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Requested date:	28-February-2022
Release date:	19-May-2023
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Source of document:	During COVID Pandemic conditions: Email FOIA Request Commander, INSCOM ATTN: IAMG-C-FOI 2600 Ernie Pyle Street Fort Meade, MD 20755-5995

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UNITED STATES ARMY INTELLIGENCE AND SECURITY COMMAND
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May 19, 2023

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Enclosure

FSTC-CS-03-02-67

Supplemented by
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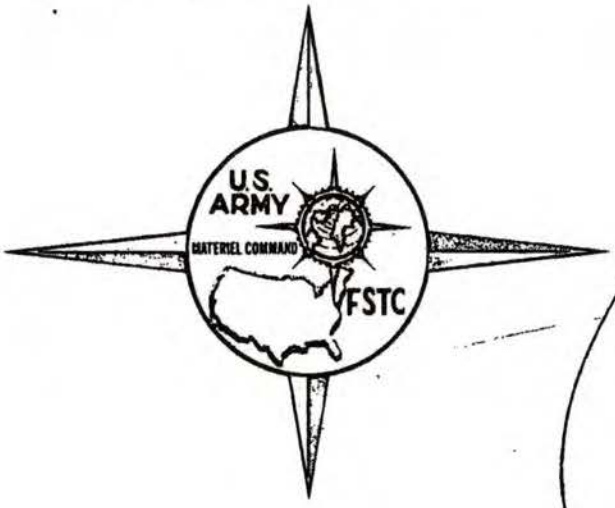

NATURAL PLANT AND ANIMAL TOXINS
(R&D FOR MILITARY TOXIC AGENTS)-FOREIGN (U)

ARC 80-CBT

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ST-S-7-2590
Cy 31

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December 1967

FSTC-CS-03-02-67, C1

Publication No.
FSTC-CS-03-02-67
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U.S. ARMY MATERIAL COMMAND
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NATURAL PLANT AND ANIMAL TOXINS
(R&D FOR MILITARY TOXIC AGENTS) - FOREIGN (U)

1. Make the following pen-and-ink changes to publication No. FSTC-CS-03-02-66, dated September 1967:

Title page, WARNING NOTICE, line 3: change "transmission of" to "transmission or".

Page v, line 6 from bottom of page: Change "Antivenom" to "Antivenin".

Page xi, para 3, line 5: Change "Thee" to "The".

Page xii, third para from bottom, line 2: Change "he" to "The".

Page xiv, last para: Change "mong" to "among".

Page 3, C.(2), line 2, end of line; add hyphen (-) after last word "high".
line 3, add hyphens (-) after "molecular" and before "weight"; also after last word "low".
line 4, add hyphen (-) between "molecular" and "weight".

Page 4, para 1: add hyphen (-) between "molecular" and "weight".

Page 6, para 11, b, line 6: Add beginning parenthesis before last word "mescaline".

Page 7, para 14, line 3: Delete last "t" in the word "interestt".

Page 8, para 18, line 4: Delete "Yadovityye i Opasnyye Ryby" and insert "Yevgeniy Sergeyevich Prosvirnov".

Page 10, para 27, b, line 5: Change "cicuta" to read "circuta".

Page 11, para 31, a, line 1: Delete last word "and".

Page 11, para 31, a, line 2: Delete first three words of line "lack of purity".

Page 13, para 34, b, line 3: Change "statment" to read "statement".

Page 17, para 46, line 7: Change "atic." to read "Katic".

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Page 25, para 70, b, (1), last line: Change "wiss-form" to read "Swiss-born".

Page 28, line 5 from top of page: Remove underline below "Japonicus".

Page 33, line 6 from top of page: Change "Ci." to "Cl".

Page 34, para 103, line 8: Delete second "e" in "be".

Page 35, para 108, line 1: Remove comma after "rain".

2. Insert new page 50.1 after page 50.

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(U)
APPENDIX II. ~~(S/NFD)~~ (Continued)
(U)
~~(S/NFD)~~ ISRAEL

