Resources for the Microbiology & Infectious Diseases Research Community

Division of Microbiology and Infectious Diseases
NIAID, NIH, DHHS

The Division of Microbiology and Infectious Diseases (DMID)

…*supports extramural basic through applied research to control and prevent diseases caused by virtually all human infectious agents except HIV*

National Institute of Allergy and Infectious Diseases

Resources for Researchers Overview

National Institute of Allergy and Infectious Diseases

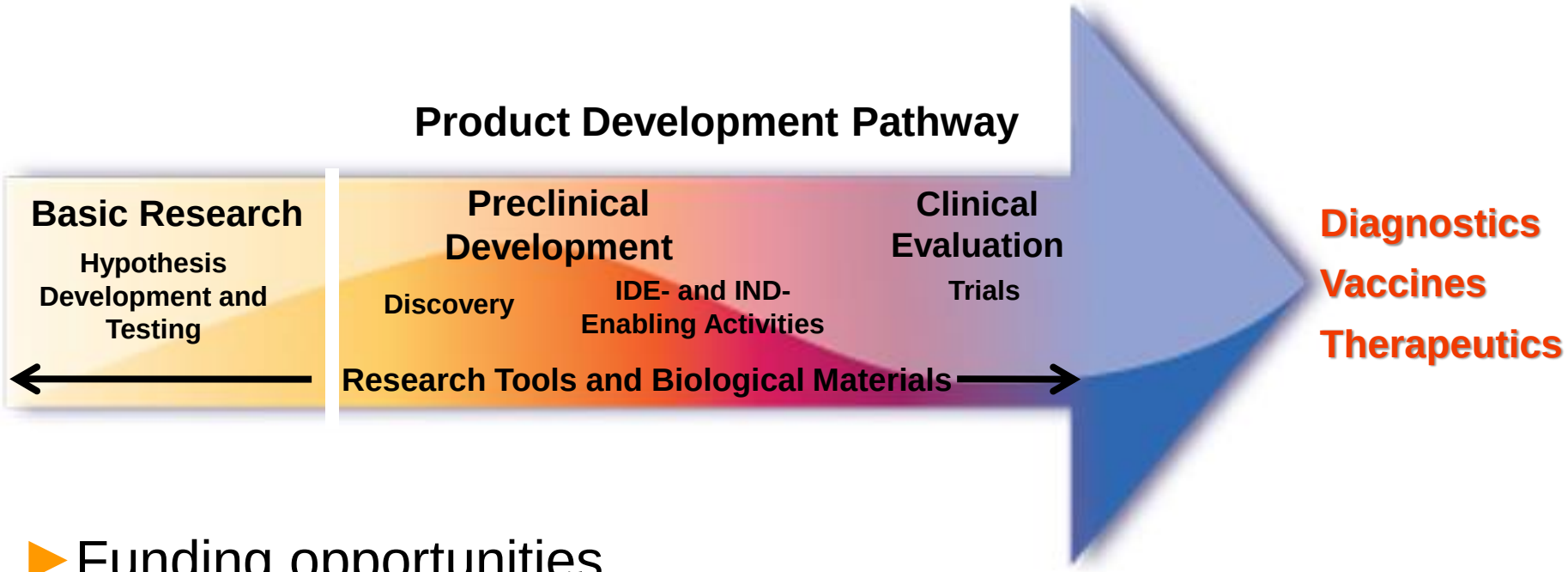
Preclinical Services (PCS) for CARB-X Fund Recipients

CARB-X funded programs will have accelerated procedures to access to NIAID's preclinical services:

- Bypass of NIAID's internal review step
- Expedited approval by Senior Leadership

National Institute of Allergy and Infectious Diseases

Resources for Researchers



- Funding opportunities
  - Research tools and biological materials
    - Preclinical and clinical services

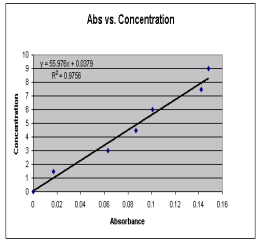
to facilitate product development

NIH National Institute of Allergy and Infectious Diseases

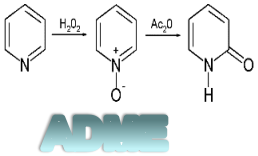
Product Development Services

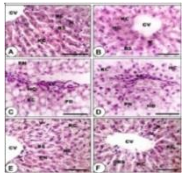
Therapeutics

In Vitro Assessment of Antimicrobial Activity



Interventional Agent



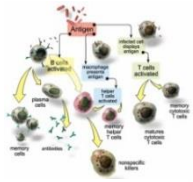


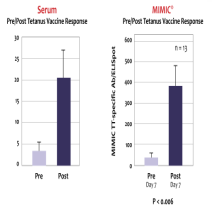
Biopharmaceutical Products

Chemistry, Manufacturing, and Controls (CMC) Documentation for IND

Vaccines

Testing





Manufacturing

Animal Models

National Institute of Allergy and Infectious Diseases

Vaccine Development Services

Supports vaccines, adjuvants, devices, challenge materials

Vaccine Manufacturing

- Feasibility, Gap Analysis, and Product Development Plan (PDP) Support
- Process Development
- Product Release Assay Development Potency Assays
- Pilot and cGMP Manufacture
- Audits
- Regulatory Activities

