GARDP
Global Antibiotic Research & Development Partnership

ACCOMPANYING NOTES TO REVIVE WEBINAR:

NIAID RESOURCES TO FACILITATE DISCOVERY & DEVELOPMENT OF ANTI-INFECTIVES

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About GARDP & REVIVE

The Global Antibiotic Research & Development Partnership (GARDP) is a not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments, while endeavouring to ensure their sustainable access. Initiated and incubated through close collaboration between the World Health Organization (WHO) and the Drugs for Neglected Diseases *initiative* (DND*i*), GARDP is part of the implementation of the Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships to encourage research and development of new antimicrobial agents and diagnostics. GARDP was hosted and facilitated by DND*i*, which provided the scientific environment, necessary personnel, and infrastructure to ensure an effective start-up phase. In 2018, the GARDP Foundation was created as a separate legal entity.

GARDP's current R&D strategy focuses on developing and delivering antibiotics for paediatric infections, neonatal sepsis, and sexually-transmitted infections as priority areas of global public health need. The decision to focus on these is based on a prioritization framework that considers the intersection between priority pathogens identified by WHO; specific populations' health needs; and individual diseases and syndromes alongside targeting indications less likely to be developed by other actors. In addition, GARDP's transversal R&D work to recover knowledge, data, and assets of forgotten or abandoned antibiotics aims to recover candidates and identify new ones for pre-clinical or clinical development to further support its priority areas. GARDP has also created REVIVE to support and connect the antimicrobial R&D community by developing educational events and materials, collating open-access resources, and helping researchers get in touch with each other.

NIAID Resources to Facilitate Discovery & Development of Anti-Infectives with Ann Eakin was part of the REVIVE webinars series and the recording is available here.

Visit revive.gardp.org and join the community now.

Contact us: revive@gardp.org

For more information about GARDP, visit www.gardp.org.

Introduction

The National Institute of Allergy and Infectious Diseases (NIAID) is one of 27 institutes and centers which make up the US National Institutes of Health (NIH). The mission of NIAID is to conduct and support basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases.

NIAID's 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 (as there is a dedicated division focused on this pathogen).

NIAID's infectious disease research has a dual mandate:

- Biomedical research – Maintain/build a robust basic and applied research portfolio
- Public health – Respond rapidly to new infectious disease threats (e.g. Ebola or Zika outbreaks, antimicrobial resistance).

DMID's responsibilities cover more than 300 pathogens. The budget of the fiscal year 2018 was 1.751B USD.

NIAID's strategies to reduce product development risk in basic research, preclinical development, and clinical evaluation, comprise three distinct mechanisms:

1. Basic & Applied Research Grants
2. Product Development Contracts
3. Preclinical and Clinical Services Contracts

NIAID may support the development of monoclonal antibodies, small molecules, non-traditional antibiotics, vaccines, diagnostics, peptides, as well as host-targeted therapies. While NIAID is US-based, all mechanisms, with the exception of Small Business Awards, are open for applications for researchers from any country in the world.

1. Basic & Applied Research – Grants

- Investigator-initiated Awards (R01, R21, etc.)
- Small Business Awards (SBIR/STTR) – United States small companies
- Standing submission deadlines – 3 times per year
- Partnerships Program – Periodic requests for applications (RFAs) targeting specific research areas, often focused on translational research/product development.

➔ For updates on Funding Opportunities, subscribe to NIAID Funding News: https://www.niaid.nih.gov/grants-contracts/funding-news-2017

➔ NIAID Council-cleared concepts – learn about upcoming potential opportunities: https://www.niaid.nih.gov/grants-contracts/potential-opportunities
  - Initiatives or concepts that were approved by the council are likely, but not guaranteed, to become a new funding opportunity

CURRENT OPPORTUNITIES SPECIFIC TO AMR:

- Program Announcements - PA-18-724, PA-18-725
  - Generating New Insights and Mechanistic Understanding of Antibiotic Resistance Development (R21/R01)
  - Researchers are particularly encouraged to submit applications in the areas of
    - Microbiome involvement in drug resistant infections
    - Efforts to understand the interactions between human microbial communities and drug resistant bacteria
    - Efforts to better understand and characterize new combinations of existing drugs to address infections caused by multidrug-resistant Gram-negative bacteria
  - Regular NIAID submission deadlines
  - https://grants.nih.gov/grants/guide/pa-files/pa-18-724.html
  - https://grants.nih.gov/grants/guide/pa-files/pa-18-725.html
- United States Small Business Administration Grants (SBIR/STTR)
  - Phase I: Feasibility and Proof of Concept (6 months – 1 year)
  - Phase II: Research/Research and Development (2 years)
  - DMID's waiver topic: Product development targeting AMR
    - Waiver topics allow to extend the base time period as well as funding limits
  - Regular NIAID submission deadlines
  - https://www.niaid.nih.gov/grants-contracts/small-businesses

2. Product Development Contracts

These are funds that are given out to companies specifically in the area of translational research and research towards developing new products targeting infectious diseases.

- Support development of therapeutics, vaccines or diagnostic products
- Up to 5-year contracts with milestone-based periods of performance
- Requests for proposals (RFPs) and Broad Agency Announcements (BAAs) typically in range of $3 - 40 M, depending on scope
- Announced on FedBizOpps (typically annually):
  https://www.fbo.gov/

In addition to being a source of funding, these contracts also provide expertise by forming of cross-functional project teams between DMID and the company to decrease development risk for the specific product and help the company mature their product development skills.

NIAID's current portfolio (Feb 2019) comprises 11 vaccines, 9 therapeutics, and 1 diagnostic.

- 2019 NIAID Omnibus Broad Agency Announcement
  - This solicitation contains opportunities to submit a proposal under the following distinct Research Areas:
    - Development of Therapeutic Products for Antibiotic Resistant Bacteria
    - Advanced Development of Vaccine Candidates for Antibiotic Resistant Bacteria
  - Deadline for proposal submission: 10 June 2019
  - https://www.fbo.gov/index?s=opportunity&mode=form&id=cd69d0728940c0e77f1ed9c6310bc6b8&tab=core&_cview=1

3.a. Preclinical and Clinical Service Contracts

NIAID has set up research service contracts with various providers and makes those services available to external scientists for determining key assays and providing key data that may help push their programmes forward.

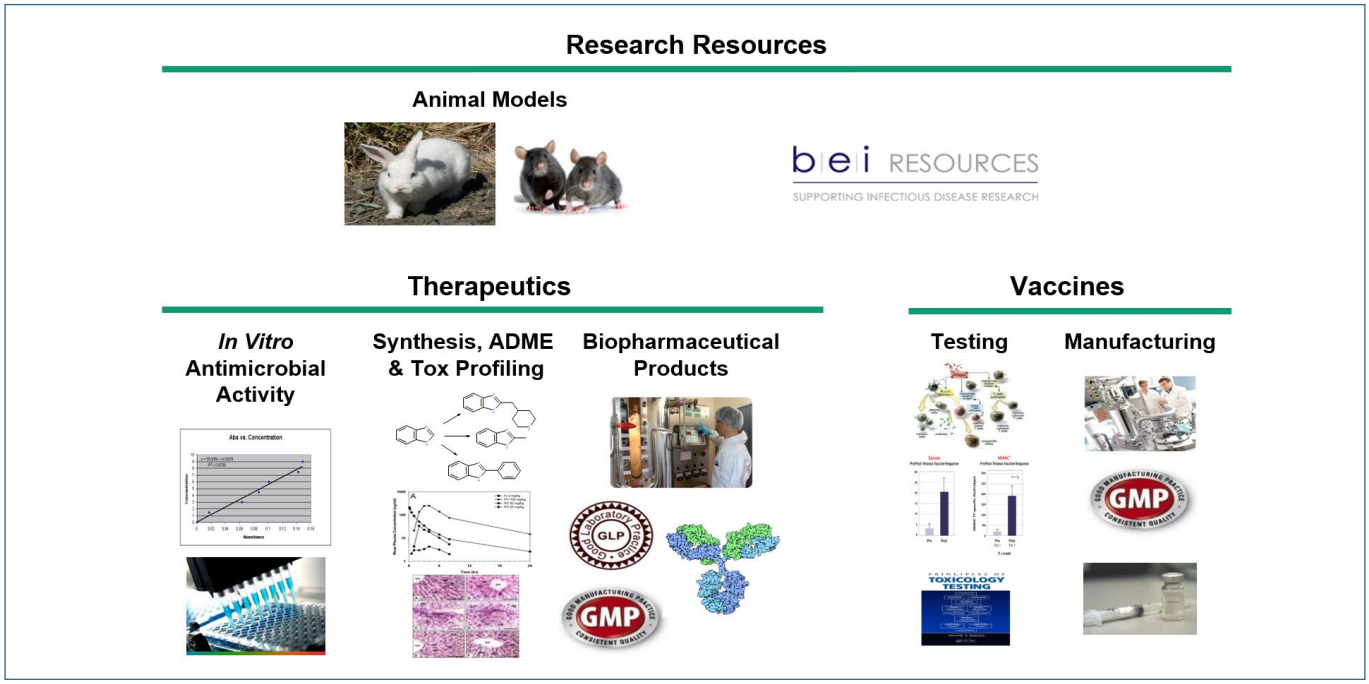
All information here.