Scientists	Research Interests	Affiliations
Adler, S.	Insect poisons	Hebrew University, Jerusalem
Ben-Tov, M.	Hallucinogens	Israel Institute for Biological Research, Ness-Ziona
Bergmann, F.[142,143]	Ergot alkaloids marine poisons	Hebrew University, Jerusalem
Bicher, H. I.[145,146]	Snake venom	University of Tel Aviv
Condrea, E.[144]	Snake venom	Rogoff Medical Research Institute
DeVries, A.[144,146]	Snake poisons	University of Tel Aviv
Edery, M.	Psychotropic drugs	Israel Institute for Biological Research, Ness-Ziona
Fisher, I. L.[141]	Toadstool poisons	Hebrew University, Abu Kabir
Gaoni, Y.[139,140]	Marihuana components	Weizmann Institute of Science, Rehovoth
Gerichter, H.	Insect poisons	Central Laboratories, Ministry of Health
Gitter, S.[145,146]	Snake venom	Hebrew University, Jerusalem
Goldblum, N.	Insect poisons	Hebrew University, Jerusalem
Goldwasser, R.	Fluorescent antibody staining technique	Israel Institute for Biological Research, Ness-Ziona
Joffe, A. Z.	Fungal poisons	Hebrew University, Jerusalem
Kidron M.[142]	Marine poisons	Hebrew University, Jerusalem
Klibansky, C.[146]	Snake venom	University of Tel Aviv
Lavie, D.	Pharmacologically active plant extractives	Weizmann Institute of Science, Rehovoth
Librus, M.[141]	Toadstool poisons	Hebrew University, Abu Kabir
Mechoulam, R.[139,140]	Marihuana components	Weizmann Institute of Science, Rehovoth
Menczel, E.	Hallucinogens	Hebrew University, Jerusalem
Parnas, I.[142]	Marine poisons	Hebrew University, Jerusalem
Peczenik, O.[141]	Toadstool poisons	Hebrew University, Abu Kabir
Reich, K.[142,143]	Marine poisons	Hebrew University, Jerusalem
Rosen, M.[145]	Snake venom	University of Tel Aviv
Shulov, A.	Insect poisons	Hebrew University, Jerusalem

FSTC-CS-03-02-67

DATA HANDLING PAGE

(U) Production Identification: FSTC-CS-03-02-67

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(U) FSTC Task No: 6-503036

(U) b3

(U) Topic Tags: Poison, natural; poison, plant; poison, marine; poison, insect; poison, bacterium; poison, fungus; poison, snake; poison, toad; venom; toxin; research and development, natural poison; natural poison, lethal; natural poison, incapacitating; toxin, animal; immunization; toxicity; antitoxin; antivenin.

(U)
~~(S)~~ Abstract: Various products from natural sources, known for their powerful effects on humans, could conceivably be used to develop new and sophisticated, lethal or incapacitating chemical warfare agents. Such natural poisons, having desirable physicochemical and pharmacological properties, may serve also as models for the design of synthetic organic substances possessing similar characteristics. The purpose of this study is to survey the international research and development activities on plant and animal poisons which could be applied to the field of chemical warfare. The data sources utilized in this study consist of open scientific literature, field intelligence reports, and hard-cover intelligence studies. The research activities on natural poisons and the laboratories and personalities associated with this research effort are covered on a country-by-country basis. Quality research on the natural poisons is being conducted throughout the world.

Pages: 70

Tables: 0

Illustrations: 0

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FSTC-CS-03-02-67

NATURAL PLANT AND ANIMAL TOXINS

(R&D FOR MILITARY TOXIC AGENTS)-FOREIGN (U)

September 1967

(Based on information available as of February 1966)

b3

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PREFACE

(U) The toxic components of plants and animals are presently being examined in various countries and attempts have been made to isolate and characterize the active principles. Thousands of natural products have already been collected from many parts of the world; undoubtedly, thousands more are yet to be found. This huge source of physiologically active substances can become a ready supply of potentially useful chemical warfare (CW) agents, or they may serve as models for the syntheses of such agents.

(U)
~~(C)~~ The limit of toxic effectiveness has not, by any means, been reached by the current array of synthetic CW agents. Some of the natural toxins are far more lethal than even the nerve agents by several orders of magnitude. An example of the fantastic level of potency characterizing the biotoxins can best be illustrated by the toxicity of the botulinum toxin produced by the bacterium, Clostridium botulinum. It has a potency about 10,000 times greater than the most toxic nerve agent. Most likely, this or some other natural poison will form the basis for future chemical agents.

(U) The importance of the natural poisons to a CW research and development program lies in the fact that among them there is a wide range of properties which could satisfy a multitude of logistic requirements. Some may be classified as lethal-type agents; others as incapacitating types. Lethal-type agents cause death or inflict various degrees of physical destruction. In the latter case, problems of medical care and rehabilitation of survivors usually become the burden of the victors. The incapacitating agents form a new concept of chemical warfare; they debilitate the civilian or military personnel temporarily with few, if any, fatalities.

