



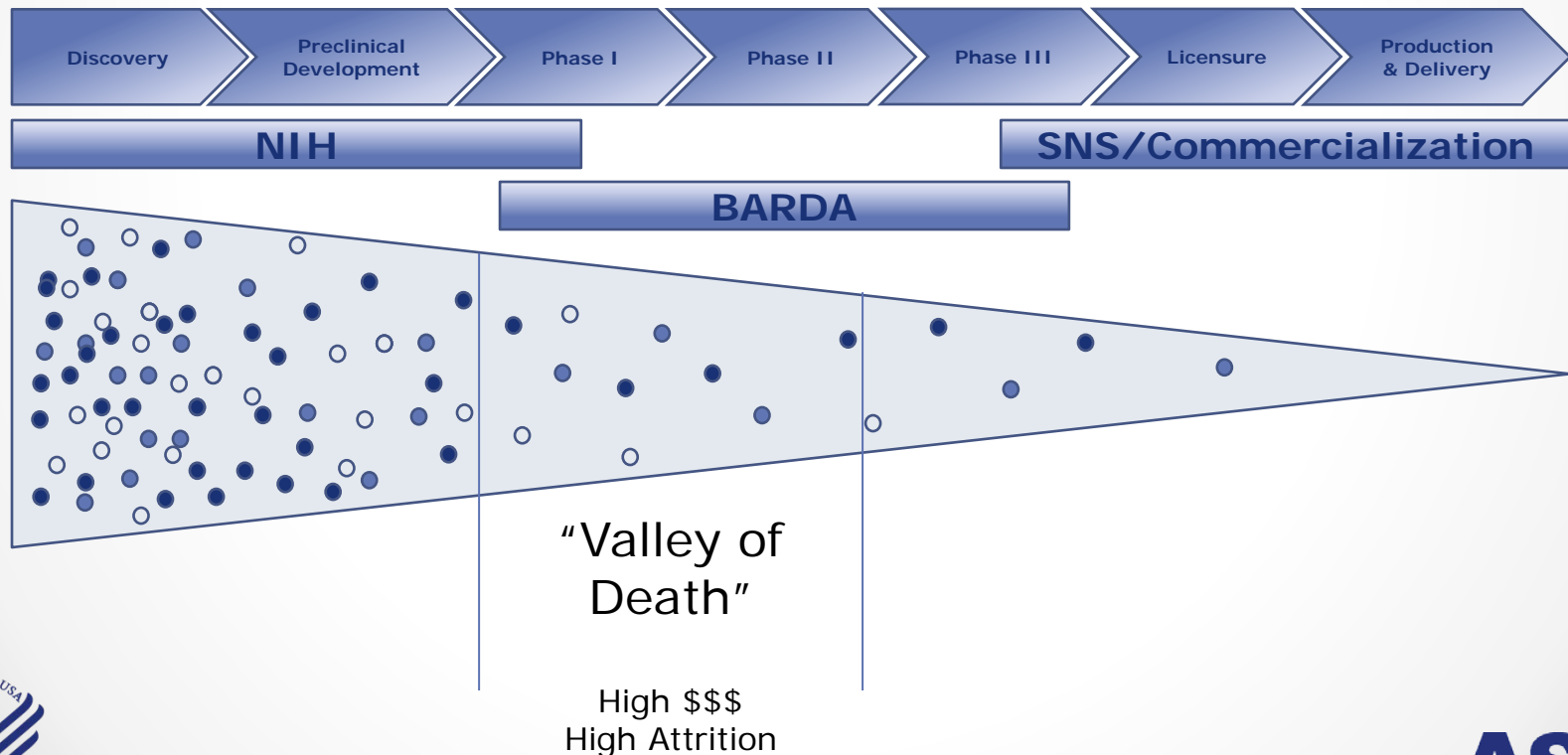
ANIMAL MODEL DEVELOPMENT IN BARDA'S NON-CLINICAL NETWORK

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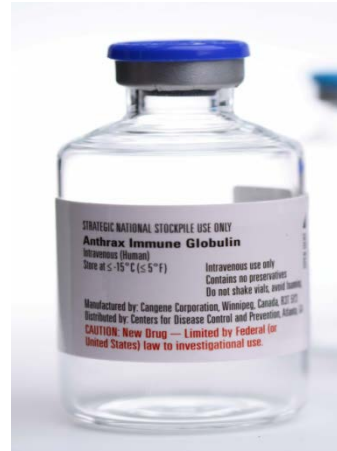
BARDA's Role within the PHEMCE

- Advanced Development & Manufacturing
- Procurement
- Chem, Bio, Rad/Nuc (CBRN) & Influenza



CBRN Portfolio

- Licensed MCMs for botulinum intoxication and inhalational anthrax



- Late-stage MCMs for smallpox
- Ebola MCMs in Phase I/II studies



- Several antibacterials in clinical development
- CARB-X



BARDA's Non-Clinical Program

- Primary objective is to support the performance of regulated studies
- Provide a non-clinical resource for advanced development of MCMs
 - Generate and publish data
 - Maintain a repository of well-characterized reagents and samples to support MCM development
- Network
 - Capabilities within biological, chemical, radiological & nuclear
 - Competitive process for Task Order award



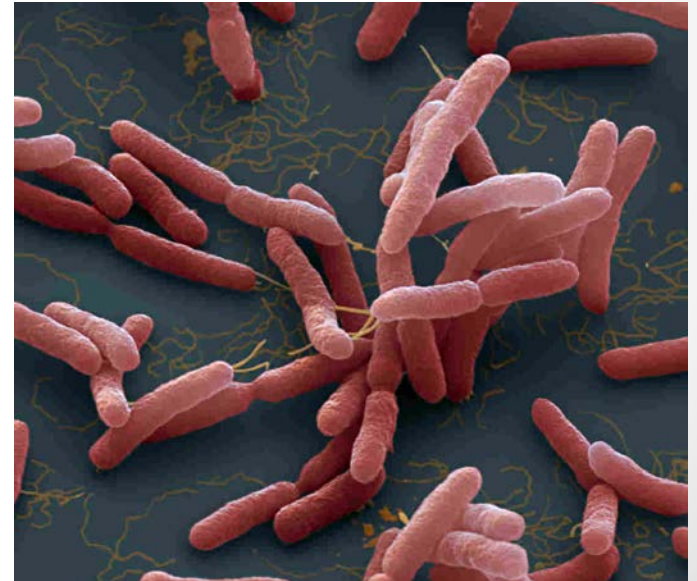
Animal Rule & Model Development

- ... *"when human efficacy studies are not ethical and field trials are not feasible"*
- Well-understood disease mechanism and prevention/reduction by the product
- Action within animal model(s) must be predictive of human response
- Endpoint related to the desired benefit in humans
- PD/PK data must allow selection of an effective dose in humans



Burkholderia Animal Model Program

- Established a clinical definition of inhalation melioidosis to guide evaluation and development of an animal model
- Developed quality controlled strain panels for *B. pseudomallei* (12 strains) and *B. mallei* (6 strains)
- Proceeded with small animal evaluations of well known strains (mice and Guinea Pigs)
- Conducted full LD₅₀ and natural history investigations in marmosets and Rhesus macaques (melioidosis) and AGMs (glanders)



C. difficile Animal Model Program

- Established a *C. difficile* strain panel (four strains)
- Development of a Syrian hamster model is ongoing
 - Qualification of clindamycin treatment
 - Dose; challenge delay
 - Microbiome analysis
 - Trigger to treat rather than fixed time
 - Includes diagnostics (ELISA, MSD, PCR)
 - Strain panel virulence
 - Natural history



Thanks!

