Operational Concerns during an Anthrax Mass Vaccination Campaign

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U.S. Licensed Anthrax Vaccine

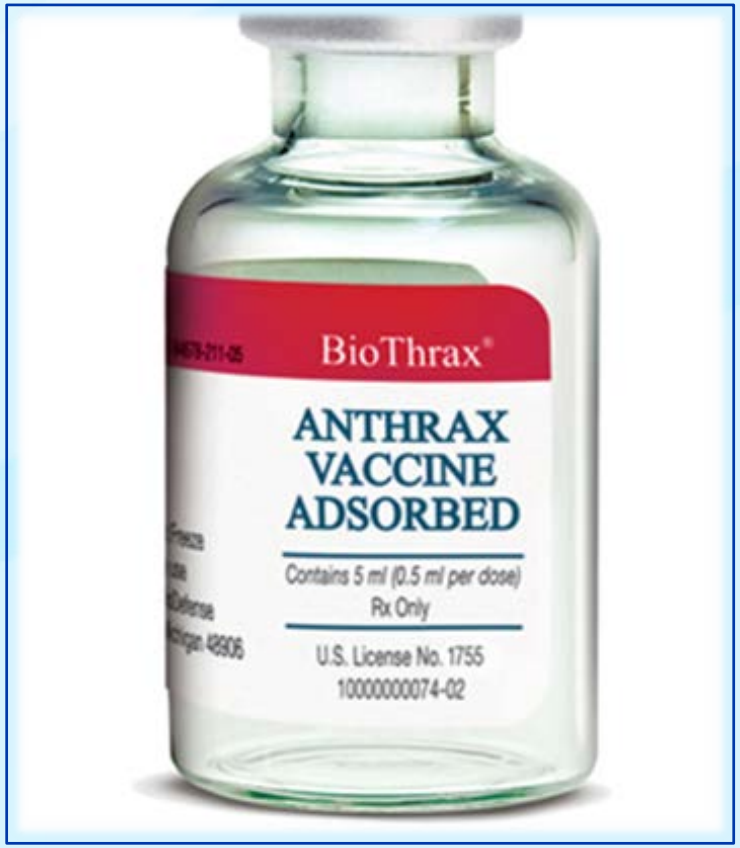
- Anthrax Vaccine Adsorbed (AVA (BioThrax®))
  - Manufactured
    - Michigan Dept of Health until 1998
    - Currently Emergent BioSolutions
  - Sterile, cell-free filtrate made from microaerophilic cultures of avirulent, non-encapsulated *B. anthracis* V770-NP1-R
- Final product
  - 1.2 mg/mL aluminum (added as aluminum hydroxide in 0.85% sodium chloride)
  - Contains as preservatives: 25 µg/mL benzethonium chloride and 100 µg/mL formaldehyde
  - Primary immunogen is protective antigen (PA)

AVA Updates Since Last ACIP Recommendations in 2010

- AVA Licensure Changes
  - Change to IM administration for pre-exposure prophylaxis – 2008
  - Elimination of priming dose at week 2 for pre-exposure prophylaxis – 2008
  - 0-1-6 month priming schedule (3-IM) – 2012
    - Protection achieved at 6 months
  - First EU approval in Germany for pre-exposure prophylaxis – 2013
    - 3-IM priming, 3-year booster
  - PEP Licensure using SC administration – 2015
- New Data
  - Additional safety studies
  - Animal models supporting AVA PEP approval and planned BLA application for next generation anthrax vaccine (AVA plus CPG 7909 (NuThrax®))
  - Dose-sparing studies

