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1. Title: Antipersonnel Chemical Immobilizers: Synthetic Opioids. 27 April 1994

2. Type Effort. S & T

3. Proposed by: Edgewood Research, Development & Engineering Center

4. Capability Sought and Uses to Which it Could be Put: The objective is to develop non-lethal chemical materials having minimal side effects for immobilizing adversaries in various military and law enforcement scenarios. Potential military applications include meeting U.S. objectives in peacekeeping missions; crowd control; embassy protection; and counterterrorism. Law enforcement application include use by local, state and national law enforcement agencies, in hostage and barricade situations; crowd control; close proximity encounters; prison riots; and to halt fleeing suspects.

5. Technical Description.

a. Technical Objectives: Develop chemical immobilizers with the desired performance characteristics, such as safety, onset time and duration of action for use in defined scenarios. Develop family of materials with performance characteristics best suited to various, specific scenarios.

b. Technical Approach.

(1) The overall development of a non-lethal chemical immobilizer is a multi-phase, multi-year process including the following steps:

Phase 1 - Develop candidate material, including design and synthesis; characterize chemical and physical properties; demonstrate effectiveness by preclinical toxicology tests.

Phase 2 - Expanded Preclinical Toxicological Tests, such as carcinogenicity, mutagenicity, teratogenicity, environmental fate, and subchronic effects, for Surgeon General, FDA and any required other agency approval.

Phase 3 - Develop delivery systems to include dissemination of candidate material for specific scenarios and hardware development.

Phase 4 - Clinical Trials for effectiveness and safety.

This proposal applies only to Phase 1.

(2) Background. The synthetic opioids were identified several years ago as prime candidate chemicals for non-lethal application. Two classes of compounds have shown promise in previous studies:

(a) The fentanyls are very potent; are among the fastest acting materials known; and show varying durations of action depending on their specific structure. They are widely used clinically as analgesics and anesthetics. Thus, they are in many respects excellent candidates for situations where a quick-knockdown agent is needed. However, they also have

drawbacks. Earlier materials showed high safety ratios in rodents, but much lower ratios in primates because of respiratory depression. Previous studies at Edgewood under the Advanced Riot Control Agent Device (ARCAD) program led to materials with dramatically improved safety ratios. This was achieved by mixing a fentanyl agonist with an antagonist that blocks the respiratory depression. As a result, the probability exists for developing a safe, quick-acting agent for some specific applications.

In the early 1990's Glaxo Pharmaceuticals patented some ultra-short acting fentanyl that have half-lives of only a few minutes in man. This offers the possibility of a greatly improved safety ratio because the extremely short duration of action should preclude serious respiratory depression. These materials are currently undergoing clinical tests (i.e., in man) in the pharmaceutical industry.

A second drawback is that many of the fentanyls are controlled narcotics. Thus, they would have to be carefully controlled among operators. Thirdly, Chemical Warfare (CW) treaties will presumably limit the use of advanced riot control agents.

(b) A class of experimental materials referred to as the "azabicyclononanes" have also been studied previously at Edgewood. Toxicity screening tests in rodents and in ferrets have shown them to be very potent and to probably have much better safety ratios than the fentanyls. These tests also indicated that the onset times are slower than with fentanyl. These materials are not controlled substances and do not appear on CW treaty schedules. Thus, they should offer advantages over fentanyls where rapid knockdown is not a prime factor.

(c) Technical Approach to Phase 1.

(1) Fentanyl/antagonist mixtures have been studied extensively under the past ARCAD program. Most of the toxicological characterization was done by intravenous or intramuscular administration. However, many of the envisioned uses require inhalation as the route of entry. Thus, studies to determine effectiveness and safety by inhalation are required to complete Phase I studies. In addition, tests in additional animal species may be necessary.

(2) A series of short acting fentanyls based on the Glaxo model have been previously synthesized at ERDEC under our 6.1 basic research program. Preliminary toxicological studies have been initiated. Once the most promising candidate(s) is selected in these preliminary tests, then extensive toxicological tests by multiple routes of entry, (intravenous, intramuscular and inhalation) and in multiple species, e.g., rat and ferret, are needed.

