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Dedicated to a safer world

USSOCOM Chemical, Biological, Radiological &
Nuclear Conference & Exhibition

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Use of Recombinant Butyrylcholinesterase in Responding to Chemical Weapon Attack

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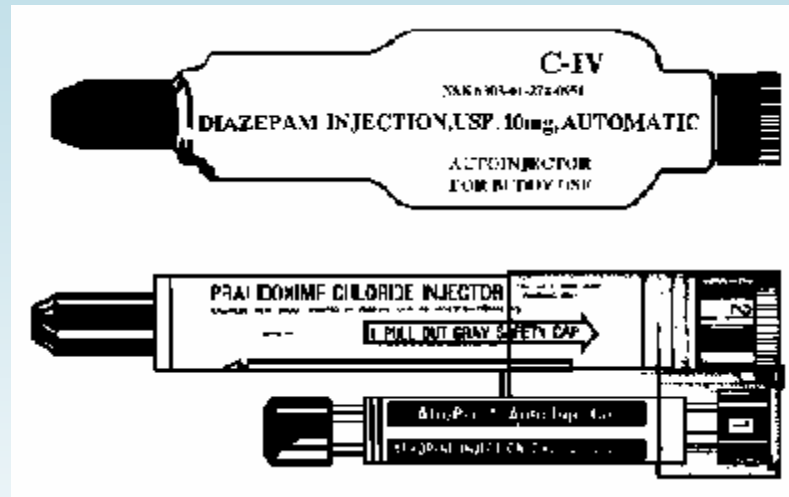
- PharmAthene's primary objective is the development of effective countermeasures to biological and chemical weapons
- PharmAthene has two lead compounds:
 - A recombinant protein, Butyrylcholinesterase (BChE), for both pre-exposure prophylaxis and post-exposure therapy of nerve agent exposure.
 - A fully human antibody designed to protect against inhalation anthrax, the most lethal form of illness in humans caused by the *Bacillus anthracis* bacterium

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Current Response Mark I and CANA



The future of rapid response to a CW threat will be greatly enhanced by development of compounds such as Protexia

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Anticipates that the needs of SOCOM may not always be identical to that of big-DOD/Army

Coordination between Industry and SOCOM early in a project may lead to SOCOM specific products

For example, SOCOM may have needs for different drug-formulations, delivery systems, or routes of administration

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Scenario 3: Chemical Agent Attack

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Scenario 3: Chemical Agent Attack

- Simultaneous Nerve Agent attack at three geographic locations
- 35,000 to 100,00 civilians in vicinity
- Initial explosions kill or maim a number of passers by
- What follows is a progressively acrid smell and onset of nerve agent symptoms

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Scenario 3: Chemical Agent Attack

- First responders don their Self-Contained Breathing Apparatus.
- Panic sets in to most of the crowded venues

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WHY IS THIS SCENARIO ALARMING?

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US: the panicked evacuation of Capitol Hill

By Bill Van Auken
13 May 2005

“Panic seized the US capital Wednesday and was transmitted in amplified form to the entire country via the broadcast airwaves. The cause was a light plane flown by two hapless pilots from rural Pennsylvania, who mistakenly strayed into the restricted airspace surrounding Washington DC.”



In the midst of the tumultuous evacuation of more than **35,000** people onto the streets of Washington,

WHAT IF THIS HAD BEEN THE PRELUDE TO A CHEMICAL ATTACK?

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**PREPARATION
OR
PANIC**

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PANIC: The Destructive Aspect of a Terrorist Attack

- In a crowd, “people behaved differently depending on who they were told the people around them were.”*
- “more mutual helping and a calmer response will result when people feel part of a group.” *



PREPARATION OR PANIC

- PharmAthene proposes to mitigate panic by:
 - Supporting multifunction Ready-Response teams
 - Providing prophylactic and therapeutic treatment for nerve agents (Protexia)
 - Increase first responder functionality
 - Decrease crowd anxiety by having first responders appear less alarming

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"DOTLMPF"

Doctrine:

Organization:

Training:

Leadership:

Material:

Personnel:

Facilities:

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Why Change Doctrine

“Mayors Recommend Greater Role for Military in Emergency Response”

October 24, 2005

- **Recommendations:**
- Enhance Military Involvement in Response
 - Allowing for greater military involvement in immediate response
 - Creating a mechanism for direct military assets during a terrorist attack
- Creating a Better Distribution System
 - Distribution of federal first responder assets directly to local areas

