



# Clinical Trials & the Military

CFR 21 50

# The Regulations

- 21CFR 50.23(d)
  - Part 50 – Protection of Human Subjects
  - Subpart B – Informed Consent
  - Sec. 50.23 – Exceptions From General Requirements
  - D1 – Presidential Waivers
- 10 USC 1107 - Notice of use of an investigational new drug or a drug unapproved for its applied use

# The Regulations

- Only the President can waive the prior consent requirement for the administration of an investigational new drug to a member of the armed forces
- Waiver must be written



# The Regulations

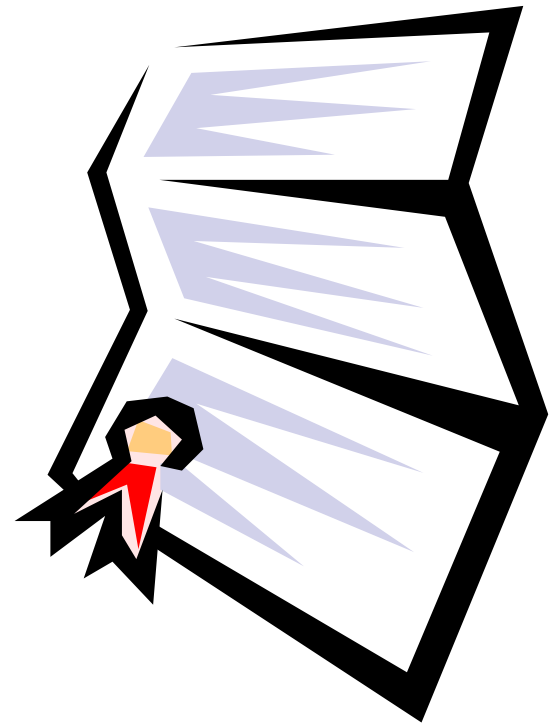
The Waiver is based on

Presidential Determination that:

- obtaining consent is not feasible
- obtaining consent is contrary to the best interests of the military member

or

- obtaining consent or is not in the interests of national security



# The Regulations

## The Secretary of Defense

- The first step in acquiring a Presidential Waiver is a request made to the President by the Secretary of Defense
- The secretary may not delegate responsibilities
- If a waiver is granted, the Secretary of Defense submits notice of the waiver along with the Secretary's justification for the waiver to the chairman & ranking minority member of each Congressional Defense Committee



# The Regulations

The **Secretary of Defense** must certify and document to the President that the following standards and criteria have been met:

- The evidence of the safety and effectiveness of the investigational new drug in relation to the medical risk that could be encountered during the military operation supports the drug's administration under an IND.
- The military operation presents a substantial risk of chemical, biological, nuclear, or other exposure likely to produce death or serious or life-threatening injury or illness.
- There is no available satisfactory alternative
- Conditioning use of the investigational new drug on voluntary participation could significantly risk the accomplishment of the military mission.
- A duly constituted institutional review board (IRB) has reviewed and approved the investigational new drug protocol

# The Regulations

## The Department of Defense IRB

- Reviews and approves the investigational new drug protocol and the administration of the investigational new drug without informed consent
- Must include at least 3 nonaffiliated members (not employees or officers of the Federal Government)
- IRB members must have proper security clearance
- IRB reviews the proposed IND protocol in a meeting at which a majority of the members are present (including at least one member whose primary concerns are in nonscientific areas)



# The Regulations

The request for a waiver includes:

- The context in which the investigational drug will be administered (self-administered or by a health professional)
- The nature of the disease or condition for which the preventive or therapeutic treatment is intended
- Where existing data is available, information on conditions that could alter the effects of the investigational drug.



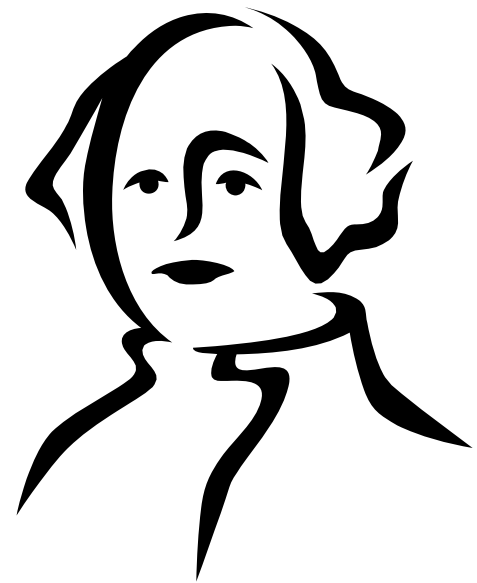
# The Regulations

## The Department of Defense Recordkeeping

- used to track the proposed treatment from supplier to the individual recipient.
- military recipient will be given a specific written information sheet concerning the investigational new drug, the risks and benefits of its use, potential side effects, and other pertinent information
- Medical records of members involved in the military operation will accurately document the receipt of the information sheets
- Medical records of members involved in the military operation will accurately document the receipt of the investigational new drug
- DOD will provide adequate follow up to assess whether there are beneficial or adverse health consequences that result from the use of the investigational new drug
- By notice in the Federal Register, DOD is to provide public notice ASAP describing each waiver of informed consent determination

# The Regulations

The statute provides that in making a “determination” to waive prior informed consent, the President shall apply the standards and criteria set forth in the relevant FDA regulations for a waiver.



# Actual Events



# Kuwait 1990 - Operation Desert Storm



## Investigational Drugs

- Pridostigmina Bromide (PB)  
(nerve agent preventative)
- Botulinum Toxoid  
(bacterial agent preventative)

# Kuwait 1990 - Operation Desert Storm

- Approximately 300,000 Military Personnel receive PB pills
- 8000 receive BT vaccine



# Kuwait 1990 - Operation Desert Storm

- Military required to provide Information Sheets to recipients
- Military required to document IND & AE's
- No procedure ever established to document which personnel received drugs, and **no AE's reported!**



# Kuwait 1990 - Operation Desert Storm

- Over 100,000 Gulf War vets report symptoms in the years following the war
- Vaccines not approved and still under investigation



# Gulf War, December 1997

- Anthrax Vaccine Absorbed (AVA)
- 2.4 Million Troops vaccinated with AVA
- Many troops protested
- Those that refused court martialed or severely punished



# Gulf War, December 1997

- AVA Manufactured by BioPort
- BioPort failed numerous FDA inspections
- BioPort cited for 23 violations

# Gulf War, December 1997

- Information Sheets “lost”
- No records kept by DOD
- No tracking of Adverse Events

