Medical Counter Measures and FDA: A Look Back

Dianne Murphy, MD, FAAP
Director, Office of Pediatric Therapeutics
Office of the Commissioner
FDA

February 15, 2012
Anthrax Drug Therapy

• The labeling of antibiotics for post-exposure prophylaxis of Inhalational Anthrax (PEIA) was an FDA initiative in 2000.*

• This was the 1st antimicrobial drug approved by the FDA for use in treating an infection due to a biological agent used intentionally.

• Dr. Friedlander and others submitted their data for review and participated in a public advisory committee on the strength of the evidence in both non-human primates, human and animal pharmacokinetics and the evidence from Sverdlovsk, in the former Soviet Union

Anthrax: Pediatrics

• Post 2001, FDA made a dosage recommendation for amoxicillin as an alternative for PEIA in pediatric patients.*
• This was based on analysis FDA performed on pharmacokinetic data in pediatric patients which it had and data from the literature.

Plague

• 2003
  FDA works with NIAID and military researchers on trials using gentamicin for treatment of pneumonic plague in non-human primates.

• FDA collaboration with CDC to study treatment with gentamicin of human plague in Madagascar

• 2005 to present
  FDA continues to work with NIAID & military to assess other antibiotics in the same non-human primate pneumonic plague model.
FDA Issues Instructions on Potassium Iodide: Pediatric Dosing included

- December 2001, FDA issues a final Guidance on Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies.
- The objective of the document is to provide guidance to other Federal agencies and to state and local governments regarding the safe and effective use of potassium iodide (KI) as an adjunct to other public health protective measures in the event that radioactive iodine is released into the environment.
Radiation Exposure: 2003
Prussian Blue Guidance

- In reaching our determination on the effectiveness of Prussian blue, we evaluated published reports of a 1987 incident in Goiania, Brazil, where approximately 250 people were contaminated with cesium-137 that had been abandoned after use in a cancer clinic (see International Atomic Energy Agency, 1998).

Forty-six patients with heavy internal contamination were treated with Prussian blue. Data on the whole-body effective half-life of cesium-137 during treatment and after treatment with Prussian blue was completed on 33 of the 46 patients. The untreated mean whole-body effective 6 half-life of cesium-137 is 80 days in adults, 62 days in adolescents, and 42 days in children.

Prussian blue reduced the mean whole-body effective half-life of cesium-137 by 69 per cent in adults, by 46 per cent in adolescents, and by 43 per cent in children (see International Atomic Energy Agency, 1998).

Data from other literature was also reviewed and reported Labeled down to 2 years of age.
SUMMARY: The Food and Drug Administration (FDA) is announcing that we have concluded that Prussian blue, when produced under conditions specified in approved new drug applications (NDAs), can be found to be safe and effective for the treatment of internal contamination with
- radioactive thallium,
- nonradioactive thallium,
- or radioactive cesium.

We encourage the submission of NDAs for Prussian blue drug products. We are also announcing the availability of a guidance for industry entitled:
“Prussian Blue Drug Products- Submitting a New Drug Application.”
This guidance is intended to assist manufacturers who plan to submit NDAs for Prussian blue.
Radiation Exposure: 2003 Ca-DTPA and Zn-DTPA

- Guidance to assist manufacturers with applications for:
  - pentetate calcium trisodium (Ca-DTPA)
  - pentetate zinc trisodium (Zn-DTPA) for:
    treatment of internal contamination with plutonium, americium, or curium.

- In the *Federal Register* of September 15, 2003 (68 FR 53984), we announced the availability of this guidance, explained in detail our findings regarding safety and effectiveness, and included a list of citations to the literature on which we partially based those findings.
Radiation Exposure: 2004 Ca-DTPA and Zn-DTPA

On August 11, 2004, revised the draft labeling for Ca- and Zn-DTPA to incorporate information considered from additional literature citations and other available clinical data. We are revising this guidance to explain our labeling revisions.

These labeling revisions reflect our current thinking on
(1) routes of administration,
(2) duration of therapy, and
(3) safety risks
FDA approves pediatric use of pralidoxime chloride for organophosphate poisoning

• September 2010, using data from a variety of sources, the FDA is able to establish dosing for children that permits labeling of pralidoxime for use in pediatrics.
• Next steps involve developing a premeasured delivery system for children.
Vaccine targets

Bacterial and Viral diseases

• Anthrax
• Tularemia
• Plague
• Glanders and Melioidosis
• Brucellosis
• Q Fever

Viruses:

• Alphaviruses
• Smallpox
• Viral Hemorrhagic Fevers
Anthrax Vaccine

NON-HUMAN PRIMATES

• Henderson DW, Peacock S, Belton FC. Observations on the prophylaxis of experimental pulmonary anthrax in the monkey. 

• Friedlander AM, Pittman PR, Parker GW. Anthrax vaccine: evidence for safety and efficacy against inhalational anthrax. 

HUMANS

• Licensed for pre-exposure only

• Post exposure to focus on providing immune safety net after discontinuation of 60 days of antimicrobial therapy-issue is spores

• Clinical Trials.gov: a number of ongoing anthrax vaccine trials
Smallpox Vaccine: Pre-event

- Historically lots of human experience
  The issue is a better and safer vaccine or approach

- Complications: high rate of myo-pericarditis with Dryvax and increasing numbers of immunocompromised individuals drive the need for a safer vaccine.


- Presently on Clinical Trials.gov a number of trials in adults.
Pandemic Preparedness

• FDA is highly involved in each year’s selection of influenza virus strains for influenza vaccine
• FDA monitors not only the vaccine reported adverse events but also the adverse events associated with antivirals used to treat influenza
Challenges for the Future: GAO

• Challenges include:

  (1) proving a countermeasure's effectiveness using animals as proxies for humans, because humans cannot ethically be used in studies involving CBRN agents;

  (2) determining appropriate doses of countermeasures for children, who may be more vulnerable to exposure to CBRN agents; and

  (3) evaluating the safety and effectiveness of medical countermeasures for use in a public health emergency if they have not yet been approved or licensed.
Gordon N. Meiklejohn, M.D.  
1911-1997