



United States Department of

Health & Human Services

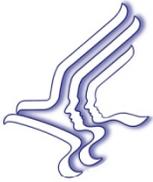
Office of the Assistant Secretary for Preparedness and Response (ASPR)

Anthrax Therapeutics: The Role of BARDA in the Development of Anthrax Medical Countermeasures

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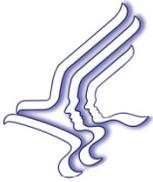
HHS/ASPR



Overview

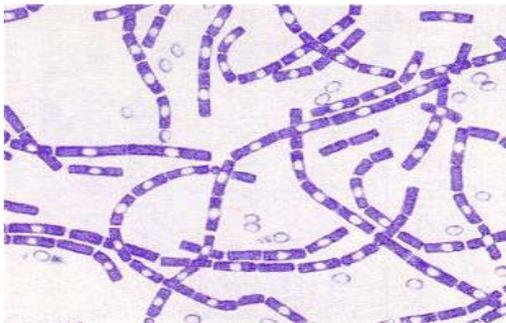


- Background
- Available Therapeutics
- USG Strategy for anthrax MCMs
- Development of anthrax antitoxins
- Licensure under the Animal Rule
- Future of anthrax MCMs
- Working with BARDA



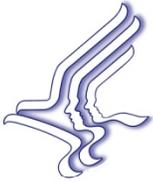
Background

- Causative agent –
Gram positive bacterium *Bacillus anthracis*



- Three clinical forms of the disease:
 - Cutaneous, gastrointestinal, inhalational (Images: CDC and Imageinvision.com)

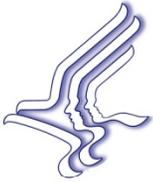




Background



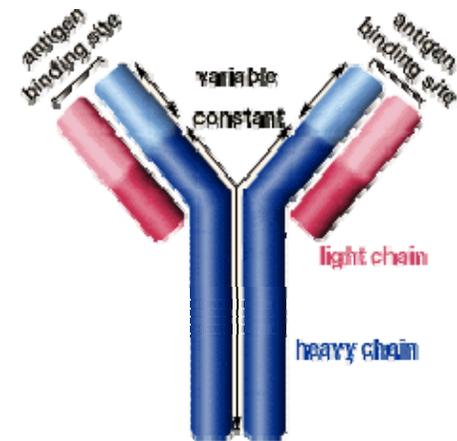
- Currently Project Bioshield anthrax therapeutics' INDs are for the indication of inhalational anthrax
- Inhalational anthrax clinical manifestations and timelines:
 - 4-14 day incubation, but spores may last for months in lungs
 - 2-3 day prodrome—fever, malaise (non-specific)
 - Death occurs rapidly without supportive care
- Not readily transmitted from person to person
- Three treatments available:
antibacterials, vaccines, antitoxins
- All three treatments part of USG strategy for preparedness and response



Available Therapeutics



- Two types of antitoxins available
 - Monoclonal antibodies produced by mammalian cell culture
 - Polyclonal antibodies produced from human plasma after vaccination

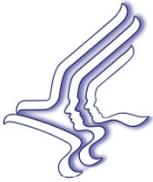


❖ Anthrax Immune Globulin (AIG) is a polyclonal anthrax antitoxin therapeutic manufactured by Cangene Corporation.



❖ Raxibacumab is a monoclonal anthrax antitoxin therapeutic manufactured by Human Genome Sciences, Inc. (HGS)

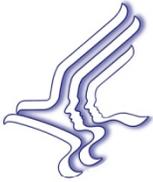




Available Therapeutics



- Both AIG and Raxibacumab:
 - Are not yet licensed
 - Have an IND held by CDC
 - Have Pre-EUA packages submitted by CDC to FDA (CBER and CDER)
- Antitoxins have been used
 - Three cases associated with African drums in US
 - The polyclonal antitoxin (AIG) was used to treat naturally-occurring cases of anthrax in both the US and the UK
 - In UK fifteen cases associated with contaminated heroin (over fifty cases total)
 - AIG used in all cases under CDC held IND

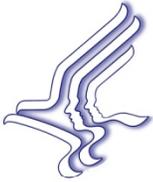


USG Strategy



- Establish antitoxin requirements
 - Completed: two requirements
 - Treatment courses for drug sensitive anthrax
 - Treatment courses for drug resistant anthrax

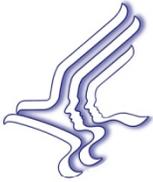
- Fulfillment of requirements
 - Acquisition of products via Project BioShield contracts
 - Development of products via Advanced Research and Development contracts
 - Review portfolio as requirements change
 - Maintain pipeline until licensed products available