Licensed Indications

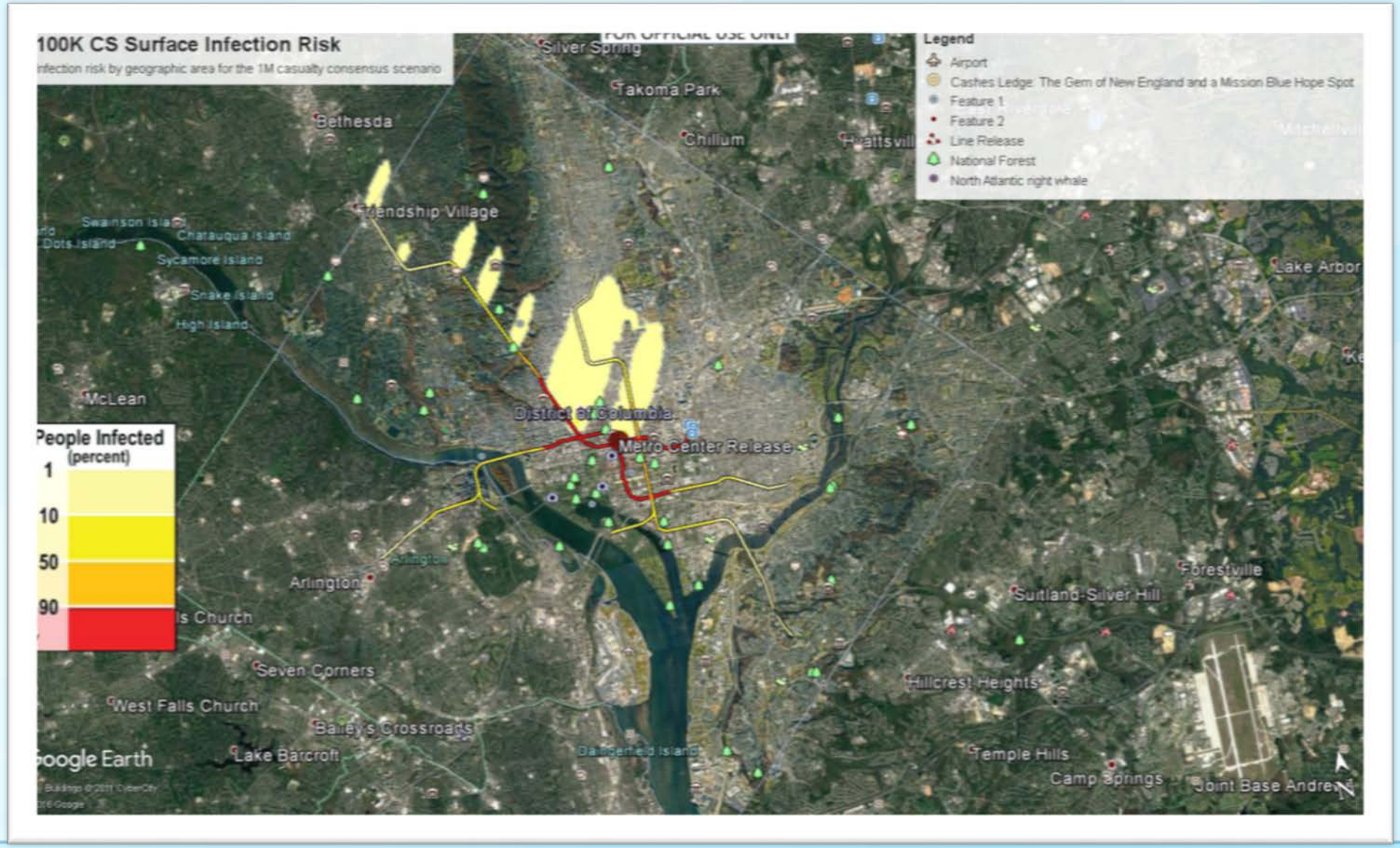
- **Pre-Exposure Prophylaxis (PrEP)**
  - Intramuscular (IM) route
  - 3-dose priming series at 0, 1 and 6 months
  - Booster doses at 12 and 18 months, then annually
- **Post-Exposure Prophylaxis (PEP)**
  - Sub-cutaneous (SC) route
  - 3-dose series at 0, 2 and 4 weeks
  - Co-administration of antibiotics for 60 days