(U) Experimental animals are used in an initial screening of plant and animal extracts to evaluate the toxic nature and degree of toxicity of the crude extracts. A promising material is subjected to various procedures to isolate the active component, determine its physical and chemical properties, and if possible, determine its molecular structure. Components with simple chemical structures can probably be synthesized and even modified to enhance a desired pharmacological effect or to reduce undesirable side reactions.. The high-molecular-weight compound may be fragmented into smaller molecules that are simpler to synthesize, providing there is no loss of biological activity. Unfortunately, many of these large molecules are protein in nature and the state-of-the-art in the synthesis of polypeptides, the building blocks of protein, is not well developed. When the toxic substance cannot be synthesized economically, availability would then depend on the supply of the natural sources. In the event the processing of the crude extract uncovers a potential CW agent and appropriate means of its dissemination have been determined, steps are finally taken to devise a suitable detection system for identifying and quantifying the poison.

(U) For the purpose of this study, the products derived from natural sources include the plant poisons (e.g., curare, ricin, and the fungal poisons), derivatives of the ergot alkaloid (e.g., LSD-25), bacterial toxins (e.g., botulinum, staphylococcus, and tetanus), marine toxins (e.g., puffer fish and shellfish

PREFACE (Continued)

toxins), snake venoms, insect and toad poisons. The synthetic poisons are not considered. This study was undertaken in order to determine the extent to which the various foreign nations, Communist and free world, have gone or could go in their research and development (R&D) efforts to attain a capability for the large-scale production of selected natural poisons as CW agents. Pharmacologically active natural poisons in sufficient quantities incapacitate or cause death; therefore, a research interest in any of these substances should not be ignored in a discussion of potentially useful CW agents.

(U) Intelligence gaps exist because much of the research in the natural poisons either has a medical orientation or is evidently of a defensive nature with regard to chemical warfare. Very little research, if any, could definitely be linked to an offensive chemical warfare program. For this reason, it is difficult to project precisely a country's capability for developing natural poisons as experimental agents for military purposes.

(U) Since a large number of scientific workers, particularly in the U.S.S.R., Czechoslovakia, and Israel, are investigating the natural poisons, a ready reference is provided in Appendix II, citing the scientists' affiliations and research interests.

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NATURAL PLANT AND ANIMAL TOXINS

(R&D FOR MILITARY TOXIC AGENTS)-FOREIGN (U)

SUMMARY

U.S.S.R.

(U)
~~(S)~~ Soviet medicine has always relied heavily on the medicinal preparations derived from natural products, particularly plant extractives, insect poisons, and snake venoms. Soviet scientists associated with the military are aware of the significance of the highly toxic natural poisons as a potential source of candidate chemical warfare (CW) agents.

(U)
~~(S)~~ The U.S.S.R. has embarked on an ambitious long-range program to cultivate many indigenous and foreign plants having useful extractives. Toward this end, scientists in Tashkent have been engaged in screening seeds and plants as possible sources of new pharmacologically active substances. Some of their findings could contribute significantly to a chemical warfare agent development program. The U.S.S.R. is particularly interested in the hallucinogenic substances LSD-25 and other indole derivatives. The research effort on bacterial toxins, especially botulinum toxin, has been very impressive. Research on snake venom appears to be concerned primarily with its medical aspects. Research on marine poisons, though limited, may point to a CW interest. Only a small amount of current study is devoted to insect, frog, and toad poisons.

(U)
~~(S)~~ Much of the research and development (R&D) on natural poisons appears to be medically-oriented, but the extent of this activity could not be justified simply from the medical point of view. Nor can any of this activity be specifically related to the development of either lethal or incapacitating CW agents. Thee Soviets appear to be primarily concerned with the application of this research to the defensive aspects of chemical warfare, such as immunization and detection techniques, but some of this effort also could be applied to the selection of compounds having potential as CW agents. If the extent of specific R&D activity in the natural poisons is any criterion, it is likely that the Soviet interest is directed toward the botulinum toxin, LSD-25, curare, and aconite alkaloids, in that order, as possible candidates in a CW agent program. There is no evidence of a large-scale production of natural poisons or the development of field dissemination techniques for delivery of such agents offensively.

(U) With the vast recent improvement in the quality of biochemical research in the U.S.S.R., there has been a concomitant Soviet development of a chemical and pharmacological expertise on which a future agent program involving natural poisons could be based.

SUMMARY (Continued)

EAST EUROPEAN COMMUNIST COUNTRIES

(U)

~~(S)~~ Both the Czechoslovaks and East Germans conduct excellent research on natural poisons. Scientists in both countries are studying the incapacitating agents, such as LSD-25, and other indole-based alkaloids. This work probably is coordinated with that done in the U.S.S.R. In studies on bacterial toxins, the East Germans appear interested in the botulinum toxin, while the Czechoslovaks tend to emphasize the tetanus and staphylococcus toxins. The quality of research in East Germany, and particularly in Czechoslovakia, is sufficiently sophisticated to yield a desirable CW agent either from the natural product or from a synthetic modeled on the natural form.

