA Filing Advice	C9 Biomarkers	C9 Drug Efficacy	---
13	B2 Product Purification	C9 Pk Studies	D2 Product Development Plan	---	---
14	C. Tox/ADME	B5 Formulations	D. Assistance & Guidance	---	---

<b>Users of RAID</b>	<b>Service #1</b>	<b>Service #2</b>	<b>Service #3</b>	<b>Service #4</b>	<b>Service #5</b>
<b>15</b>	<b>A. Small Scale Synthesis</b>	<b>D2 Product Development Plan</b>	<b>B3 Analytical Methods</b>	<b>C. Tox/ADME</b>	<b>---</b>
<b>16</b>	<b>C. Tox/ADME</b>	<b>---</b>	<b>---</b>	<b>---</b>	<b>---</b>
<b>17</b>	<b>D. Assistance</b>	<b>B5 Formulations</b>	<b>A. Small Scale Synthesis</b>	<b>C. Tox/ADME</b>	<b>---</b>
<b>18</b>	<b>A. Small Scale Synthesis</b>	<b>B1 Scale-Up Synthesis</b>	<b>B2 Purification</b>	<b>C. Tox/ADME</b>	<b>D. Assistance &amp; Guidance</b>
<b>19</b>	<b>B1 Scale-Up Synthesis</b>	<b>B5 Formulations</b>	<b>B7 cGMP Manufacture</b>	<b>---</b>	<b>---</b>

Most of those interviewed, with only one exception (out of the 19) found the list of pre-clinical services to be quite comprehensive. While some interviewees would provide detailed rankings, others would only rank by general categories such as A, B, C, etc. Some would provide their top 8 choices while others only provided their top two choices. Therefore, the level of detail varies with the interview.

Nonetheless, clear trends can be seen in Table #4. If we examine which pre-clinical service was most often cited, regardless of priority ranking, we see that “Process Development” was most often cited. Process development was cited ~ 47% of the time. Tox/ADME was second most cited at 28%; while Assistance and Guidance was chosen ~ 18% of the time; and the lowest category cited was Small Scale Synthesis at ~7%. The #1 priority, most frequently chosen was again in Process Development. The general category of Process Development was chosen as the first priority in ~ 42% of the interviews. More specifically B1, “streamline and scale-up synthesis” was cited most frequently as the first priority, ~ 32% of the time. The #2 priority was also Process Development, or more specifically, “Formulation Studies”. Several that were interviewed emphasized the importance of GLP for Tox/ADME studies; as well as emphasized that manufacturing production of the product must be cGMP.

It should be noted that pre-clinical services for Extramural Research Directors were not examined since these scientists were not considered as potential users (customers) of the RAID services. Nonetheless, all commented that this list of pre-clinical services seemed very reasonable for supporting drug development.

## Other Pre-Clinical Services Requested

The following is a complete list of pre-clinical services that interviewees suggested we write-in:

1. *In vivo* Immunogenicity
2. *In vivo* Inflammatory response
3. Awareness training on FDA requirements
4. FDA e-filing rules (i.e. electronic Common Technical Documents, e-CTD)
5. Bio-availability assays
6. Assessing biomarkers
7. Assessing *in vivo* drug efficacy
8. PK assays and studies

## Chapter 6

### Types of Products for NIH-RAID Support

Historically, NIH-RAID has only, until very recently, supported the development of small molecules. The rationale was that proteins and biologics were very expensive to support. The preference was to support a greater number of small molecule projects. NIH-RAID has recently changed its policy such that later stage pre-clinical development of proteins, biologics, and gene therapy agents will be considered for support, with the exception of product production. The policy can now be found on the NIH-RAID website at: <http://grants.nih.gov/grants/guide/notice-files/NOT-RM-08-005.html>. It could be argued that one should focus upon a concise research (such as small molecules) area to have the maximum impact. Alternatively, one might argue that there is a variety of important therapeutic agents that fall outside of the “small molecule” category. To resolve these two schools of thought, we asked our experts in drug development to select the top 2 or 3 categories of products that would have the greatest impact on translational medicine (in their specific discipline). The questions asked during the interview followed the following outline of products. Much like the previous list of services, this list was not meant to be an all-encompassing list of products; rather this list was designed to stimulate discussion:

- A. Small Molecules**
- B. Peptides**
- C. Oligonucleotides**
- D. Proteins/Biologics:**
  - 1. Antibodies
  - 2. Vaccines
  - 3. Therapeutics
  - 4. Enzymes
  - 5. Monoclonal Ab therapeutic
  - 6. Other
- E. Cellular Therapies**
- F. Diagnostics**
- G. Others**