Bioterrorism

- ***Bacillus anthracis* spores: the most likely bioweapon**
  - Relatively easy and cheap to produce
  - Can be stored for a long time
  - Can be aerially dispersed a variety of ways
  - Odorless, colorless, tasteless
  - Inhalation anthrax is highly lethal
  - May survive > 40 yrs
- **Can cause widespread illness and death among unprotected persons**
  - Sverdlosk incident, 1979
  - US mail incident, 2001

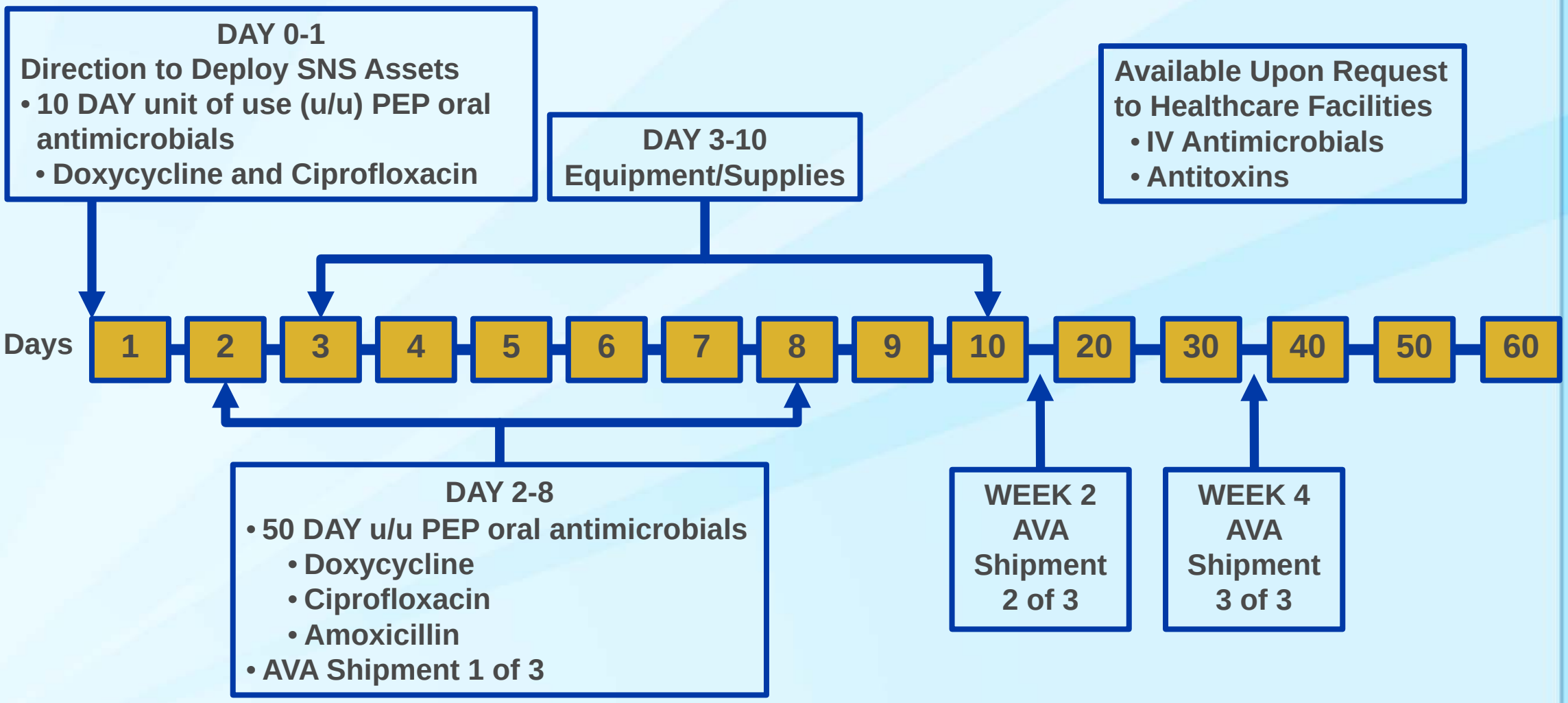
Hypothetical Wide Area Outdoor Release



Federal Response to a Wide-area Release of *B. anthracis* Spores

- CDC stockpiles medical countermeasures
  - Oral antimicrobials and vaccine for PEP
  - Parenteral antimicrobials and antitoxin for treatment
  - Ancillary supplies
- Individuals exposed to aerosolized *B. anthracis* spores should receive 60 days of oral antimicrobial in conjunction with a three-dose course of anthrax vaccine
- PEP should be started as soon as possible

60-day Anthrax Response Timeline



Operational Concerns

- Supplies for administering vaccine
  - CDC SNS does not stockpile sufficient numbers of 5/8” needles to administer stockpiled vaccine via SC route
  - Manufacturer supply chain does not have sufficient 5/8” needles either
  - 1” needles supplies are more available and come closer to meeting needs
- CDC SNS will start transitioning to AVA plus CPG 7909 (NuThrax®) in 2018
  - During the transition over next 4-5 years, SNS will have two vaccines with two different routes of administration
- In a large anthrax event, efficiency of administering vaccine to a large number of people is a major concern
  - IM administration could be technically easier and faster than SC

Adherence to Antimicrobial PEP – Anthrax Event 2001

- Approximately 10,000 persons were recommended for at least 60 days of antimicrobial prophylaxis to prevent inhalational anthrax

- Interviews on 6,178 persons recommended PEP
  - Most of the respondents were 40–64 years of age
  - 60% were men

Shepard CW, Soriano-Gabarro M, Zell ER, Hayslett J, Lukacs S, Goldstein S, et al. Antimicrobial Postexposure Prophylaxis for Anthrax: Adverse Events and Adherence. Emerg Infect Dis. 2002;8(10):1124-1132.

Adherence to Antimicrobial PEP – Anthrax Event 2001

- 787 (13%) never started their antimicrobial prophylaxis
- 2712 (44%) persons reported taking antimicrobial prophylaxis for 60 days
- Reasons for stopping included
  - Adverse events (43%)
  - Perceived a low risk for anthrax (25%)
  - Identified fear of long-term side effects from antimicrobial PEP (7%)

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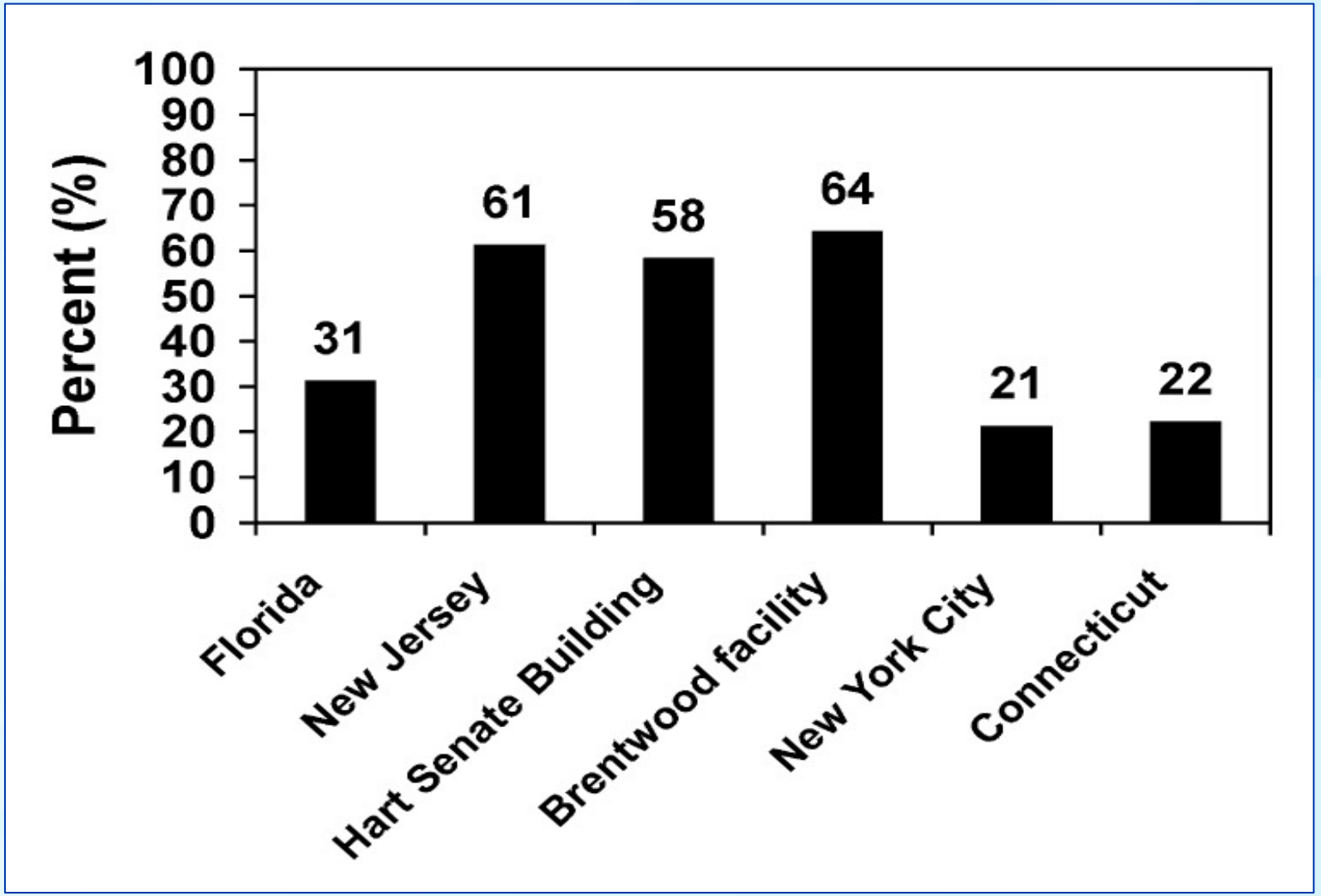