(U)

~~(S)~~ The "natural poison" research effort in Poland, Hungary, and Yugoslavia is mainly on botulinum toxin. The only connection with any military effort would appear to be from a defensive point of view. Hungary's interest in the ergot alkaloids apparently is due primarily to their importance as a medical export item. The contribution of these countries, as well as of Bulgaria, to a military-oriented CW research program in natural poisons is minor, if it exists at all.

ASIAN COMMUNIST COUNTRIES

(U)

~~(C)~~ Communist China's Chemical-Biological-Radiological program had been patterned after that of the U.S.S.R. until 1960, when the Sino-Soviet split forced China to develop its own program. But China's scientific development will be retarded for several years, because the nation's strong emphasis on political standing and class origin, rather than on educational qualifications, hampers the training of gifted students.

(U)

~~(S)~~ The large plantations belonging to the State serve as a rich source of pharmacologically active plant extracts, some of which could be applied to chemical warfare R&D on natural poisons. Communist China has many institutes which are capable of conducting biochemical, pharmacological, and physiological investigations.

(U)

~~(S)~~ Only a small amount of R&D is done on the bacterial toxin, botulinum (type E); interest in the insect, snake, and marine poisons is not evident. he Chinese military shows a strong interest in the ergot alkaloids and uses expensive experimental animals (e.g., monkeys) for these studies. Interest in LSD-25 probably is more than required for medical purposes and may indicate a Chinese desire to push its development as a CW agent.

(U) The Communist rebels in South Vietnam (Vietcong) are reportedly using toxic plant extracts for preparing poison-tipped bamboo stakes and arrow traps in their military operations against the government and allied forces.

FRANCE

(U)

~~(S/NFD)~~ France has shown some interest in the natural poisons as possible CW agents. The military evidently has supported R&D on the psychochemicals (LSD-25)

SUMMARY (Continued)

and on the bacterial toxins (botulinum toxin), but none of these substances has been standardized for military use in chemical warfare. France will probably accelerate its program on natural poisons in an effort to develop an offensive capability in new and sophisticated agents.

ISRAEL

(U) ~~(S/NFD)~~ Some government-sponsored classified research involving BW agents has been reported. Possibly a study of bacterial toxins is included in this program. A systematic collection of plants and other natural products is being carried on for the purpose of preparing pharmacologically active substances, especially those having psychotropic effects. Marine, insect, and snake poisons are also studied. A competent group of scientific investigators is conducting an excellent program on substances derived from natural sources. No definite evidence links this research with a chemical warfare agent program, but the extensive investigations in this field may disclose substances potentially useful for this purpose.

ITALY

(U) ~~(S/NFD)~~ The military organization sponsors little or no R&D on natural poisons. This type of study is performed by a small corps of competent Italian scientists in the civilian research institutions or in nonmilitary governmental facilities. Several extracts from insect, plant, and marine sources could prove to be potentially useful, incapacitating CW agents. Impressive results were seen in their large-scale production of the ergot alkaloids by improved fermentation techniques.

JAPAN

(U) ~~(S/NFD)~~ Japan is very active in research on the chemistry of natural poisons. Much R&D is devoted to the determination of the pharmacological properties of plant extracts, bacterial toxins, marine poisons, snake venoms, and toad poisons.

(U) ~~(S/NFD)~~ Japanese interest in plant extractives is primarily for the purpose of preparing drugs. However, some purified active components and their derivatives (e.g., LSD-25) that have been studied are potential chemical warfare agent candidates. The animal poisons (tetrodotoxin from puffer fish, bufotenidine from the Chinese toad, and snake venoms) have also been investigated, and these too may be considered as possible candidates for such a program. The military, however, appears to have little or no direct interest in this type of research, except as it may pertain to public health.

NETHERLANDS

(U) ~~(S/NFD)~~ Dutch researchers have shown an interest in natural poisons derived from the insect, bacterium, and plant. No evidence exists that the military desires to develop an R&D capability in this field. Bongkrekic acid, a bacterial

SUMMARY (Continued)

toxin prepared by a Dutch scientist, is being tested as a possible chemical warfare agent.

SWEDEN

(U)
~~(S/NFD)~~ Sweden has shown a general interest in plant, bacterial, and toad poisons. A worldwide search for pharmacologically active plant extractives is being undertaken by one of Sweden's research institutes. Interest in bacterial toxins appears to focus on the large-scale production of tetanus toxin. The very toxic batrachotoxin from the Colombian frog, Phyllobates bicolor, is undergoing investigation. Although there appears to be no direct military involvement, these studies could lead to the development of potential CW agents. The Swedes are developing expertise in this type of research.