Vaccine Testing

- Assay Development for Non-Clinical and Clinical Samples
- Non-Clinical Immunogenicity and Efficacy Studies (including non-GLP, GLP and 'Animal Rule' studies)
- Clinical and Non-Clinical Sample Testing
- Safety and Toxicity Testing

Preclinical Services

In vitro Assessment for Antimicrobial Activity

- Screening for bacteria & fungi, viruses, parasites & vectors, and toxins
- High throughput as well as specific and broad spectrum screens
- To stimulate research towards discovery of improved antimicrobial therapies

Bacterial In Vitro Screening: Public Health Pathogens

Species	Strains for Initial MIC Screen	Strains Represented in MIC90 Panels
Staphylococcus aureus	1. MRSA USA300 2. MRSA USA100 3. MSSA	MRSA USA100, MRSA USA200, MRSA USA300, MRSA USA400, MRSA ST398, Vancomycin-resistant *Staphylococcus aureus*
***Enterococcus* species**	1. Vancomycin-resistant *E. faecalis/E. faecium* 2. Penicillin-resistant *E. faecalis/E. faecium*	Vancomycin-resistant *E. faecalis/E. faecium*, Penicillin-resistant *E. faecalis/E. faecium*
Streptococcus pneumoniae	1. Pan-susceptible *S. pneumoniae* 2. Penicillin-resistant *S. pneumoniae* 3. Quinolone-resistant *S. pneumonia*	Tetracycline-minocycline-R, tet(M), macrolide-R; cefuroxime-R, trimethoprim-sulfamethoxazole-R, fluoroquinolone-R
Streptococcus pyogenes	1. Susceptible *S. pyogenes* 2. MDR *S. pyogenes*	Pen-R, Macrolide-R, Lincosamide-R, StreptograminB-R
Streptococcus agalactiae	1. Susceptible *S. agalactiae* 2. MDR *S. agalactiae*	Tetracycline-minocycline-R, macrolide-R
Klebsiella pneumoniae	1. Susceptible *K. pneumoniae* 2. MDR *K. penumoniae*	Fluorquinolone-resistant strain(s), Carbapenem-Resistant strain(s), 3rd Generation Cephalosporin-Resistant strain(s), Colistin-resistant strain(s)
Acinetobacter baumannii	1. Susceptible *A. baumannii* 2. MDR *A. baumannii*	Fluoroquinolone-resistant strain(s), Carbapenem-Resistant strain(s), 3rd Generation Cephalosporin-Resistant strain(s)
Pseudomonas aeruginosa	1. MDR *P. aeruginosa* 2. PAO1 *P. aeruginosa* (efflux pump wild-type)	Fluoroquinolone-resistant strain(s), 3rd Generation Cephalosporin-Resistant strain(s), Carbapenem-Resistant strain(s) *Will include PAO1 strain(s) with efflux pump deletions (e.g., PAO200 or PAO750)
Enterobacter species	*Enterobacter* sp.	Fluoroquinolone-resistant strain(s), Carbapenem-Resistant strain(s), 3rd Generation Cephalosporin-Resistant strain(s)
E. coli	1. *E. coli* WT (ΔtolC parent strain) 2. *E. coli* (ΔtolC strain) 3. Extraintestinal pathogenic MDR *E. coli*	Fluoroquinolone-resistant strain(s), Carbapenem-Resistant strain(s), 3rd Generation Cephalosporin-Resistant strain(s)

MIC90s and specialized panels (e.g. NDM-1 strains, CREs, etc.) are possible too.

CDC & FDA Antibiotic Resistance Isolate Bank strains available for testing

NIH National Institute of Allergy and Infectious Diseases

Bacterial In Vitro Screening: Bio-Defense

Table 2 – Biodefense Bacteria strains for MIC+

	Number of Strains in MIC+ panel	*Strains for MIC+ determination (identified by BEI catalog number)*
Bacillus anthracis	**12**	*NR-3838, NR-415, NR-21670, NR-21689, NR-411, NR-412, NR-41, NR-46, NR-414, NR-1202, NR-1355, NR-9564 (Bacillus cereus)*
Yersinia pestis	8	*NR-641, NR-635, NR-636, NR-637, NR-638, NR-639, NR-640, NR-642*
Francisella tularensis	6	*NR-643, NR-644, NR-645, NR-646, NR-647, NR-648*
Burkholderia mallei	7	*NR-23 NR-36122, NR-36126, NR-36127,NR-4071, NR-36128, NR-8073*
Burkholderia pseudomallei	16	*NR-24 NR-4073, NR-4074, NR-4072 NR-8068, NR-8071, NR-8072, NR-9915, NR-9921, NR-9922, NR-9923, NR-36132,NR-36133, NR-36134, NR-36138, NR-36139*

Strains were chosen with CDC input,
Initial pass only on framed strains

NIH National Institute of Allergy and Infectious Diseases

Animal Models of Infectious Diseases

- Provision of a broad range of *in vivo* models (small animal, non-human primate, and non-traditional models)
- Development of novel models
- Refinement of existing models
- Screening of products and efficacy testing to support FDA submissions

Therapeutics Development Services

Nonclinical Services for the Development of Interventional Agents for Infectious Diseases

Therapeutics (and *in vivo* diagnostics, e.g., imaging and skin test reagents)

- Lead identification and development
- Chemistry and manufacturing
- *In vitro* and *in vivo* preclinical safety, toxicology and pharmacokinetics
- Preclinical development, planning and evaluation

Preclinical Development of BioPharmaceutical Agents

Core task areas:

A: Feasibility Assessments, Audits

B: Product Assays, Bioanalytical Development

C: Process Development

D: Manufacturing, including pilot and cGMP

E: Regulatory documentation support

NIH National Institute of Allergy and Infectious Diseases

Preclinical Services Access

- Resources are limited
- Services provide critical information needed to move a product forward
- Not intended as the sole source of development
- Preliminary data required to proceed through each stage of development

Preclinical Services Eligibility Criteria

- Investigators in academia, not-for-profit organizations, industry, and government
- National/international
- Don’t need to be funded by NIH

Preclinical Services Assurances Provided

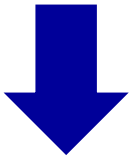
- Confidentiality
- Materials Transfer Agreement (MTA)
- Non-Clinical Evaluation Agreement (NCEA)

Preclinical Services Requirements for All Users

- Shipping and handling charges
- Acknowledging the contribution of NIAID contract support in publications and presentations
- Submitting manuscripts, abstracts and presentations for NIAID review
- Reporting achievements to NIAID annually

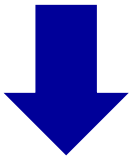
Preclinical Services Standard Application and Approval Process

Program Officer and Requestor
explore request informally



Branch/Office Review*
Not needed for CARB-X recipients

Program Officer invites Requestor with promising
Proposal to submit formal request for approval



Senior Leadership Review*
Expedited for CARB-X recipients

Studies/protocols are carried out under contract

*Based on standard criteria

NIH National Institute of Allergy and Infectious Diseases

Preclinical Services (PCS) for CARB-X Fund Recipients

Companies funded by CARB-X will need to complete:

- Non-Clinical Evaluation Agreement (NCEA)
- Service Request Form (SRF)

There will be expedited procedures to leverage NIAID services in the most impactful way to advance CARB-X funded programs.

Preclinical Services Standard Criteria

1. Proposed studies within DMID/NIAID mission
2. Proposed studies within scope of and/or technology provided by contract services
3. Sufficient quality and/or quantity of product available
4. Proposed studies in compliance with animal welfare regulations
5. Proposed work not supported by/available from other funding sources
6. Previous use of DMID resources for assessment of the same or similar product (Repeat use of DMID resources may be undertaken with strong justification.)

Preclinical Services Standard Criteria (Cont'd)

7. Preliminary data adequate to support the request to advance the product to the next step in the product development pipeline
8. Likelihood that services will contribute significantly to the eventual development and/or evaluation of a product of high quality
9. Purported public health impact
10. Improvements in health benefits offered beyond current measure(s)
11. Availability of a plan for advancing the product beyond completion of the services requested
12. Rank of requested studies among competing priorities

Preclinical Services (PCS) for CARB-X Fund Recipients

Consultation with NIAID is required before completing SRF to determine optimal use of NIAID PCS to specific needs of project

NIAID contacts:

Erin Zeituni (erin.zeituni@nih.gov)

Anita Sheoran (anita.sheoran@nih.gov)

NIAID CARB-X Team (DMIDCarbXPCS@mail.nih.gov)

National Institute of Allergy and Infectious Diseases