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Doctrine

- Standing-up, and strategically staging prophylactically-protected, multi-purpose, CONUS “ready-teams”
- Emphasis is on targeting panic and site control

Organization/Personnel

- Stand-by teams consisting of experts in security, psychological operations, crowd control, local government affairs, medical counter measures, patient treatment, and science and technology
- Personnel protected enroute with nerve agent Bioscavenger Protexia

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Leadership

- On-site temporary authority (over both Federal and State assets) to coordinate first responders and other assets
- Requires significant change in current local policy and doctrine
- Could avoid scenarios such as an apparent slow response to the Katrina Disaster in New Orleans

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Training

- Response times within a few hours of an event
- Site control and containment
- Establishing command centers
- Coordinating Federal and State responders (i.e., local security, medical, and decontamination)

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Training

- Use of Protexia by first responders
- Triage those in need of Protexia
- Distribution of strategically stockpiled Protexia to local medical facilities
- Educating local medical personnel in the use of Protexia

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WHY PROTEXIA

In animal studies sponsored by the US Army

Protexia pre-treatment (18 hr) prior to 5.5 x LD50
Soman or VX

- 100% survivability
- no signs of toxicity
- no weight loss and no impairment of motor coordination

Conventional therapy following 1.5 x LD50 Soman or
VX

- 50% survivability of Soman and 100% of VX
- Severe toxic signs (transient)
- weight loss and impairment of motor coordination

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EFFICACY OF PROTEXIA

As you heard yesterday, in order to get a product fielded for use, we are required to do animal studies.

For nerve agent pre-treatments we use Guinea Pigs to test efficacy of compounds

The very short (very fast) movie clip attached shows an untreated/unexposed guinea pig walking a balance beam to test neurologic function;

The color lines you see allow us to use computers to monitor and compare neurologic function



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EFFICACY OF PROTEXIA

The following clip shows a guinea pig that was pretreated with Protexia and then 18 hrs later exposed to 5.5 x LD50 of Soman

We treated more than 24 animals with different V or G series nerve agents and 100% of the animals pretreated with Protexia survived with no signs of poisoning.

What you will see is a perfectly normal guinea pig which would have no impact in a functional field setting



EFFICACY OF PROTEXIA

The next clip shows an animal that was exposed to only 1.5 x LD50 of Soman and immediately given the conventional treatment of atropine/2-PAM/Diazepam

And Yes, We do employ Model: (1) Guinea-Pig Emergency Capture/Safety Device



WHY PROTEXIA

- BChE testing has been conducted in collaboration with US and Canadian Defense Departments
- Efficacy studies indicate that prophylactic Protexia can protect animals against the toxicity of multiple lethal dosages (LD₅₀s) of VX and soman
- Protexia administered up to 1 hour post nerve agent exposure in animal models can rescue up to 90% of guinea pigs from an otherwise lethal exposure to VX