UNITED KINGDOM

(U)
~~(S/NFD)~~ The British have an excellent, but small, R&D program on natural poisons. Some of this work is conducted at military installations. British interest in plant poisons is evidently concentrated on ricin, the toxic protein obtained from the castor bean, and on andromedotoxin from the leaves of a rhododendron plant. The action of the phospholipases from snake venom and of the bacterial toxin, bongkrekic acid, has also been studied. These poisons could be a valuable contribution to a chemical warfare agent evaluation program.

WEST GERMANY

(U)
~~(S/NFD)~~ West Germany has shown a strong interest in the botulinum toxin and in the very toxic plant poison, andromedotoxin. Research in these natural poisons could be linked to a chemical warfare effort either in the search for sophisticated toxic agents or as part of a defensive program.

MISCELLANEOUS FREE-WORLD COUNTRIES

(U)
~~(S/NFD)~~ Austria is investigating the venom of the orange-speckled toad. Nationalist China is interested in such toxalbumins as ricin, croton, and abrin. The Chemical-Biological-Radiological facility in the U.A.R. Army is sending personnel to the U.S.S.R. for extensive biological warfare training, reportedly on poisons. Some of this training may have included background study on the potentialities of the natural poisons as chemical warfare agents. The military and civilian investigators of Switzerland have indicated a strong interest in botulinum toxin. In India's small R&D program on natural poisons, attempts have been made to identify the pharmacologically active substances in the Indian stinging nettle. Canada indicated an interest in the ergot alkaloids and the bacterial toxins. The venom of the orange-speckled toad, ricin, botulinum toxin, and ergot alkaloids are mong those natural poisons potentially useful as CW agents. However, the research of these free-world countries in all probability will not evolve anything of value to an independent CW program.

NATURAL PLANT AND ANIMAL TOXINS

(R&D FOR MILITARY TOXIC AGENTS)-FOREIGN (U)

Section I. (U) ~~(S/NFD)~~ U.S.S.R.

A. (U) ~~(S)~~ INTRODUCTION

1. (U) ~~(S)~~ MEDICAL INTEREST IN NATURAL POISONS

Soviet medicine has always relied heavily on medicinal preparations derived from natural products. For example, bee venom has been used for rheumatism, denatured bacterial toxins for the production of antitoxins, and plant alkaloids for various therapeutic purposes. In studying the natural poisons, the Soviets appear to emphasize particularly the bacterial toxins and plant alkaloids, with only a relatively minor interest in the marine, insect, and toad poisons.

2. (U) ~~(S)~~ QUALITY OF BIOCHEMICAL RESEARCH

Soviet biochemistry is now well supported by the state and is no longer forced to premature practical applications as was formerly the case. The liberation of scientists from political restrictions after Stalin's death was partially responsible for this transformation. The total available space in the biochemical laboratories of most institutes is extensive and generally well equipped, though they continue to be overcrowded. Techniques for extracting, purifying, and testing natural substances have become more refined in recent years as the quality of Soviet biochemical research has improved. Research on protein and polypeptide structures, enzymes, metabolic studies, and animal and plant poisons appears to exceed the probable value of these results to medicine, suggesting that the Soviets may be interested in applying this type of research to a chemical warfare (CW) agent program.

B. (U) ~~(S/NFD)~~ BACTERIAL TOXINS

3. (U) ~~(C)~~ GENERAL

Soviet research and development on bacterial toxins has been conducted at both military and civilian institutions. The emphasis is on botulinum toxin, but research is increasing at a rapid rate on other toxins (perfringens, tetanus, staphylococcus, diphtheria, and plague).[1] There is no unequivocal evidence of any Soviet research and development (R&D) on large-scale production of toxins or of toxin-filled munitions. Obviously, this information would not be published in the open literature, and covert sources seem to be almost completely lacking for this type of information. Their interest in these toxins, the Soviets claim, is brought on by fears that an enemy would use these substances against them either offensively, as in a military operation, or covertly, by poisoning their drinking water. The Soviets evidently try to stress this apprehension by publishing only those studies which cover the defensive aspects of bacterial poison intoxication.

4. (U) ~~(S/NFD)~~ BOTULINUM TOXIN

a. (U) ~~(S)~~ Physiological Effects and Immunization

(1) (U) ~~(S)~~ Research on botulinum toxin, obtained from the bacterium Clostridium botulinum, has been carried on in the U.S.S.R. for the past several years.[2-5] In studies on mice and guinea pigs, Dr. A. M. Yakovlev, Military Medical Order of Lenin Academy imeni S. M. Kirov, Moscow, introduced aerosolized botulinum toxin, types A and B, into experimental animals via the respiratory route, which he found more effective than the oral, and even the subcutaneous, routes. Active immunization by subcutaneous injection of botulinum toxoid or passive immunization by injection of botulinum antitoxin protected the animals from respiratory intoxication.