**Table #5 --- Ranking of Top 3 Product Priorities for NIH-RAID Support**

<b>Non-Users:</b>	<b>Product #1</b>	<b>Product #2</b>	<b>Product #3</b>
<b>1</b>	<b>D. Protein/Biologics</b>	<b>B. Peptides</b>	<b>---</b>
<b>2</b>	<b>D2 Vaccines</b>	<b>D5 Monoclonal Ab</b>	<b>D3 Prophylaxis</b>
<b>3</b>	<b>D. Protein/Biologics</b>	<b>---</b>	<b>---</b>
<b>4</b>	<b>A. Small Molecules</b>	<b>D. Protein/Biologics</b>	<b>E. Cell Therapies</b>
<b>5</b>	<b>D5 Monoclonal Ab</b>	<b>C. Oligonucleotides</b>	<b>D6 Growth Factors</b>
<b>6</b>	<b>A. Small Molecules</b>	<b>---</b>	<b>---</b>
<b>7</b>	<b>D. Protein/Biologics</b>	<b>---</b>	<b>---</b>
<b>8</b>	<b>B. Peptides</b>	<b>C. Oligonucleotides</b>	<b>A. Small Molecules</b>
<b>9</b>	<b>A. Small Molecules</b>	<b>D. Protein/Biologics</b>	<b>---</b>
<b>10</b>	<b>A. Small Molecules</b>	<b>B. Peptides</b>	<b>---</b>
<b>11</b>	<b>A. Small Molecules</b>	<b>---</b>	<b>---</b>
<b>12</b>	<b>A. Small Molecules</b>	<b>D. Protein/Biologics</b>	<b>---</b>
<b>13</b>	<b>A. Small Molecules</b>	<b>B. Peptides</b>	<b>---</b>
<b>14</b>	<b>D. Protein/Biologics</b>	<b>D5 Monoclonal Ab</b>	<b>---</b>
<b>NIH Extramural Non-Users</b>	<b>Product #1</b>	<b>Product #2</b>	<b>Product #3</b>
<b>15</b>	<b>---</b>	<b>---</b>	<b>---</b>
<b>16</b>	<b>A. Small Molecules</b>	<b>E. Cell Therapies</b>	<b>F. Diagnostics</b>
<b>17</b>	<b>A. Small Molecules</b>	<b>E. Cell Therapies</b>	<b>G. Gene Therapies</b>
<b>18</b>	<b>A. Small Molecules</b>	<b>E. Cell Therapies</b>	<b>B. Peptides</b>
<b>RAID Users</b>	<b>Product #1</b>	<b>Product #2</b>	<b>Product #3</b>
<b>19</b>	<b>A. Small Molecules</b>	<b>G. Biomarkers</b>	<b>D. Protein/Biologics</b>
<b>20</b>	<b>C. Oligonucleotides</b>	<b>D. Protein/Biologics</b>	<b>D5 Monoclonal Ab</b>
<b>21</b>	<b>B. Peptides</b>	<b>A. Small Molecules</b>	<b>D5 Monoclonal Ab</b>
<b>22</b>	<b>E. Cell Therapies</b>	<b>A. Small Molecules</b>	<b>B. Peptides</b>
<b>23</b>	<b>A. Small Molecules</b>	<b>---</b>	<b>---</b>

Table #5, above, shows the distribution and priority of products for drug development. There was a diversity of opinion on which products should be supported by NIH-RAID. The product most cited to be worthy of RAID support was “protein/biologics” at ~33%. The 2<sup>nd</sup> most cited product was “small molecules” with ~26% of the vote. The 3<sup>rd</sup> most cited product was peptides with ~15% of the vote; and cellular therapies were referenced ~ 9% of the time. Small molecules received ~54% of the vote in the number one priority category; in the second priority category was “proteins and biologics” at 40% of the total vote.

## **Traditional Small Molecules *versus* Proteins and Biologics:**

It appears that proteins and biologics molecules were most often cited in spite of the strong feelings by many traditional medicinal chemists and pharmacologists. Many saw this rift in therapeutics as traditional technology *versus* the future therapeutics. The differences can be summed up by the following comments on proteins and biologics: It is "...where the industry is headed". "We must translate how biologics work for new therapeutics"; "This is the future hope for many therapeutics". "RAID should be open to biologics, for especially since this is where modern pharma is moving". "in spite of the higher costs and quantities needed for studies – we should allow this area since the trend is moving towards biologic areas." Another offered, ""Biologics are needed to broaden the pool of applicants". Although the preponderance of responses favored proteins and biologics, one researcher stated, "I do not wish to see support of biologics"; while others simply had no opinion.

Four interviewees stated the utility of specialized antibodies; and as such would like support for these monoclonal antibodies. These drug developers did not wish to use the monoclonal antibodies as a therapeutic, but rather as a specialized reagent. They all stated that monoclonal antibodies are extremely valuable as a tool; but they are restricted by the extreme cost to develop monoclonal antibodies.

## **Cellular and Gene Therapies:**

Gene therapies and Cellular therapies were each cited in 4 responses or ~7%. Although these technologies are in their infancy, they hold the best promise for cures for specific diseases. Several felt that these types of therapeutics should not be excluded from RAID support. For example, ocular stem cells had been used to effectively treat corneal damage.

## **Other Products:**

Some cited the value of electronic chip implants and prosthetic devices; and others discussed the value of fast and quick point of use diagnostics.

## Chapter 7

### Possible Sources of Funding for RAID-Like Support

In order to assure that there is not a wide array of RAID-like programs available to those needing pre-clinical support, two similar questions were posed to our drug development experts. 1) *Are you aware of similar/comparable resources available to support pre-clinical drug development?* 2) *What are your primary sources of funding for pre-clinical drug development programs?*

The table below depicts the type of institution, i.e. biotech, pharma, contract research organization (CRO), or non-profit institutions; and the knowledge of other types of pre-clinical drug development support available.

**Table # 6 --- Resources Available to Support Pre-Clinical Drug Development**

<b>Type of Institute Interviewed</b>	<b>No Knowledge of Other Sources</b>	<b>Knowledge of Other Sources</b>	<b>1° Source of Their Lab Funding</b>	<b>Possible Source for Drug Support</b>
<b>CRO</b>		<b>X</b>	<b>Client Fees</b>	<b>North Carolina Biotech Center</b>
<b>CRO/Consulting</b>		<b>X</b>	<b>Client Fees</b>	<b>SBIR/STTR Grants</b>
<b>Biotech</b>		<b>X</b>	<b>Venture Capital (VC), Gates Foundation, Welcome Trust</b>	<b>DOD SBIR</b>
<b>Biotech</b>		<b>X</b>	<b>VC, Stock &amp; Product Sales</b>	<b>FDA- Orphan Drugs (post-IND only)</b>
<b>Biotech</b>	<b>X</b>		<b>VC</b>	
<b>Biotech</b>		<b>X</b>	<b>Stock Sales &amp; Pharma Partnerships</b>	<b>SBIR &amp; STTR</b>
<b>Pharmaceutical</b>		<b>X</b>	<b>Stock &amp; Product Sales</b>	<b>Partnerships with Pharma</b>
<b>Academic (Med. School)</b>		<b>X</b>	<b>NIH grants (CTSA)</b>	<b>Inst. Trans. Med. &amp; Ther.</b>

				<b>(Penn's ITMAT)</b>
<b>Academic (Med. School)</b>		<b>X</b>	<b>NHLBI</b>	<b>Nat. Gene Vector Lab &amp; Prod. Assist. For Cellular Ther. (PACT)</b>
<b>Academic (Med School)</b>	<b>X</b>		<b>NIH</b>	
<b>Academic</b>		<b>X</b>	<b>NIH</b>	<b>Penn's ITMAT</b>
<b>Academic</b>		<b>X</b>	<b>NIDA &amp; NCI</b>	<b>NIDA, Northeastern Center for Drug Discovery (CDD)</b>
<b>Academic (Med School)</b>	<b>X</b>		<b>NIDDK</b>	
<b>Academic (Med School)</b>	<b>X</b>		<b>Pharma Partner</b>	
<b>Academic</b>		<b>X</b>	<b>NCI</b>	<b>NCI RAND</b>
<b>Academic</b>		<b>X</b>	<b>NIA</b>	<b>VC &amp; SBIR</b>
<b>FDA</b>		<b>X</b>	<b>(NA)</b>	<b>NIH R01</b>
<b>Research Inst.</b>		<b>X</b>	<b>NIH</b>	<b>University Grant</b>
<b>Research Inst.</b>	<b>X</b>		<b>NIH</b>	
<b>Research Inst.</b>		<b>X</b>	<b>NIH</b>	<b>Johns Hopkins CIDR</b>
<b>Research Inst.</b>	<b>X</b>		<b>NIH</b>	

Table #6 clearly indicates that a significant portion of the funding mentioned is through NIH sources. The closest competition for NIH-RAID might be considered NIH IC programs; for example, NCI's RAND program. The IC drug development programs are of course limited to select diseases. Upon analysis of the alternative sources of funding, we found no program with either the focus or funding capabilities of NIH-RAID. There were very few programs that were established to specifically support pre-clinical research (i.e. pre-IND). For example, the FDA program for orphan drug support is only available to candidates after a successful IND filing. It appears that the only grant mechanism for biotech is the SBIR/STTR grants; these mechanisms cover a very broad range of scientific areas. There are focused programs such as University of Pennsylvania's ITMAT, and Northeastern University's CDD programs. These programs are established primarily for in-house funding and do not have the resources to fund numerous outside projects. Perhaps the deepest funding pockets for drug development could be provided by pharmaceutical partnerships. Although this funding route looks attractive, pharmaceutical companies are reluctant to fund research until the drug candidates are well into their clinical trials. The Bill and Melinda Gates Foundation and the Wellcome Trust fund an incredible number

of worthy medical research projects. Nonetheless, there has not been a specifically targeted program for pre-clinical drug development. In summary, we found no significant national funding alternative to the NIH-RAID program. The NIH-RAID program appears to fulfill a unique market niche.

## Chapter 8

### Perceived Barriers to Using NIH-RAID

As discussed in the Outreach chapter and elsewhere, part of the impetus for a “Needs Assessment” was that the NIH-RAID program had relatively low numbers of applicants. It was concluded that a focused outreach/marketing program would no doubt address some aspects of this issue. Related to this, the chapter describing “Awareness of the RAID program” discussed the relatively low awareness level of the RAID program within the drug development community. However, awareness alone may be insufficient to explain the low number of applications. In reality, a number of factors are likely to contribute to the paucity of applicants of this relatively new NIH-RAID initiative. This chapter will analyze the results of asking interviewees the direct question: “*What are the potential barriers to your use of the program?*” We have already established, in the chapter on “Need for the NIH-RAID Program”, that there is a strongly perceived need for the NIH-RAID program. Consequently, in addition to previously covered marketing/outreach and awareness deficiencies, this chapter will analyze the responses of our interviewees to the following questions concerning additional barriers to applying for NIH-RAID services:

#### Specific questions for “non-RAID users”

- What are the potential barriers to your use of the program?
  - Eligibility restriction?
  - Application Process
  - Intellectual Property?
  - Speed/Timeliness?
  - Other?

