

U.S. Army Chemical Corps Research and Development Command  
U.S. ARMY CHEMICAL RESEARCH AND DEVELOPMENT LABORATORIES  
Army Chemical Center, Maryland

U.S. ARMY CHEMICAL RESEARCH AND DEVELOPMENT LABORATORIES  
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C. (C) Directorate of Medical Research

1. (C) EA 2277

a. (C) Plan "B" for EA 2277, an agent-munitions capability in 12 calendar months, has been a top priority program since early 1961. The plan was to have been included in Project 112, phase II, and was to be funded for implementation on or about 1 January 1962.

b. (U) It has been decided that a field demonstration (sometimes referred to as a "troop test") at Dugway will not be required.

c. (C) Using EA 2277 labelled with tritium in the 3-position of the quinuclidinol structure it was found that EA 2277 distributes rapidly into the brain, though it has been hard to measure. Using P<sup>32</sup>-labelled compounds it was revealed that EA 2277 inhibits incorporation of phosphorus into brain phosphatidic acid and phosphatidyl choline. Tetrahydro-9-aminoacridine (THA) inhibits this effect to some degree.

d. (U) Information from Dr. Samuel Gershon, University of Melbourne, Australia, indicates that THA is considered "primitive" as a benzilate antagonist and that more effective compounds are known. Since they are proprietary in nature, details are not presently available. A grant of the order of \$20,000 is being negotiated with Dr. Gershon to obtain more information.

e. (C) Persistent efforts by medical research personnel have paid off with a breakthrough in the form of a percutaneously active incapacitator. Contrary to predictions and lack of encouragement, they have been able to get EA 2277 through the skin in 20 microliters of 20%

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solution in benzyl alcohol. The onset of the psychosis is delayed to about 36 hours, but the duration thereafter is unimpaired (72-96 hours so far).

f. (C) It is of some interest to the Laboratories that Hoffman-LaRoche is marketing a drug called Quarzan as one component (along with a tranquilizer) of a proprietary called Librax, which is supposed to be good for the troubled intestine. The dose of Quarzan orally is 2.5 mg and Quarzan is nothing more than the quaternary (methyl bromide) salt of EA 2277, which is psychotogenic (as free base or hydrobromide) in oral dose of 0.5 mg.

2. (C) Anticholinesterases

a. (C) Work continues in the VX vapor-aerosol field, but nothing new has developed. Some data have been obtained to confirm the previous impression that, even though toxicity increases with wind speed to 15 mph, toxicity falls off at 20 mph. The practical import of this is not great.

b. (U) Dr. Van M. Sim, Chief, Clinical Research Facility, recently attended a meeting on oximes at the Office of The Surgeon General (OTSG) set up by Colonel Arnold, Chief Pharmacy Consultant. The result was that these Laboratories will be called upon officially to recommend dosage form, schedule, and amount of drug to be administered. This the Laboratories are prepared to do, provided it is recognized that specific recommendations along these lines necessarily imply assumptions and decisions pertinent to doctrine, supply and training.

c. (U) To such extent data obtained from industry, estimated (incorporated into Project 112) on cost of large-scale procurement of oximes does not yet appear to be in error. However, the job is formidable. It is estimated that 250 metric tons of the oxime (enough for 30-day prophylaxis for 1 million men) will require the whole of one year of U. S. production of alpha-picoline.

d. (C) Treatment of GD poisoning is still being investigated. It has been clearly confirmed in man that oximes are of no value in either treatment or prophylaxis of GD poisoning. In vitro, the oximes initially reactivate GD-poisoned enzyme as rapidly as GB-poisoned enzyme, but the reaction stops at about 20% of reversal. GF is not too bad so far as treatment is concerned, but prophylaxis is very poor.

3. (C) Flechettes

Subject to revision of the primary data, it would appear that flechette rounds can virtually negate the effect of body armor. Obviously the flechette can completely negate the effect of chemical-protective clothing. Toxic flechette rounds are in the development stage in the United States, and progressing nicely. The course of recent scientific history would indicate that the Soviets are thinking along the same lines, and are at the same state in the art. So far, most of the U. S. studies have been with VX toxic fills; this is by no means the ideal choice, and a few studies have been made with other types of agents.

4. (C) EA 3000, Botulinum Toxin

Responsibility for development of an agent-munitions system for EA 3000 has been assigned to CRDL. The non-living toxin of Clostridium botulinum is a chemical compound that probably works by inhibiting either the synthesis or release of acetylcholine at certain

synapses. Nevertheless, no toxicologist or pharmacologist (not even an expert in cholinergic mechanisms) can consider himself qualified by normal training on botulism. The people who understand botulism are either microbiologists or immunologist. The biological problems are enormous in computing human LD50 inhalation estimates for various concentrations and particle sizes.

5. (U) Military Chemicals

a. Dr. Keith Jacobson, Coordinator of Military Chemicals, recently attended a meeting at Army Research Office (ARO) on the future organization of the recently-relinquished Advanced Research Projects Agency (ARPA) program on "Toxicological Research." Dr. Jacobson presented the views of the Director of Medical Research as follows:

(1) The work should be done in a medical institution, and our definition of the emphasized term is that our own laboratories qualify.

(2) The funds and the program should be separately identified, or "noncompetitive" with other research programs; otherwise they may be forced to take a back seat.

(3) The program by and of itself is not escalating; it will go at a reasonable steady and predictable level for many years and can well be matched with fixed personnel resources.