(2) (U) In 1957, V. M. Sergeyev (affiliation unknown) and others studied mass immunization effects of aerosolized botulinum toxoid powder on human volunteers. A single aerosol immunization was somewhat less effective than subcutaneous inoculation, but a second immunization by aerosolization resulted in a marked increase in antibody titer. In similar experiments with dust toxoids on human volunteers, P. N. Burgasov, (affiliation unknown) demonstrated in 1959 that reimmunization by aerosolization was no less effective than subcutaneous reimmunization.[6] Since aerosols of botulinum toxin rarely occur in nature, this study was obviously conducted with chemical warfare in mind. A sizable group of Soviet microbiological researchers at the N. F. Gamaleya Institute of Epidemiology and Microbiology, Moscow (Gamaleya Institute), has conducted an intensive study of botulinum toxoids. They have prepared harmless botulinum toxoids effective against types A,B,C,D, and E in the form of a polyvalent toxoid. Since antibodies are type-specific, the use of polyvalent toxoids (or antitoxins) for mass immunization of humans has definite advantages. One unconfirmed report states that these toxoids are effective and inexpensive, and that a major portion of the population has been immunized.

(3) (U) A number of Soviet papers have been published on the morphological, physiological, and clinical aspects of botulinum intoxication. These studies have shown that the toxin reduces the phagocytic properties of the host leucocytes, causes necrosis of cells, upsets tissue respiration, and results in neuromuscular paralysis of respiratory organs. Dr. L. M. Shredov, (affiliation unknown) reported that botulinum toxin, fed orally in combination with Clostridium botulinum organisms, gave rise to a considerably more severe intoxication than the toxin alone.

b. (U) ~~(S/NFD)~~ Production

(1) (U) ~~(S/NFD)~~ A West German source has reported that the Gamaleya Institute possesses breeding and tank facilities, which permit a relatively large production of botulinum toxin.

(2) (U) T. I. Bulatova, of the Gamaleya Institute, reported in 1965 that the Clostridium botulinum, type E, produced an inactive protoxin as well as a toxin.[7] The former could be converted to the active toxin by treatment with trypsin, yeast proteinase, or other proteinases. The toxin obtained by activation was strictly type-specific. By indirect hemagglutination tests, the activated and nonactivated protoxins were found to have the same antigenic activity, although

the biological toxicity of the activated protoxin was markedly greater than the nonactivated protoxin. These studies are interesting insofar as they suggest a relatively stable form of the toxin which can be stored safely as the inactive toxin. Furthermore, if the location and identity of the chemical grouping in the protoxin (bound to the active site) can be determined, a means of detoxifying the active toxin reversibly becomes a possibility. It also may be possible to degrade the large botulinum toxin molecule into fragments without losing toxicity, by protecting the active site with this or similar chemical groupings.

c. (U) ~~(S)~~ Detoxification

(1) (U) ~~(S)~~ V. M. Khil'ko, Perm Medical Institute, Perm, also a captain in the military medical service, has published papers on using gelatin foam filters for collecting aerosolized botulinum toxin.[8] This technique could serve as an efficient means for removing airborne bacterial toxins from the atmosphere.

(2) (U) Detoxification of botulinum toxin, type A, with formalin into a toxoid, results in a sharp decrease in free amino nitrogen, an increase in high molecular weight protein and polypeptide content, and a decrease in content of low molecular weight nitrogeneous substances.[9] Evidently, detoxification with formalin is associated with polymerization of toxin to larger molecules.

(3) (U) The chlorine content, usually found in treated water, is insufficient to destroy the toxin, types A,B, and C. However, researchers at the Military Medical Academy imeni Kirov, Leningrad, reported that high chlorination (9.6 to 13.7 ppm) can destroy the toxin in 30 to 40 minutes. Boiling the water for 10 to 15 minutes will also destroy the toxin. Ye. V. Shtannikov and V. A. Zhuraylev, Perm Medical Institute, Perm, studied the stability of the toxin in various concentrations of acids and bases and also attempted to remove botulinum toxin from water by the use of ion-exchange polymers.[10] Activated charcoal and carboferrogel have been successfully used in removing the toxin from drinking water.