#### General questions for “RAID users” who had already applied to the RAID program for support:

- Were there barriers or impediments to using the program?
- Were there any areas of concern when making the decision to apply?

## Data Collected from Interviewing Target Audience:

Table #7 --- Barriers to Using NIH-RAID

Interview #	Eligibility Restriction	Application Process	Intellectual Property	Speed/Timeliness	Other Barriers
1	---	X	---	---	---
2	X	---	---	---	---
3	X	---	---	---	---
4	X	---	---	X	X
5	X	---	X	X	---
6	X	X	---	X	X
7	X	---	X	X	---
8	X	---	---	---	X
9	---	X	---	---	X
10	X	---	---	X	X
11	X	---	---	---	X
12	X	X	X	X	---
13	X	X	X	X	---
14	X	X	X	X	---
15	---	X	---	X	---
16	X	X	---	X	---
17	X	---	X	---	---
18	X	---	---	X	---
19	X	---	---	X	---
20	X	---	---	X	---
21	---	X	---	---	X
22	X	---	X	---	---
23	---	---	---	---	---

Of the 23 total interviews conducted, 18 interviewees were non-users of the RAID program and the remaining 5 (yellow shading) are RAID applicants that either have RAID support or are re-applying for that support (See Sections A and B for more details).

### Eligibility Restriction

Table #6 above clearly shows that, by far, the greatest perceived barrier to applying for RAID services is Eligibility for the program. Fully 83%, or 15 out of 18 non-users, felt that the eligibility restrictions substantially limited the number of applicants to the program. Even 3 of the 5 RAID users (60%) had this opinion. Both groups most often cited the need and wisdom of expanding the program to include biologics, and many felt that small companies, with careful guidelines, should also be eligible. They are already eligible when associated with an academic “grantee”, but only in that situation. One comment was: “The goal should be to find the best possible drug candidates...the best source of candidates is found in biotech or pharma and RAID

should look at the drugs that have the most promising future.” Another comment was: “The eligibility requirements need to be changed in order for RAID to be successful, not just by broadening the eligible compound types to biologics, but there is no reason to exclude for-profit institutions....” Section D on Types of Products has additional comments from interviewees supporting the eligibility of biologics.

***Note:** NIH-RAID recently announced, after these interviews had been conducted, that it has expanded its program services to include biologics, but generally not for synthesis. The announcement may be viewed at the following link:*

<http://grants.nih.gov/grants/guide/notice-files/NOT-RM-08-005.html>.

### **Speed/Timeliness**

The second largest category selected by 11 of the 18 RAID non-users (61%), and 2 of the 5 RAID users (40%) was Speed/Timeliness. The main concern for non-users was the amount of time it would take from submitting an application to go through the review process and actually begin services. Most felt this cycle needed to occur in a 4-6 month timeframe. Otherwise, the opportunity window will have closed, as the most important fields are advancing quickly and the compounds proposed may even be obsolete by the time they are available for testing. The two RAID users that mentioned speed/timeliness referred to the seemingly slow progress of an existing program, and to the decision making process for granting support being too slow and needing a faster turn-around.

### **Application Process, Intellectual Property and Other Barriers**

The interviewee responses in the remaining 3 categories of Application Process, Intellectual Property and Other Barriers were essentially equally distributed. Of the 18 non-RAID-users, the Application Process was selected 8 times (35%), while IP and Other were chosen 6 times (33%) each. Only 1 in 5 (20%) RAID users had comments in each of these 3 categories.

Application Process – There was a preponderance of perceptions from non-users (non-applicants) that the application process was likely to be “onerous.” This was based largely from their experience with RO-1 grant applications, after which RAID applications have been patterned, and not on any first-hand knowledge of the RAID application process itself. Some commented that it may be a lower priority, if not a deterrent, for an investigator to spend time applying for services rather than for actual funds. There were also comments expressed about the review process. Some questioned whether the reviewers themselves were sufficiently experienced and knowledgeable in drug development to adequately decide which projects were most appropriate to approve. Another suggested that both FDA and academics should be involved in the review process. One RAID user commented that the application process “needs more clarity on what is expected...” Notably, another RAID user thought that the highly constructive and professional review process was literally responsible for the survival of his program and critically important to his own drug development education. We heard similar comments by other users on the importance of the program review and the advice given by the review committee.

Intellectual Property – The roughly one-third of non-users who thought IP might present a potential barrier were, after discussion, actually less intensely concerned than that number might

suggest, but it remains a perceived barrier to applying for services. Interviewees from small companies tended to think it would likely be an issue only if royalties were expected, and otherwise felt it would be a “case-by-case” assessment. Academic faculty noted that IP may be a complex issue where universities want to protect IP that can interfere with future company interest/partnership in advancing compounds.