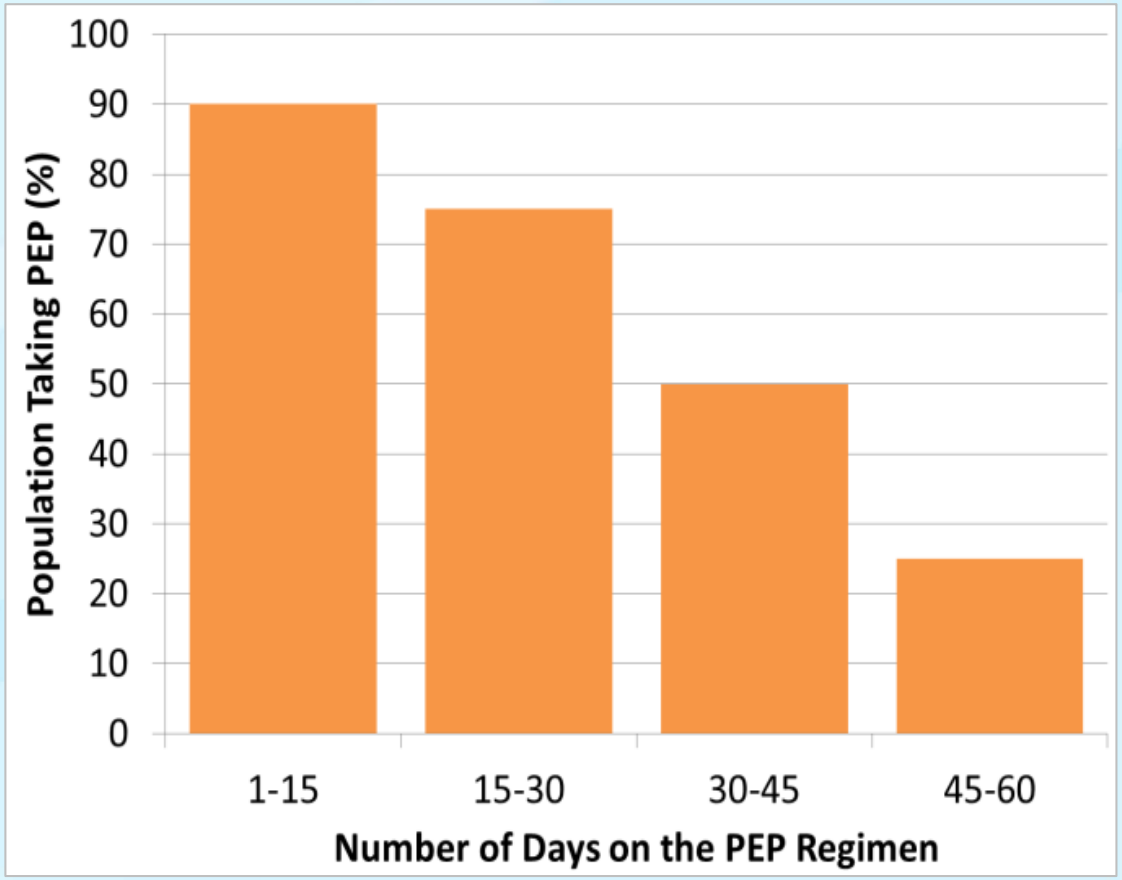
PEP Following Laboratory Incident at CDC

- 42 individuals potential exposed to *B. anthracis* spores were recommended to receive 60 days of antimicrobials and AVA 3-dose series
- Information regarding antimicrobial adherence was available for
  - 29 (69%) at day 30 of PEP
  - 18 (43%) at day 60 of PEP
- Of the 29 individuals who responded to the survey
  - 28 (97%) started the antimicrobial PEP course
  - 15 (52%) reported discontinuation by day 30
- Of the 18 who responded at day 60, only 6 (33%) surveyed reported completion of the 60-day antimicrobial PEP
- Reasons for stopping antimicrobial PEP early
  - Low perceived risk (9/14 (64%))
  - Experiencing AEs (5/14 (35%))

Nolen LD, Traxler RM, Kharod GA, Kache PA, Katharios-Lanwermeyer S, Hendricks KA, et al. Postexposure Prophylaxis After Possible Anthrax Exposure: Adherence and Adverse Events. Health Secur. 2016 Nov/Dec;14(6):419-423

Estimates of Adherence to Antimicrobial PEP

- 10% who get PEP will not take it
- 90% still take PEP at 1-15 days
- 75% still taking PEP at 15-30 days
- 50% still taking PEP at 30-45 days
- 25% still taking PEP at 45-60 days



Adherence to PEP Vaccine

- Little data on the effect of adverse events and vaccine adherence in emergency situations
- AVRP study evaluated an alternative administration route and a reduced priming and booster schedule
- Intramuscular administration results in a lower proportion of injection site adverse events compared to subcutaneous administration
- No association between drop-out rate and route of administration

Summary of Work Group Discussions

- **Operational Concerns**
  - Supplies to administer vaccine
  - Two vaccines with different routes of administration
  - Efficiency of response
- **Adherence to antimicrobial PEP**
- **Adherence to vaccine PEP**

Discussion