d. (U) ~~(S)~~ Detection

The Soviet military medical service has shown considerable interest in the rapid detection of botulinum toxin. In 1959, Yu. A. Vladimerov, State University imeni M. V. Lomonosov, Moscow, was ordered by the highest Soviet scientific authorities to apply fluorescence techniques and instrumentation to R&D on bacterial toxin detection, with particular emphasis on botulinum toxin. In association with E. A. Burshtein and G. M. Zimina, he published the results of a study on fluorescence analysis.[11] In 1961, T. I. Bulatova and Ye. A. Kabanova, of the Gamaleya Institute, reported on the detection and identification of botulinum toxin, types A and B, by means of fluorescent antibody staining technique. This method holds great promise as a sensitive, rapid detection and identification technique for bacterial toxins. Dr. Bulatova also found the indirect (passive) hemagglutination reaction to be a rather rapid and sensitive method for detection, but differentiating botulinum toxins of the A and B types by this method was impossible.[12] Major V. A. Sinitsyn of the medical corps described the application of the indirect hemagglutination reaction in which red blood cells are sensitized with botulinum antiserum.[13,14] The test could be completed in 1.5 to 2 hours. R. Ye. Konikova, Military Medical Academy, Leningrad, found this test to be much more sensitive than the ring precipitation test; additionally, it had an advantage over animal testing in that it was able to detect toxoids as well as toxins.[15] The

fluorescent antibody staining and the hemagglutination techniques could conceivably be applied to instrumental methods for the rapid, specific detection of botulinum toxin and other high-molecular weight poisons that have antigenic properties.

e. (U) Treatment of Botulism

(1) (U) Methods of treating cases of botulism are relatively ineffectual; however, Dr. Yakovlev has reported that treatment of experimental animals with antisera following the respiratory introduction of botulinum toxins types A and B could be effective if administered in a sufficient dose and not later than 10 to 12 hours after intoxication. F. F. Rezepov (affiliation unknown), found that the best therapeutic effect, with types A,B,C, and E antisera, was obtained by prompt administration of antiserum at the very start of illness. In fact, the greater the dose of botulinum toxin which led to intoxication, the sooner the antiserum had to be administered to obtain any therapeutic effect. Intravenous injection of doses larger than optimal seemed to have no better effect than smaller doses, but the larger doses were more effective when administered intramuscularly.

(2) (U) V. B. Derkach, Kishinev Medical Institute of Microbiology, Kishinev, conducted investigations to determine the therapeutic effects of mycerin, which is generally employed as an antibiotic, on the botulinum, tetanus, diphtheria, and staphylococcus toxins. Experiments on mice established that mycerin alleviated the toxic effects of these poisons. The effectiveness of mycerin depended on the dosages used, the maximally tolerated doses being more effective than small doses.[16]

5. (U) PERFRINGENS TOXIN

a. Several articles have been published on the toxin produced by Clostridium perfringens. Dr. G. T. Patrikeev (affiliation unknown), was able to inactivate the toxin with formalin in the presence of proteinase inhibitors and oxidizing agents with minimal losses of antigenicity.[17] Dr. T. A. Zanchevskaya, Odessa Medical Institute imeni N. I. Pirogov, found that a protoxin was produced in parallel with the toxin in normal broth cultures. The protoxin was remarkably stable and could be activated to toxin by calcium chloride.[18]

b. B. D. Bychenko, N. V. Ploskirev, L. G. Ivanova, Z. M. Volkova, L. M. Samorodov and others at the Gamaleya Institute have conducted significant research related to production methods and antigenic properties of the perfringens toxin.

6. (U) TETANUS TOXIN

a. Drs. A. D. Ado (affiliation unknown), and V. V. Mikhaylov, Saratov Medical Institute, Saratov, studied the pharmacological mechanism of the bacterial neurotoxins (tetanus and botulinum) in terms of their specific effects on the central and peripheral nervous systems. M. A. Torban (affiliation unknown), studied the mechanism for the inactivation of the tetanus toxin by formalin.[19] He suggested that aggregation of the tetanus toxin molecules occurs, during which there is a fixation of the toxophoric groups. The product of inactivation (toxoid) is characterized by its stability and chemical inertness; these, in turn, explain the resistance of the toxoid to heating, prolonged storage, or the action of the proteases.

b. Dr. Derkach found that mycerin reduces the toxic effects of the tetanus toxin.[16]

7. (U) STAPHYLOCOCCUS TOXIN

a. Dr. N. V. Karnitskaya, Institute of Epidemiology, Microbiology, and Hygiene, Rostov-on-Don, has studied the toxins produced by various staphylococcus strains.[20] Dr. A. D. Brisker, Medical Institute, Chelyabinsk, has studied the clinical picture in alimentary intoxications produced by staphylococcus and the effect of its toxin on the human cardiovascular and nervous system.[21]

b. Dr. Derkach has found that mycerin reduces the hemolytic, necrotic, and lethal effects of the staphylococcus toxin.[16] V. Ya. Pochinok, Medical Institute, Kiev, has reported that the aqueous extract of the leaves of Eucalyptus globulus inactivated staphylococcus toxin.