In addition, an update literature review is needed to determine what, if any, additional data has been published on recent pre-clinical or clinical studies. Also, studies to characterize the chemical and physical properties, for decontamination, determining compatibility with various media, and thermal and storage stability are required.

(3) Azabicyclononanes. The primary toxicity screen in the mouse has been completed on a series of these compounds. A limited study was completed

in the ferret to indicate promise by intramuscular injection. Extensive toxicological studies to determine safety and effectiveness by multiple routes of entry and in multiple species are required. An update literature review is needed to determine if additional data is available. Studies to characterize chemical and physical properties are needed.

6. Risk and Limitations: These were outlined in the discussion above. However, to expand on this:

a. Fentanyl/antagonist mixture offers a good probability of success in quickly developing a rapid knockdown agent for use in certain situations where the CW treaty does not prohibit their use. Extensive studies have been carried out in the past and the most advanced technology exists for the fentanyls than for any other chemical immobilizer candidates. However, as also previously pointed out, many of these materials are controlled substances and may require special accountability procedures for operators.

b. Quick-acting fentanyls have only undergone preliminary evaluation at ERDEC. Extensive clinical trials for their use as analgesics/anesthetics are progressing. If this data is available it will help in their evaluation. However, extensive tests to demonstrate safety and effectiveness for use as chemical immobilizers is required. Information available to date indicates a moderate to good probability of success. However, as with the other fentanyls these materials may present the same problems with CW treaty and controlled substance issues.

c. Azabicyclononanes. Only preliminary data is available, but results so far indicate real promise for a safe, potent chemical immobilizer for use where an onset of several minutes is acceptable. Problems with CW treaty and controlled substance issues should be much less than with the fentanyls.

All of these substances are solids that have to be disseminated as aerosols for inhalation effectiveness. Thus, a protective mask should serve as an effective countermeasure. Effective antidotes are available for the fentanyls. These antidotes may also be effective against the azabicyclononanes, but we do not have specific knowledge of this.

7. Project Plan: This proposal is designed to provide data for the proposed ACTD ERDEC effort, entitled "Demonstration of Chemical Immobilizers"; and to provide data for next generation chemical immobilizers to improve or expand the capability.

Task	Completion Date
Synthesize Materials	2Q FY95
Toxicology tests: multiple species, im/iv	4Q FY95
Chemical Studies: decon, thermal stability	2Q FY96
Toxicology Tests: inhalation	4Q FY96

8. Project Cost by Fiscal Year.

FY95 - $300K FY96 - $300K Total $600K

9. ERDEC POC:

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IN REPLY REFER TO:

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LAW
27 OCT 03

Mr. Edward Hammond, III
The Sunshine Project
101 West 6th Street, Suite 607
Austin, TX 78701

Re: Freedom of Information Act Request 084F-01, Referrals for Determination

Dear Mr. Hammond:

This responds to your Freedom of Information (FOIA) Request 084F-01. Department of Defense Instruction 5230.29 directs that prior to release of any information concerning chemical, biological, nuclear, or radiological information, the request for the information shall be referred to the Directorate for Freedom of Information and Security Review (DFOISR). Consequently, this office has referred the following documents listed in the subject request, along with release determination suggestions, to DFOISR:

1. Anti-Personnel Calmative Agents (94-085.pdf)
2. Anti-Personnel Chemical Immobilizers: Synthetic Opioids (94-086.pdf)
3. Biological Infared Sensor to Ascertain Human Targets and Determine Their Physical Characteristics, (5/11/98, P98-013.pdf)
4. Controlled Lachrymating Agents (97-010.pdf)
5. Demonstration of Chemical Immobilizers (94-084.pdf)

DFOISR will determine the appropriate release disposition of those four documents and respond to you directly. Please be advised that the official having cognizance over the subject matter of this portion of your request is: