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December 10, 1997

Dockets Management Branch  
HFA-305  
FDA  
12420 Parklawn Dr  
Room 1-23  
Rockville, MD 20857

RE: Docket No. 90N-0302

Dear FDA:

Yesterday, I learned of the 7/31/97 Federal Register notice.

Please accept my comments.

The 12/90 first-of-its-kind waiver of informed consent for competent research subjects should not have been granted on both legal and scientific grounds.

The legal grounds are reviewed excellently in several reports and editorials in the 11/27/96 issue of **JAMA** (which served the legal/ethical basis for my 3/5/97 comments in **JAMA**) and the 10/24/97 docket submission of George **Annas**, Leonard **Glantz**, and Michael Grodin.

Scientific evidence establishes that PB is not a nerve-agent protectant, decreases the protection conferred by actual protectants, and would be harmful in healthy individuals. Old and new evidence indicates that PB toxicity is exacerbated under conditions of stress and activity.

My 1994 submissions to Senator Rockefeller, 4/95-9/97 submissions and 11/12/96 testimony to the Presidential Advisory Committee on Gulf War Illnesses, and 4/24/97 testimony to the US House review this extensive evidence.

The PAC concluded in its final report that PB is not a nerve-agent protectant.

DOD failure to meet any of the conditions of the 12/90 waiver and IND support FDA and PAC conclusions that DOD is incapable of carrying out its obligations to protect soldiers

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being used as experimental subjects. DOD agrees, stating in a letter to the PAC that it "did not comply with the letter or spirit of its agreement with FDA for use of BT vaccine or PB or that conducting an IND during a combat deployment might not be feasible." (see PAC 'special report')

Regarding FDA's requested comments:

**A(1).** Yes, because the interim rule is a violation of the Nuremberg Code and various other rules, and because of the abysmal record of implementing the rule.

A(2). No. Soldiers should never be experimental subjects, and certainly never without informed consent, never without sound evidence, and never with evidence against the experiment.

A(3). No.

A(4). Soldiers should not be research subjects - especially in view of evidence against the experiment.

A(5). Soldiers should not be research subjects - especially in view of evidence against the experiment.

**A(6).** Not needed. Experimenting on soldiers should be abandoned.

A(7). Yes, to zero.

**A(8)(a).** Yes, because of the abysmal record.

**A(8)(b).** Yes, because of the abysmal record of allowing DOD violations.

**A(8)(c).** Yes. Given the abysmal record, FDA should have no latitude.

**A(9)(d).** **Yes.** Announce to all soldiers that they have the right not to participate in any experiment.

**A(10)(e).** Yes. Soldiers should not receive investigational products, especially in view of evidence against the experiment.

**A(10)(f).** Yes. Create an advisory board independent of FDA, DOD, and DVA as well as require prior Presidential findings of safety and efficacy.

**A(8)(g).** Yes.

B. Human efficacy trial are typically done. There is no need to change the system. Contrary to the use of PB, however, clinical experiments should not be performed when there is so much evidence against the experiment.

C. The same quality of evidence necessary for any drug or medical device claim of safety or efficacy.

C(1). **Yes**, just as FDA promulgates clinical guidelines now. Without 'substantial evidence' there is no basis for safety or efficacy claims.

C(2). **Yes**. The advantage - soldiers would not be experimental subjects, especially futile when there is so much evidence against the experiment.

C(3). **Yes**. Notably, PB was not used for victims of the Tokyo subway incident. In fact, PB is contraindicated after **nerve-**agent exposure, and in view of the evidence it should be contraindicated before nerve-agent exposure.

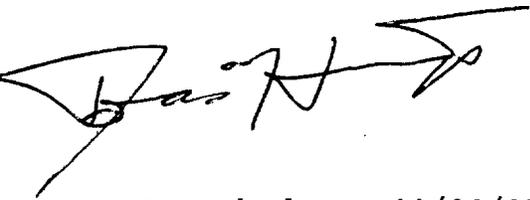
What is most troubling about the evidence against the use of PB is that DOD sponsored and/or performed it prior to the Gulf War. There was no scientific or rational basis for the PB experiment.

FDA's premise for its interim rule and 7/31/97 notice is erroneous. While data indicates that PB + atropine confers protection, when PB is removed from the mixture protection is greater and far less toxicity results.

In view of the significant evidence record, Gulf War illnesses were easily predictable. The majority of the complaints appear to be the consequence of exposure to nerve enzyme inhibitors, eg PB, sarin, and pesticides - whose toxicities synergize with each other and in the presence of DEET insect repellent.

I understand the only country not to report gulf war illnesses was the only country not to use PB on its soldiers (France).

Sincerely,

A handwritten signature in black ink, appearing to be 'D. H. S.', written in a cursive style.

Attached: My 11/30/97 submission.