Other Barriers- One in three non-users constructively suggested additional barriers to using the RAID program, though no single suggestion was voiced by more than one or just a few individuals. One believed that NIH has experience in clinical research but not drug development. Similarly, another believed there are “very few people with the appropriate skill set to shepherd a drug through to clinical trials. RAID needs to partner with the appropriate scientists that can take the drug beyond the IND.” One non-RAID user stated that a barrier was that the program is limited by small funding and other issues in conceptualizing the program. Several non-users said that new concepts sometimes confuse recipients and they don’t know how to adapt – they “don’t know what to think about RAID.” Still another thought that investigators do not immediately recognize or fully appreciate the potentially high value offering of RAID. This is because they do not consider regulatory strategies, filings, FDA discussions, etc. until they are imminent. The RAID user who commented, and who is actually very pleased with the RAID program, suggested that the central control of services could be improved by providing some direct interaction with contractors. This would improve the investigator’s education. In this regard, he had a better prior experience with one of the ICs.

As alluded to above in Application Process, another barrier may be the perceived difference between dollars granted and support services. In most conversations there was little concern regarding the difference between service support and dollars granted. However, two researchers asked “How will the university judge me when it comes time for tenure”. One suggested that “\$1M in services may not be seen in the same light as a \$1M grant”. In the case of a grant, “the university gets to add on their overhead charge”. Another said, “Dollars are not the same as services; and dollars are sometimes needed to keep a lab afloat”. It was speculated that perhaps the RAID program might have a greater appeal to those who already have stable funding, and need not worry about dollars coming into their institutions.

## Chapter 9

### Outreach and Marketing of NIH-RAID

In early discussions, it was clear that the NIH-RAID program had relatively low numbers of applicants. As stated in our chapter on “Awareness”, there is a relatively low level of awareness of NIH-RAID within the drug development community. The low level of awareness and the lower numbers of applicants likely go hand-in-hand. There need not necessarily be a connection between the awareness and the number of applications, if there is not a clear need for the NIH-RAID program. In our chapter on “Need for the NIH-RAID Program”, we have already established that there is a clear and unfulfilled niche for the NIH-RAID program. Application barriers, either perceived or real, could also reduce application rate. However, we know that this is not solely the case from analysis of our interview data (please see our chapter on “Perceived Barriers”). The low application rate is also not a reflection on concerted efforts of the NIH-RAID staff; and should not diminish the efforts of Dr. David Badman, Dr. Tom Miller, Mr. Tony Jackson, and others who have worked arduously and enthusiastically to promote the NIH-RAID program awareness.

#### Data Collected from Interviewing Target Audience:

In multiple discussions with both the RAID staff and the Working Group members, the question often arose, “What is the best way to reach the NIH-RAID target audience?” In order to resolve the RAID marketing challenge, this is a question that must be answered in order to be fully successful in recruiting applicants to the NIH-RAID program. In order to help answer this fundamental question, we first asked the users of the NIH-RAID program, “How did you become aware of the NIH-RAID Pilot Program? We also devised a series of questions to better understand how potential applicants gather information. In this information age, as technology changes, we are changing the ways we gather our scientific information. The following is a list of questions that were used in our interviews with drug development experts (See also Appendix A):

- What are the primary sources of information/data gathering you rely on?
  - Printed journals? Which?
  - Online journals? Which?
  - Specific websites? Which?
  - Information through society/professional memberships?
  - Online searches/browsing?
  - Newspapers/Magazines? Which?
  - Other?

**Table #8 --- How Interviewees Gather Information**

<b>Interview #</b>	<b>Printed Journal</b>	<b>Online Journal</b>	<b>Specific Website</b>	<b>Professional Society Membership</b>	<b>Online Searches</b>	<b>Trade Newspaper</b>	<b>Other</b>
1	X	X	X	X		X	
2	X		X	X	X	X	
3	X		X	X	X		
4		X	X	X	X		
5			X	X			Workshops
6		X	X	X	X		Symposia
7			X	X	X		
8		X	X	X	X		
9	X	X	X	X	X		
10	X		X	X	X		
11	---	---	---	---	---		
12		X	X	X	X		
13		X	X	X	X		
14	X				X	X	
15	X	X	X	X	X		
16	X	X	X	X	X		
17				X			
18			X	X			

The majority of those interviewed by Tunnell utilized specific websites, online searches, and professional society memberships to gather information. In many cases, the specific websites utilized were the same as those of the professional societies. As seen in Table #8, above those interviewed seemed to be equally divided on printed and online journal utilization; although, there is a future trend towards electronic media. Approximately half of those that read journals, (in print or online) volunteered that they do not read advertisements. Not all scientists interviewed regularly read journals; many conduct a search on a particular topic and read only pertinent research articles. This suggests that advertisements in specific journals may not be totally effective in reaching the target audience for the NIH-RAID program.