USG Strategy



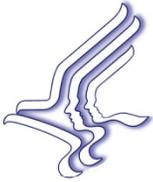
- Acquisition Strategy
 - Near term- fulfill requirements with technologies immediately available, acquisitions based on fit between technology and concept of operations (antibody-based antitoxins)
 - Mid-term- improve technologies immediately available (improved ease of administration, formulation, stability)
 - Long term- investment in next generation technologies (small molecule antitoxins)



Project BioShield



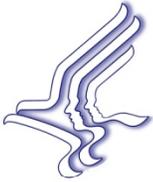
- PBS acquisition contract with Human Genome Sciences, Inc. for up to 100,000 treatment courses of raxibacumab
 - Base award for 20,001 treatment courses
 - Options exercised for 45,000 additional treatment courses
 - To date, ~49,000 doses of raxibacumab delivered to SNS
- PBS acquisition contract with Cangene Corporation for up to 100,000 treatment courses of Anthrax Immune Globulin (AIG)
 - Base award for 10,000 treatment courses
 - To date, 10,000 doses of AIG delivered to SNS



Anthrax Therapeutics Contract Summary



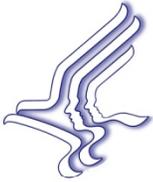
- Seven contracted companies developing anthrax therapeutics in varying stages of development
- All contracts funded by BARDA; some contracts managed by NIAID
- Two companies currently delivering product to the SNS (1 polyclonal and 1 monoclonal)
 - 2 polyclonal therapies; all polyclonals stored at -20°C
 - 5 monoclonal therapies; all monoclonals stored at 2-8°C



Animal Rule Licensure



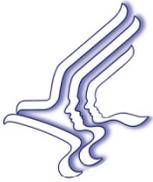
- Clinical trials with anthrax not feasible
- Safety demonstrated in humans
- Efficacy demonstrated in animal models
 - NOT “Two Animal Rule”
 - Small animal model for “statistical data”
 - Large animal model for bridging correlates or surrogates
 - Models must be accepted before pivotal studies possible
 - Model reflect the disease in humans
 - Treatment predict human response
- Identify human dosage
 - Evaluate repeat-dose safety



Additional Issues to Consider

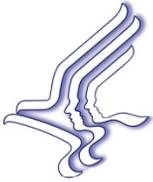


- Concomitant use of other MCMs
 - Vaccines, antivirals, antibacterials
- Anthrax antitoxins will be used with antibacterials
 - FDA requires demonstration of “added benefit” before approval
 - Development of antibacterial treatment model required
 - All three models- monotherapy, antibacterial, and combination therapy- must be accepted by FDA
 - Antibacterial treatment model must reflect results of use in humans
- Antibacterials have a label indication for use as Post Exposure Prophylaxis only.



Model Expectations

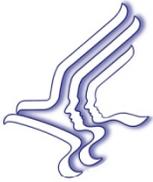
- Antibacterial model parameters established by FDA
 - Antibacterial dosage- full human equivalent
 - Treatment initiation- clinically relevant data
 - Treatment duration- five days minimum
- Model goal
 - 50% survival of animals treated with antibacterial alone
 - Defined added benefit in combination treatment groups
 - Statistical significance required



Sponsor Consortium



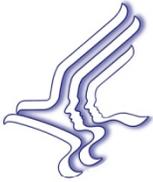
- USG funding development of multiple products to mitigate risk
- Each sponsor required to demonstrate added benefit
- Inefficient for USG to fund parallel development of several models independently
- Inefficient use of limited model development and testing resources
- All USG-funded sponsors participating in consortium
 - Control data from studies pooled for meta-analysis
 - Effort started spring 2010, first report expected this spring
 - Correlation with human data if possible



Future of Anthrax Therapeutics



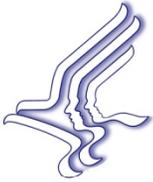
- Address gaps in advanced development portfolio
- Targets
 - All antitoxins in advanced development target Protective Antigen
 - Solicit white papers/proposals regarding antibody-based antitoxins based on other targets (lethal factor, edema factor)
- Administration and storage
 - All antitoxins in advanced development administered as IVs
 - Solicit white papers/proposals for improved formulation, alternate administration routes, storage without cold-chain



Future of Anthrax Therapeutics



- All antitoxins in advanced development based on antibodies (monoclonal/polyclonal)
 - Solicit white papers/proposals regarding small molecule antitoxins or antidotes
 - Keep in mind TRL requirements: must have active IND and initiated clinical trial



Interfacing with BARDA



- www.phe.gov
 - Program description, information, news, announcements
- www.medicalcountermeasures.gov
 - Portal to BARDA
 - Register, request a meeting
 - Tech Watch
- www.fedbizopps.gov
 - Official announcements and detailed information about all government contract solicitations