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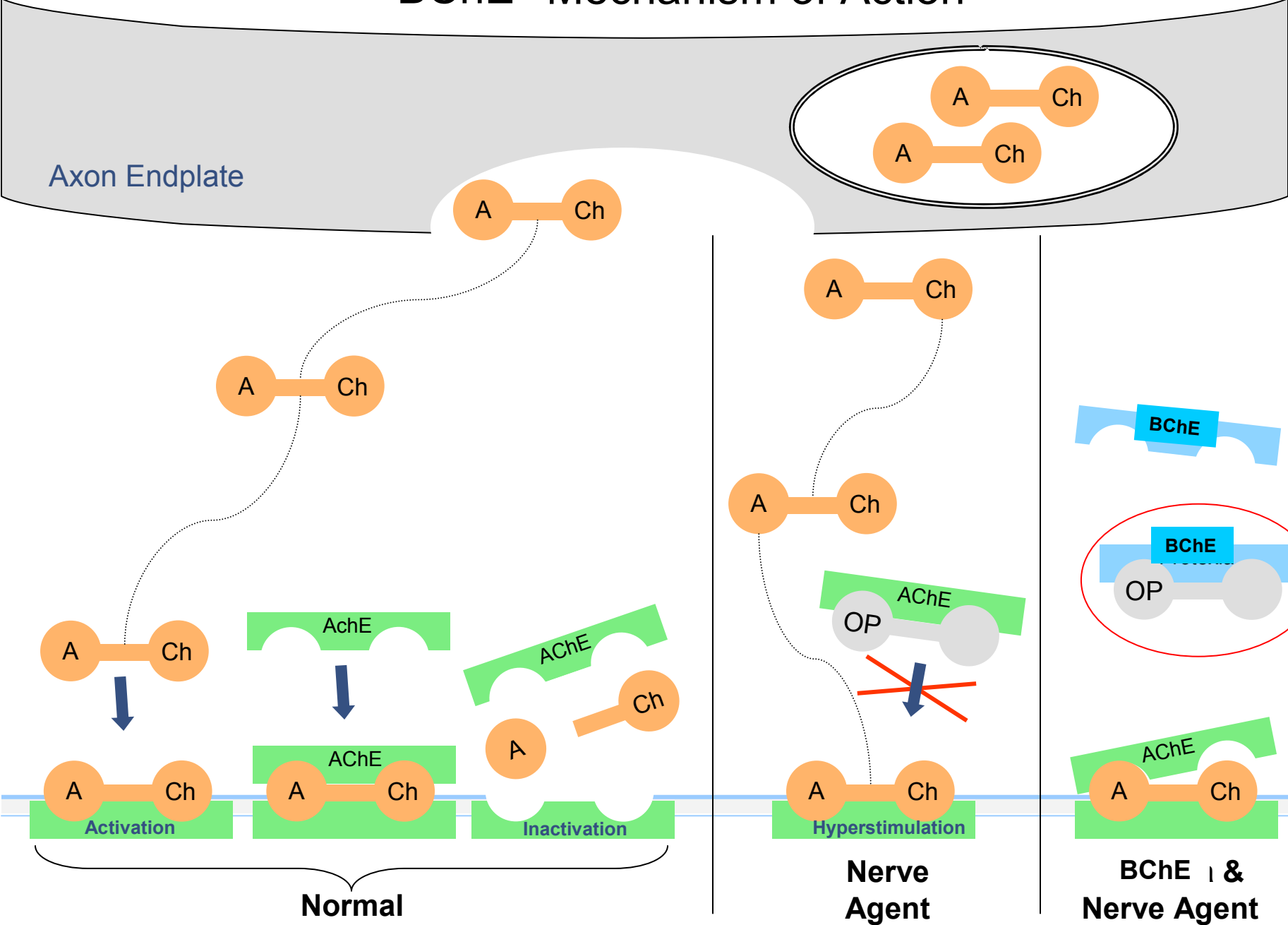
PROTEXIA: Why Does it Work

- Butyrylcholinesterase (BChE) is a naturally occurring protein found in extremely small quantities in blood.
- PharmAthene has developed a technology to produce large amounts of BChE/Protexia in the milk of Goats
- BChE functions as a natural bioscavenger, like a sponge, to absorb and degrade nerve agents before they cause neurological damage.

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BChE Mechanism of Action



Protexia May Provide:

- Prophylactic protection from large doses of nerve agent
- Ease of administration for first responders
- Comfort of knowing protection is “on board”
- Increased ability to operate freely in contaminated areas
- Decreased levels of PPE/MOPP gear

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Material

- Rapid air and ground transportation
- Less restrictive Personal Protective Equipment
- Protexia
 - Available to First Responders
 - Stockpiled for distribution to Aid Stations
 - Distributed to local hospitals for potential use as therapy

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Current Response Personal Protective Equipment



DuPont Tychem®



Photos by Karen Fleming, Michael

Possible Post-Prophylaxis Personal Protective Equipment?



Nitrile Flock-Lined



SOFLOOP™



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Facilities

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SIMULATED EAST COAST CONUS

RESPONSE TEAM STAGING LOCATIONS

- 1: MacDill AFB
- 2: Bolling AFB
- 3: Hanscom AFB
- 4: Fort Bragg
- 5: Rickenbacker AFB
- 6: Robins AFB
- 7: Gunter AFB
- 8: Fort Knox
- 9: Kellogg AGS
- 10: Fort McCoy
- 11: Glenview NAS
- 12: Des Moines AGS
- 13: Fort Leonard Wood
- 14: Little Rock AFB
- 15: Fitzsimmons AMC



Conclusion

- It is anticipated that data to be collected will support the use of Protexia as a nerve agent countermeasure in the future
 - Anticipated filing of IND in 2007
 - Anticipated filing of BLA in 2012
- Our intent is to demonstrate that anticipating future technology, such as Protexia, can play a role in future doctrine/policy

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- **QUESTIONS?**

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