The journals, websites, search engines, and professional societies visited on a regular basis were diverse, and reflect a researcher's specific interests. The following lists document the sources of information that may be considered for creating an effective outreach campaign:

**Journals and Publications (in printed & online formats) cited:**

1. BioPharm International
2. BioProcess International
3. Biotech Journal
4. Cell
5. Contract Pharma

6. Dev. Biology
7. Downstream Processing
8. Drug Discovery Today
9. Genetic Engineering News
10. Infect. & Immunity
11. J. Bio. Chem.
12. J. Clin. Invest.
13. J. of Immunology
14. J. Pediatrics
15. Nature
16. Nature Biotechnology
17. Nature Genetics
18. Neuron
19. Neurosciences
20. New Eng. J. Med
21. Pediatrics Research
22. PNAS
23. Science
24. Vaccine

### **Specific Websites cited:**

1. [www.biospace.com](http://www.biospace.com)
2. [http://news.yahoo.com/fc/science/biotechnology\\_and\\_genetics](http://news.yahoo.com/fc/science/biotechnology_and_genetics)
3. [www.FierceBiotech.com](http://www.FierceBiotech.com)
4. [www.bio.org](http://www.bio.org)
5. [www.pharmabiz.com](http://www.pharmabiz.com)
6. [www.cdc.gov](http://www.cdc.gov)
7. [www.nih.gov](http://www.nih.gov)
8. [www.hhs.gov](http://www.hhs.gov)
9. [www.alzforum.org](http://www.alzforum.org)

### **Specific Search Engines cited:**

1. [www.datamonitor.com](http://www.datamonitor.com)
2. [www.nlm.nih.gov](http://www.nlm.nih.gov)
3. [www.google.com](http://www.google.com)
4. [www.pubmedcentral.nih.gov](http://www.pubmedcentral.nih.gov)
5. [www.cas.org](http://www.cas.org)

## **Professional Societies cited:**

1. AAAS
2. AAN
3. AAO
4. AAPS
5. ACNP
6. AGS
7. ANA
8. ARVO
9. ASCARS
10. ASCI
11. ASCPT
12. AVPO
13. BIO
14. CASSSS
15. CINP
16. CPDD
17. GSA
18. NJ Biotech
19. PDA
20. RAPS
21. SFN
22. SGI
23. SOT

## **Impact of Current Marketing Efforts:**

Marketing a program like NIH-RAID is a long term project where multiple activities will be additive if properly choreographed. Although Dr. Badman has made many fine NIH-RAID presentations, it will take a multi-prong marketing approach to achieve long-term, nation-wide awareness goals. NIH-RAID has begun new and sustained marketing efforts within the past half year; therefore it is perhaps too early to judge the effectiveness of the new outreach efforts. Although short term gains may be seen; significant movement towards awareness goals are usually only achieved in the long term.

## **Suggestions for Improved Awareness through Marketing/Outreach:**

Unlike most scientific disciplines, marketing is not an exact science because it involves the intricacies of human behavior and human interactions that are not entirely predictable. Even the best conceived marketing plan will likely take two to two and a half years to create national community awareness (as was true for NHLBI's PACT marketing campaign). There are simple rules of marketing that are utilized to develop a comprehensive marketing plan. The plan is

devised and executed with expectations that some activities will produce great results, while other activities may fall short of their goals. This is why a multi-pronged approach to marketing is prudent and reasonable. As components of the plan are executed, the outcome should always be judged in relationship to the cost of the activity, i.e. Return on Investment (ROI). For example, it is easy to judge the effectiveness of a tradeshow by the total cost of the tradeshow and dividing it by the total number of “qualified leads” (i.e. the number of people who are very interested in applying to the NIH-RAID program). In this hypothetical example, a cost per qualified lead would be calculated, and subsequently used to gauge future marketing activities. In this same manner, other outreach/marketing activities should be judged to find the best possible outreach approaches.

## **Mechanisms of Outreach/Marketing:**

Many NIH scientists admitted that marketing is not a core area of expertise at NIH. Most commented that NIH has tremendous scientific talent, however doesn't have the expertise or FTEs to conduct a true marketing campaign. The following outreach mechanisms arose in recent discussions with scientists:

1. **Journals** (Tunnell survey observations)
  - a. Only approximately half of all surveyed regularly read specific journals
  - b. Journal readers were equally divided between printed and online journals
  - c. Approximately half of all readers skip advertisements in journals
2. **Webinars**
  - a. Can be influential with good scientific societies and known scientists
  - b. Commercial webinars are not well attended
3. **Website Links**
  - a. SBIR/STTR websites should have a link to the NIH-RAID program.
  - b. Collaborate with FDA website to have a NIH-RAID link for drug development support
4. **Scientific Meeting Workshops**
  - a. This was very effective media for NHLBI's PACT outreach. [PACT would sponsor a session in exchange for a time slot to present PACT at the workshops].
  - b. Scientist will always attend, if the workshop will help find funding or funding options
  - c. This expands the network of positive “word of mouth” comments as scientists return to their respective institutions
5. **Publish Journal Articles**
  - a. Introductory articles can be very effective if published in prestigious journals
  - b. Introductory articles should be published in multiple journals to find “hidden customers” in specific scientific disciplines that need pre-clinical services for drug development
  - c. Successful drug advancement (through NIH-RAID) should be published to portray what can be accomplished with NIH-RAID's support. These stories will serve as excellent examples to others.