(4) There is no reason for this program to be run by a "Program Manager" at some higher level. Contract research should be run

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by the "man at the bench" who is running comparable in-house research. One man, down at the working level, should have responsibility for the total program.

b. In the light of uncompleted experiments by Dr. Richard Lindenberg, one of our Military Chemicals contractors, we are beginning to feel that presently accepted safe concentrations of CO are too high, and that brain changes may be secondary to cardiovascular dysfunction, rather than the reverse.

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D. (C) Directorate of Research.

1. (U) Prime Contract - Research, Evaluation and Synthesis of Chemical Compounds.

The prime contract relating to the search for chemical agents was placed with the Du Pont Company, the successful bidder among thirteen companies. Most of the research work will be conducted in their Stire Laboratories.

2. (C) Incapacitating and Lethal Compounds.

a. Active research programs are in progress in the field of EA 1476, EA 1729, EA 2228, CS 4640 and certain selected irritants. A method for the synthesis of CS 4640 which lends itself to production of at least pound quantities has been worked out.

b. In the search for percutaneously active benzilates, several have been synthesized which are viscous liquids miscible in all proportions in solvents such as orthodichlorobenzene and benzyl alcohol. EA 3167 is an example of such a compound. Biological evaluation is in progress to determine their activity compared to EA 2277.

c. An assay procedure for the procurement of EA 2277 has been developed.

3. (OFLUSE) G and V Agents.

a. (OFLUSE) The intravenous toxicities of GB and GF are increased approximately six and ninefold, respectively, upon prior administration of a nonlethal dose (25 per cent of the LD50) of the systemic insecticide, ethyl p-nitrophenyl thionobenzenephosphate (EPN). It appears that this pre-treatment inhibits certain enzymes responsible for detoxication of G agents. No potentiating effect was found when VX was substituted for G agents.

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b. (U) A program has been initiated which is designed to overcome the partial or complete refractoriness of certain anticholinesterases (GD, GF, V 12, EA 1464) to prophylaxis and treatment by present procedures (atropine, 2-PAM, EA 1814). Data are being accumulated to obtain a consistent picture of rates of enzyme reactivation, development of refractoriness of inhibited enzyme, and prophylactic and therapeutic effectiveness. A synthetic program designed to yield more effective treatment agents has been started.

4. (C) EA 2277.

The applicability of a reaction of EA 2277 with the dye, Tro-paeoline 00 to the detection and estimation of EA 2277 in field water supplies has been studied further. The previously noted high sensitivity has been confirmed; compounds known to interfere (e.g., non-polar amines) are, however, additional possible water contaminants, and research is continuing on the elimination of such interferences.

5. (C) EA 3000.

Under contract, considerable progress has been made in the separation of hydrolytic products of crystalline toxin following treatment with acid and salts. Fractions which retained as much as 20 per cent of the specific toxicity of the original material have been separated. Replication of these results, and molecular weight determinations, are in progress.

6. (U) Toxicity Screening.

Approximately 149 EA compounds and 221 CS compounds have been screened for biological activity. Sixteen of these merited more thorough evaluation as potential incapacitating agents. In the tests for prophylaxis against nerve agent poisoning, approximately twelve appeared worthy of further study.

7. (U) Industrial Liaison Program.

Approximately 2,070 structures and 460 samples were received and about 425 screening reports processed during the quarter. The one-year extension of the Stanford Research Institute information gathering contract was signed.

8. (C) Physical and Mathematical Dissemination Studies.

a. (U) A device was designed and developed for the rapid sampling of aerosol clouds in the field. This device, which catches an aerosol sample by the rapid closing of an open cylinder that moves transversely to the direction of motion of an aerosol cloud, will, because of features in its design be applicable generally, be independent of cloud flow conditions and allow extremely short sampling times.

b. (U) The installation of the Univac SS-90 computer system was completed during this period, and significant progress has been made in converting the Burrough's 205 computer programs to the SS-90. Fifteen programs have been converted and are in operation, and most of the remaining programs have been completed and are being debugged.

c. (U) Slide rules have been contrived for evaluating the Sutton's mathematical models for estimating down-wind travel and area coverage from an instantaneous point source of vapor or very fine aerosol disseminated and sampled at ground level. A low-cost circular slide rule for determining area coverage from aerial spray munitions has also been designed. These slide rules permit making preliminary weapons predictions in a simplified manner.

d. (U) Through a statistical evaluation, the CARAMU breathing function model which requires 9 distributions with 43 parameters has been

replaced with an improved model having 3 distributions and 6 parameters. A study of the SD-2 and SD-5 surveillance drones and the North American Army Low Cost Training Target Missile has been conducted to determine optimum effectiveness under practicable spray conditions. The study has developed area coverages achievable, together with the optimum practicable spray operating conditions.

e. (U) A flash X-ray camera has been installed for use in dissemination studies. Preliminary calibration is now under way.

f. (C) Dissemination studies on toxic proteins (EA 3000) by cold gas atomization have shown a total initial recovery of about 66 per cent with a toxin recovery by bioassay of 33 per cent. Approximately 80 per cent of the particles produced have a mass medium diameter of 10 microns or less.

g. (C) Tests were conducted on the shaped-charge follow-through principle against steel plate targets over bunker entrances using GB. Two of the tests resulted in well over 30 per cent of the 170 centimeters of agent being injected into the breached bunker, which is considerably higher than previously achieved with any experimental designs.

h. (U) Under Contract DA-18-108-405-CML-891, recently completed, the design parameters for a bread-board retro-rocket for flame thrower applications have been established. Several alternate systems were also proposed for pressurization of the fuel. A bread-board model is planned for fabrication based on the parameters, to permit experimental determination of thrust, transient phenomena, ranges, etc., as a function of fuel consistency and pressure.

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