GOALS:

- Lower the risk and advance promising discoveries along product development pathway
- Gap-filling services, not intended to take a product to licensure
- Provide expertise/capability in product development
- No loss of intellectual property (IP), strict confidentiality maintained
- Provide data to support/address
  - Research/knowledge gaps
  - New/continued funding
  - Go/no-go decisions
  - Lifting of FDA clinical hold

SUITE OF CONTRACTS:

NIAID offers a suite of contracts that provide a broad range of assays and capabilities to the extramural community free-of-charge.



Link BEI Resources: https://www.beiresources.org/Home.aspx

THERAPEUTICS DEVELOPMENT SERVICES:

IN VITRO ASSESSMENT OF ANTIMICROBIAL ACTIVITY:

- Screening of therapeutic candidates against bacteria & fungi, viruses, parasites & vectors, and toxins
- High-throughput as well as specific and broad-spectrum screens
- Minimum inhibitory concentration (MIC) and MIC90, monotherapy and combinations
- CDC & FDA Antibiotic Resistance (AR) Isolate Bank and other isolates: https://www.cdc.gov/drugresistance/resistance-bank/index.html
- Biodefense pathogens

CHEMICAL SYNTHESIS AND ADME & TOXICOLOGY PROFILING:

- Medicinal chemistry and process chemistry/scale-up (incl. GMP*)
- In vitro and in vivo preclinical toxicology and pharmacokinetics (incl. IND*-enabling GLP* studies)
- Rapid ADMET* & PK screening for optimization of lead series
- Preclinical development, planning and evaluation, IND documentation

* GMP – good manufacturing practice; IND – investigational new drug; GLP – good laboratory practice; ADMET – absorption, distribution, metabolism, excretion, toxicity; PK - pharmacokinetics

BIOTHERAPEUTICS DEVELOPMENT SERVICES:

Support for products derived from biotechnology processes, e.g. monoclonal antibodies, recombinant proteins, peptides, nucleic acid-based products:

- Product development planning and evaluation
- Assay development and product release testing
- Process development and formulation
- GMP manufacturing
- Reagents for diagnostics products
- Regulatory CMC* documentation support

* CMC – chemistry, manufacturing, and controls

PRECLINICAL MODELS OF INFECTIOUS DISEASES:

- Broad range of infection models
  - Rodents, mini-pigs, non-human primate, and non-traditional models
- Efficacy testing to support screening and pharmacodynamics and pharmacokinetics (PK/PD)
- Murine thigh & lung infection models
- Urinary tract infection (UTI) models in diabetic & normal mice
- Hamster model of *Clostridium difficile* infections (CDI)
- Development of novel models

VACCINE DEVELOPMENT SERVICES:

MANUFACTURING SERVICES:

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

TESTING SERVICES:

- 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

ELIGIBILITY:

- Innovators from academia, non-profit organizations, industry, and government
- US-based or foreign institutions
- Do not need to have prior or current NIH funding
- Simplified Request Process – available year-round
- Support determined based on:
  - Priority of research area, significance and innovativeness of the programme, preliminary data, value, overall product development plan and how the requested data will fit into that

3.b. NIAID/DMID Clinical Services Contracts

All information here.

GENERAL CAPABILITIES:

- Provide a ready resource for the conduct of clinical trials to evaluate promising vaccines, treatments, devices, and diagnostics for all infectious diseases except HIV
- Contracts provide services, not direct funding, for all aspects of the clinical trial

PHASE I CLINICAL TRIAL UNITS FOR THERAPEUTICS:

- Support Phase I clinical trials of new drugs

VACCINE AND TREATMENT EVALUATION UNITS (VTEUs):

- Phase I-IV clinical trials
- Prevention and Treatment of all DMID pathogens
- Access to clinical samples, e.g. for diagnostics validation

NIAID Antibacterial Resistance Leadership Group (ARLG):

- Purpose: To prioritize, design and execute clinical research that will reduce the public health threat of AMR
- ARLG Clinical Research Scope
  - Gram-positive and Gram-negative infections (new agents for CRE)
  - Infection control/stewardship
  - Diagnostics:
    - Virtual repository
    - Clinical specimen collection
    - Master Protocol Development for validation of multiple diagnostics simultaneously
- To date, the ARLG has
  - initiated >35 studies
  - included data from >18,000 subjects
  - published >100 manuscripts.

➔ http://arlg.org

Further links and contact information:

- DMID Product Development Resources: https://www.niaid.nih.gov/research/microbiology-and-infectious-diseases-resources

  ➔ http://arlg.org
- NIAID Funding News: https://www.niaid.nih.gov/grants-contracts/funding-news-2017
- Ann Eakin, Senior Scientific Officer, Office of Biodefense, Research Resources & Translational Research, DMID/NIAID/NIH: Ann.Eakin@nih.gov