## **Outreach Suggestions within NIH:**

Several of those interviewed believed that there was not adequate understanding of the RAID program within the NIH Extramural Research community. One of the IC's Directors, possessing an exceptionally good awareness of the NIH-RAID program, offered that only approximately one third of their Program Officers had a full understanding of the NIH-RAID program. Although it is difficult to quantify the exact degree of RAID awareness within ICs, the awareness can no doubt be improved. There were several suggestions offered regarding improvement of NIH-RAID program awareness at NIH:

- One Extramural Director had a Program Officer that is incredibly enthusiastic, and this person has made a huge difference in their IC awareness. Therefore, suggested that NIH-RAID program should train Project Officers on the features and benefits of the program.
- Dr. Badman's slides should be developed for inclusion within all Extramural presentations and mailings. These materials could be especially powerful persuaders if the materials contained a success story of drug development, i.e. a poster child.
- The NIH-RAID website should better reflect Dr. David Badman's RAID PowerPoint presentation.
- All IC websites should have a link to the NIH-RAID website; and all websites should have metrics to track the website usage.

## **Summary of Outreach/Marketing Observations and Suggestions:**

Outreach/marketing is critical to the creation of awareness. It is this customer awareness that will drive the success of a program or corporation. The same is true of the NIH-RAID program; marketing will ultimately determine whether the program's growth remains flat, or grows exponentially. In order to find and support the very best therapeutics, the pool of applicants must be expanded. Expansion of the program will grow with awareness of the NIH-RAID program. Even the best conceived marketing plans require time and dedication in order to see the fruits of their labors. As mentioned above, even a well-conceived marketing plan may take > 2 years to achieve the desired level of program awareness. Therefore, we suggest that attention currently be focused upon marketing of the NIH-RAID program. To be successful in outreach there must first be a detailed, well-coordinated strategic marketing plan. Secondly, there must be specific and dedicated resources to accomplish the multiple outreach goals. Third, we suggest that the marketing effectiveness be measured by return on investment (ROI).

# Chapter 10

## NIH-RAID Pilot Program Summary of Results and Suggestions

### Summary:

Tunnell Consulting conducted 23 interviews to collect data about the NIH-RAID Pilot program. Scientists interviewed were from a wide variety of disciplines and represented large and small, profit and non-profit institutes. Data was collected from academic institutions, research foundations, biotech and pharmaceutical companies. The interviewees were subdivided into 4 major categories and an interview form for each group was developed (see Appendix A). The interview groups were: 1) RAID users, 2) RAID non-users, 3) NIH ICs, and 4) NIH-RAID-like Service Providers.

### 1. NIH-RAID Need Assessment:

- The overwhelming response to the question of whether or not the RAID program services are needed in the translational research community was “Yes”.
- A majority of interviewees were interested in learning more about NIH-RAID.
- Interviewees from biotech and pharma companies were less interested in RAID services, but several agreed it was worthwhile for them to forward RAID information to friends and colleagues.

### 2. Awareness of NIH-RAID Program:

- Among non-users, there was generally low or no awareness of the RAID program. Less than 25% of the non-users interviewed had a good awareness of the details of the RAID program and its services.
- Two of 4 NIH-IC Extramural Research Directors (unaffiliated with the RAID working group) interviewed had a medium to high level of awareness of the program.
- Awareness of the RAID program among non-users was most often communicated by word of mouth and by contact with a RAID reviewer or applicant.
- RAID program applicants became aware of RAID through Dr. Badman or through other direct or indirect word of mouth contacts.

### 3. Ranking of Pre-Clinical Development Services:

- Interviewees rated the most important development services to their programs. The list of services used for them to make their choices was:

#### **E. Small Scale Synthesis**

#### **F. Process Development:**

1. Streamline and scale-up synthesis
2. Bulk product purification
3. Analytical methods development (purity, identity, stability, potency, specifications)
4. Perform analytical methods for agent characterization
5. Formulation studies
6. Consistency runs to demonstrate process control
7. Technology transfer of processes to cGMP manufacturing
8. Demonstration of reproducibility and process control (multiple lots)
9. Stability on representative product lot(s)
10. Other

#### **G. Tox/ADME for IND (GLP or non-GLP):**

1. Metabolic Stability
2. Metabolite ID
3. Protein Binding
4. Cyp Inhibition and Induction
5. Cell-based Toxicity
6. *In vivo* studies
  - i. MTD
  - ii. Dose range
  - iii. Other
7. Caco-2 permeability
8. Cardiotoxicity (hERG) testing
9. Other

#### **H. Assistance & Guidance**

1. Provide primer to steps in preclinical plan
2. Provide specific product development plan
3. IND filing
4. Other

- All, with the exception of 1, out of 18 interviewees found the list of pre-clinical drug development services to be comprehensive. The strong suggestion from the one respondent was that RAID needs to take a Systems Biology approach to all translational science development.
- **Process Development** was most often cited as a valuable service, followed by **Tox/ADME** testing. Within Process Development, “streamline and scale-up synthesis” was the first priority, and “Formulation Studies” was the second priority.

