BARDA Programs to Foster Technological Innovation

Brian Dattilo, Ph.D.
Project Officer
Strategic Science and Technology Division (SST)
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How Does BARDA Support Technology Innovation?

• **Intramural Research Projects**
  - Multiple projects per year for FDA and CDC laboratories
  - Program dates back to 2005

• **Workshops**
  - Organized and sponsored “Mechanisms of Lung Injury and Immunomodulator Interventions in Influenza” workshop March 2010
  - In conjunction with 2010 Gordon Research Conference “Biology of Acute Respiratory Infection”

• **Extramural Research Projects**
  - “Science and Technology Platforms Applied to Medical Countermeasure Development” BAA published July 8, 2009, reissued January 1, 2011 (BARDA-BAA-11-100-SOL-00001)
  - FedBizOps ([www.fbo.gov](http://www.fbo.gov)) keyword search “BARDA”
  - Links through [www.medicalcountermeasures.gov](http://www.medicalcountermeasures.gov)
Use of the Term “Platform Technology” has Increased in the Literature

- Publications in *Nanotechnology, Chirality, Expert Opinion on Drug Delivery, Biomaterials, Vaccine, etc.*
Innovation – What are the guidelines?

Platform Technologies and Applications

CBRN Division

Product Specific Applications – e.g. Anthrax vaccine, etc.

SST Platform Technologies – Process Oriented

Ex vivo Immune System  Adjuvant/Delivery  Analytical Assays
Protein Stabilization  Molecular Tools / Methods for Diagnostic Tests  Biomanufacturing

Applied to Late Stage Products – Integrated Development Activities

Product Specific Applications – e.g. H1N1 vaccine, etc.

Influenza & Emerging Diseases Divisions
SST BAA Areas of Interest

• SST Area of Interest #1: Technologies to accelerate evaluation of candidate vaccines and therapeutics

• SST Area of Interest #2: Formulation chemistry, protein stabilization, and vaccine delivery technologies

• SST Area of Interest #3: Innovative methods in bioprocess development and manufacturing

• SST Area of Interest #4: Methods and technologies to advance development of tests for rapid diagnosis of human injury and infections
BARDA Interest: Stage of Platform Technology and Product Development

Integrated Regulatory Pathway

- Stage of Maturity -
  - High
  - Low

Innovative Platform
  - Basic/Applied
  - Advanced Development
  - Advanced Research

Stage of Product Development
  - TRL-3
  - TRL-5
  - TRL-6
  - TRL-8

BARDA Interest
  - Low
  - High
Accelerating Vaccine and Therapeutic Evaluation

• Technology
  – MIMIC® (Modular IMmune In vitro Construct) models both the innate and adaptive immune responses through 2 modules

• Maturity and Project Scope
  – MIMIC® has been evaluated with commercial vaccines – Influenza and Yellow Fever
  – Further development and verification that the in vitro system is correlated to in vivo response

• Application to BARDA’s mission
  – MIMIC® may greatly accelerate evaluation of candidate vaccines and reduce dependence on animals
  – System would apply to biodefense, influenza, and emerging diseases
  – Platform potential extends to many aspects of product development (e.g. formulation) and applies to vaccines and therapeutics

http://www.vaxdesign.com/mimic-technology
Improved Stability of Influenza Vaccines

• Technology
  — PATH coordinated team for liquid (Arecor) and dried (Aridis) formulation strategies

• Maturity and Project Scope
  — Both technologies have been applied to products used in clinical development for commercial applications
  — Both technologies will be applied to subunit and live attenuated influenza vaccines (2009 H1N1) and subsequently to a second strain to demonstrate robustness
  — Formulation and pre-clinical studies

• Application to BARDA’s mission
  — Technologies address an immediate for improved stockpiled flu vaccine stability (especially live)
  — Impact to BARDA’s international program by reducing cold-chain requirements
  — Both technologies would be broadly applicable to biothreat and emerging disease candidate biologicals


http://www.aridispharma.com/stabilizationofbiopharma.html
Adjuvants

• **Technology**
  – IDRI’s stable emulsions combined with GLA TLR4 agonist represent emerging adjuvant candidates

• **Maturity and Project Scope**
  – GLA-SE has entered clinical evaluation with multiple late stage products
  – Adjuvant technologies will be evaluated with other TLR agonists and emulsion formulations to evaluate a toolbox to tailor the immune response to the needs of a particular pathogen
  – Formulation and pre-clinical studies with influenza vaccines

• **Application to BARDA’s mission**
  – Dose- and dosage-sparing are immediate needs in influenza
  – Applicable to current and future biodefense, influenza, and emerging disease requirements

Protein Expression

• **Technology**
  – Pfenex’s *Pseudomonas fluorescens* protein engineering uses high throughput strain development and screening for efficient production of soluble protein

• **Maturity and Scope of Work**
  – *P. fluorescens* expression platform has successfully produced protein used in clinical development of commercial products
  – Pfenex is demonstrating through strain development and pre-clinical studies the capability to produce rPA as a candidate anthrax vaccine

• **Application to BARDA’s mission**
  – *P. fluorescens* expression system is a platform technology capable of producing proteins that are unsuccessfully produced in other expression systems
  – Supplementing the anthrax vaccine program’s product pipeline

http://www.pfenex.com/page/platform-technology
Influenza Manufacturing Platforms

• Technology
  – Rapid Micro Biosystems’ Growth Direct System (GDS) for rapid sterility testing takes advantage of cell auto-fluorescence to rapidly detect contaminating cell growth
  – Novartis’s flu vaccine manufacturing and J Craig Venter Institute’s gene synthesis capabilities

• Maturity and Scope of Work
  – GDS is commercially available technology for bioburden screening being developed and optimized for rapid sterility testing
  – Influenza seed viruses fit into nearly all egg- and cell-based vaccine products

• Application to BARDA’s Mission
  – Reducing sterility testing assay time to < 14 days and reducing virus reassortant processes will greatly accelerate vaccine release
  – Platform technologies applicable to other parenterals and virus-based products

• Projects accomplish many objectives
  – Evaluating and supporting further development of platform technologies
  – Supporting earlier development to expand product pipeline for CBRN and Influenza
  – Addressing critical mission goals such as flu manufacturing and BARDA’s international program
  – Typical 2-3 year timelines allows fluidity to rotate in new technologies as existing projects mature and transition

• Innovation capitalizes on established infrastructure
  – Formulations designed to streamline into existing manufacturing processes
  – Biomanufacturing improvements are compatible with existing infrastructure (e.g. fermentation facilities)
  – I.e. innovation doesn’t require a complete restructuring of the entire MCM infrastructure
Further Thoughts

• Most projects applied to influenza vaccine
  – Easier system to evaluate technologies due to licensed products with historical data and established assays and animal models
  – Application to other pathogens is applicable

• Represented Technologies
  – Adjuvants and protein stabilization
  – Expression and influenza vaccine manufacturing
  – Diagnostics

• Underrepresented Technologies
  – Formulations for alternate delivery
  – Accelerated vaccine and therapeutic design
  – Other technologies in the future?
Questions?