Thomas N. **Tiedt, Ph.D.**  
PO Box 422  
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**941-747-7281**

November 30, 1997

Dockets Management Branch  
HFA-305  
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Rockville, MD 20857

RE: USE OF INVESTIGATIONAL AGENTS IN SOLDIERS - STOP ILLICIT  
WAIVERS OF INFORMED CONSENT

Dear FDA:

I write as a deeply concerned scientist. I have previously spoken about these issues to the US Senate during **1994, to the Presidential Advisory Committee on Gulf War Veterans' Illnesses 1995-1997, to the US House 1997, on 60 MINUTES 9/96, and in the Journal of the American Medical Association 4/97 (1).** I published relevant research **1977-1978 (2-5)**, which has been extended by several DOD and civilian laboratories - who established the futility of the reckless PB experiment years before the Gulf War (6).

**The** unconscionable use of pyridostigmine (PB) as a nerve-agent protectant contradicted scientific evidence, ethical principles, and several international and US laws and regulations,

Extensive scientific evidence developed during the **1970s and 1980s**, sponsored mostly by DOD, established that PB would be harmful in healthy individuals, and even more harmful in stressed individuals (6). **PB's** toxicology is well understood, including why PB is less toxic in Myasthenia **Gravis** patients, whose pathophysiology provides protections against PB toxicity.

This same array of research established that PB is not a nerve-gas protectant (notably recognized by the Presidential Advisory Committee **(7)**), decreases the effectiveness of actual protectants (eg, atropine), and has synergistic toxicity with nerve agents and pesticides **(6)**. Given the evidence framed by thousands of relevant studies, Gulf War illnesses were easily , predictable.

Outrageously, the pattern of deceit practiced by DOD for the Gulf War and the Bosnia conflict are part of a 50-year legacy according to Senator John Rockefeller (9).

Also consider that 1) DOD's Captain Michael Doubleday held a press conference **9/26/96**, stating that a conscious decision was made by **DOD** not to inform our troops of **PB's** health hazards, 2) DOD sent an urgent fax to 60 MINUTES **9/27/97**, stating that it prepared brochures about PB toxicity but no one received them, and 3) **DOD's** Dr. Bernard Rotsker held a press conference **12/5/96**, stating that DOD confirmed with tests prior to the Khamasiya bunker destruction that it held **sarin** and mustard warheads.

Therefore:

- 1) the Interim Rule must be revoked,
- 2) a true Institutional Review Board, independent of **FDA/DOD** and cognizant of the scientific literature, must be adopted.

Without informed consent and scientific evidence, it is never ethical to expose humans, including soldiers in war, to toxic substances. Agents proven to not protect and to be harmful must never again be used in the name of protection. Most certainly, PB was not the best available protection against nerve gases as indicated by **FDA** in its comment invitation; arguably, it was the worst.

Sincerely,



1. T. N. Tiedt. The Nuremberg Code, Informed Consent, and Involuntary Treatment. **JAMA** 277, 712-713, 1997.
2. T. N. Tiedt, et al. Neurotrophic regulation of resting membrane potential and acetylcholine sensitivity in rat extensor digitorum **longus** muscle. **Exp Neurol** 57, 766-791, 1977.
3. T. N. Tiedt, et al. Neostigmine-induced alterations at the mammalian neuromuscular junction. I. Muscle contraction and electrophysiology. **JPET** 205, 326-339, 1978.
4. C. S. Hudson, et al. Neostigmine-induced alterations at the mammalian neuromuscular junction. II. Ultrastructure. **JPET** 205, 340-356, 1978.
5. T. N. Tiedt, et al. Degenerating nerve fiber products do not alter physiological properties of adjacent innervated **skeletal muscle** fibers. **Science** 198, 839-841, 1977.
6. T. N. Tiedt. Gulf War Syndrome. Sworn testimony to House

# Memorial Day: A- time for nation to reflect

**T**oday is Memorial Day, a solemn day of reflection since 1866 and the end of the Civil War. We honor the men and women who sacrificed their lives, the ultimate sacrifice, in all American wars.

Our collective memorial is symbolized by a silent ceremony at the Tomb of the Unknown Soldiers in the National Cemetery on the southern bank of the Potomac River opposite Washington. Everyone who attends — and everyone should attend at least once in their lives — will be humbled and inspired.



**Thomas N.  
Tiedt**

Also, we honor our fallen patriots in every town and city in the United States.

We will display our most treasured and unifying symbol — the U.S. flag. It waves and snaps our bold red, white and blue arrangement of 50 stars representing our 50 states and 13 stripes representing our 13 original colonies.

We will organize parades to tie our community together. We will assemble our trans-generation families, from toddlers to grandparents, for a holiday dinner.

As we should We owe our freedom to our fallen patriots.

And, we owe them for their most unambiguous message — that their lives mattered, and by subtle-but-stirring implication so do our own lives. These Americans deserve every ounce of respect we can muster.

We are proud of our country — what it was, what it is, and what it will be.

The United States, its glorious land and ideals, is the stage for the American Dream. We have the world's stage for equality and equal opportunity for all.

As an evolving experiment of human intellect and pursuit, the United States is the most successful social experiment on earth

Let's keep it that way.

DAY, FROM PAGE 4

**This way, we will most significantly honor those Americans who fought and died in war**

**The better we do this, the better we will prevent unnecessary and counterproductive re-enactments and casualties — and better evolve the American mission.**