- **Assistance and Guidance** was the next most-often cited service, though praise for its value among those who did cite this was notably very high. This was seen as a critical offering by most RAID applicants. Several non-users (especially FDA), suggested additional emphasis on Regulatory Guidance.
- **Small Scale Synthesis** was the service least cited as a priority.
- The following is a list of additional pre-clinical services suggested by interviewees. Many of these have new relevance since Proteins and Biologics have recently become eligible for consideration to receive NIH-RAID service support:
  9. *In vivo* Immunogenicity
  10. *In vivo* Inflammatory response
  11. Awareness training on FDA requirements
  12. FDA e-filing rules (i.e. electronic Common Technical Documents, e-CTD)
  13. Bio-availability assays
  14. Assessing biomarkers
  15. Assessing *in vivo* drug efficacy
  16. PK assays and studies

#### 4. Types of Products for NIH-RAID Support

- Interviews were conducted when only small synthetic molecules were eligible for consideration for RAID development support. Data was collected on the desirability for inclusion of other compound types, particularly biologics such as protein therapeutics and monoclonal antibodies. As noted above, NIH-RAID recently announced that biologics will now be accepted for review. See: <http://grants.nih.gov/grants/guide/notice-files/NOT-RM-08-005.html>.
- The list of compound types presented to interviewees for discussion was:
  - H. Small Molecules**
  - I. Peptides**
  - J. Oligonucleotides**
  - K. Proteins/Biologics**
    1. Antibodies
    2. Vaccines
    3. Therapeutics
    4. Enzymes
    5. Monoclonal Ab therapeutic
    6. Other
  - L. Cellular Therapies**
  - M. Diagnostics**
  - N. Others**
- The product most recognized to be in need of RAID support was **Proteins/Biologics**.
- The 2<sup>nd</sup> most cited product was **Small Molecules**
- The 3<sup>rd</sup> most cited product was **Peptides**, followed by **Cellular Therapies**.
- In overall priority rankings, **Small Molecules** was number one, followed by **Proteins/Biologics**.

- Several respondents stated that **Cellular and Gene Therapies** should not be excluded from consideration of RAID support.

## 5. Sources of Funding for NIH-RAID-Like Support

- No significant national funding alternative to the NIH-RAID program was identified by the respondents. The NIH-RAID program appears to fulfill a unique market niche.
- It appears that the only viable grant mechanism for biotech is the SBIR/STTR grants; these mechanisms cover a very broad range of scientific areas.
- Archival analysis identified numerous non-profit and for-profit centers engaged in translational drug development programs. The RAID pilot program is unique, and is differentiated from these support functions primarily by providing comprehensive drug development services rather than direct funding to program recipients.
- Drug development services within university consortiums are limited in scope, funding and access. RAID is comprehensive and available to a much wider range of eligible investigators.

## 6. Barriers to Using NIH-RAID

- RAID non-users most often identified, by far, the **Eligibility Restrictions** of the RAID program as their primary barrier to using RAID services.
- Much of this perception was based on the exclusion of product types other than small molecules, but this has been partially addressed by the recent acceptance of Biologics applications by NIH-RAID.
- All biotech interviewees and others, thought that small **Biotech** should be eligible, and suggested using guidelines similar to those of SBIR/STTR.
- The second most cited concern was **Speed/Timeliness**, in most cases referring to the time from submission to start of services. Many thought that <6 months was an important target.
- The interviewee responses in the remaining 3 barrier categories of **Application Process**, **Intellectual Property** and **Other Barriers** were equally distributed.
- The **Application Process** was perceived as “likely to be onerous” by non-users familiar with ROIs. A deterrent for some was also applying for services as opposed to actual funds.
- **Intellectual Property** was perceived, as a complex and potentially large issue to about a third of interviewees. Small company representatives thought it may be less troublesome on a case-by-case basis, provided royalties were not involved.
- **Other Barriers** included: 1) a perception that NIH has experience in clinical research, but not in drug development. 2) A perception that there are very few people at NIH with the appropriate skill set for drug development. 3) the program is limited by small funding and other issues in conceptualizing the program. 4) several non-users said that RAID is a new concept, and recipients don’t know what to think about RAID. 5) investigators do not immediately recognize or fully appreciate the potentially high value offering of RAID support.

## 7. Outreach/Marketing

- The majority of those interviewed by Tunnell utilized specific websites, online searches, and professional society memberships to gather information. Websites used were often those of the professional societies. Interviewees were equally divided on use of printed and online journal utilization, but the trend is towards electronic media.
- Respondents mainly did not read advertisements and searched particular topics to read. This suggests that advertisements in specific journals may not be totally effective in reaching the target audience for the NIH-RAID program.
- Specific journals, websites and professional societies were compiled from the interviewees (see Outreach/Marketing chapter).
- A multi-pronged marketing approach is needed to achieve long-term, nation-wide awareness goals.
- Scientists stated that marketing is not a core area of expertise at NIH. Most commented that NIH has tremendous scientific talent, however doesn't have the expertise or FTEs to conduct a true marketing campaign.
- Several suggestions were also offered regarding improvement of NIH-RAID program awareness within NIH, including Project Officer training and strategic locations for links to the RAID website (see Outreach/Marketing chapter).