8. (U) DIPHTHERIA TOXIN

a. P. V. Pavlov, et al, (affiliation unknown), used special stainless steel reactors for obtaining diphtheria toxin under deep-culturing conditions.[22] Yu. A. Khavkin, M. A. Morozova, and N. S. Kristallinskaya, Scientific Research Institute of Vaccines and Sera, Tashkent, attempted to purify the toxin by gel filtration and ammonium sulfate precipitation.[23] Drs. N. I. Shapiro and I. V. Moskvicheva, Research Institute of Vaccines and Sera, Leningrad, reported on the detoxification of diphtheria toxin by means of formalin.[24] I. N. Morgunov, S. I. Yagud, and Yu. A. Barshteyn, Kiev Epidemiology and Microbiological Institute, Kiev Medical Institute, were able to potentiate toxoid antigen action with sublethal doses of specific toxins. Immunization with a diphtheria toxoid and a sublethal dose of diphtheria toxin, for example, produced a stronger titer than with the diphtheria toxoid alone.[25]

b. Dr. Derkach has reported on the detoxifying effect of mycerin on diphtheria toxin.[16]

9. (U) PLAGUE TOXIN

a. A. A. Kanchukh, N. L. Loseva, N. N. Basova, and N. N. Novosel'tsev, Rostov-on-Don Research Antiplague Institute, were able to purify the toxin of the plague bacillus, Pasteurella pestis, by starch block electrophoresis. V. Yu. Gavrilenkova and V. I. Ivanov (affiliation unknown), Moscow, isolated a toxic fraction from a vaccine strain of Pasteurella pestis EV76 by precipitation with ammonium sulfate.[26] One of the preparations had a lethal dose of 1.5 μg for mice. V. I. Krupenina, Irkutsk Scientific Research Antiplague Institute of Siberia and the Far East, reported that plague toxin poisoning resulted in three types of oxygen deficiency--circulatory, hypoxic, and histotoxic.[27] The basis for the toxic effects is believed to be due to an indirect effect on the oxidative enzymes, e.g. cytochrome oxidase. N. I. Aleksandrov, Military Medical Academy imeni S. M. Kirov, Leningrad, in association with several other scientists, conducted an investigation of aerosol immunization of large numbers of people with powdered plague vaccine. A double aerosol immunization with a 5-day interval provoked a stronger general protective reaction than a single aerosol immunization.[28]

have been assisting in this work on peptides. N. K. Kochetkov and Yu. A. Ovchinnikov apparently serve as deputy directors of the Institute.

(U)
15. ~~(S)~~ EVALUATION

Of the plant poisons, the lysergic acid derivatives, curare, and the aconite alkaloids appear to occupy most Soviet attention. However, there is no evidence that these are being developed as standard CW agents. Since plant extractives are an important source of medicinal items, the U.S.S.R. has embarked on an ambitious program to be independent with respect to these items. Possibly new substances, having desirable pharmacological properties, will be discovered which can contribute to a future CW experimental program. The Soviets appear particularly interested in hallucinogenic agents based on the indole group.

(U)
D. ~~(S)~~ MARINE POISONS

16. (U) INTRODUCTION

Dr. Bruce W. Halstead, of the World Life Research Institute in California and a specialist in plant-animal poisons, has stated that the important role of the marine toxins in the study of human ecology with reference to military operations has long been recognized by Soviet military physicians and scientists.[52]

(U)
17. ~~(C)~~ SEA SNAKE VENOM

Sea snakes are among the most poisonous animals in the world and are found in the tropical seas of the Indian and Pacific Oceans, and in the Gulf of Tonkin. Except for a study on a dead sea snake (Pelamis platurus L.) in 1929, little more had been written until 1962 when V. R. Shuntov published a treatise on sea snakes.

(U)
18. ~~(S)~~ FISH TOXIN

A definite pattern of their intensive interest in marine poisons is seen by the current work of Soviet scientists on the toxins of the catfish (Saccobranchus fossilis) and the nonprotein tetrodotoxin found in the Japanese fish "fugu" and the American newt. In 1963, Yadovityye i Opasnyye Ryby wrote a book on Poisonous and Dangerous Fish. Dr. I. L. Knunyants, an academician involved in the Soviet military CW program, is aware of the toxicity of shellfish toxin, although little or no research has been reported on this toxin.[53]

(U)
19. ~~(S)~~ EVALUATION

Apparently, the limited research program on marine organisms is being done with full realization of CW implication and application. There is little question, however, that much of this research is medically oriented.

(U)
E. ~~(S)~~ SNAKE VENOM

20. (U) INTRODUCTION

General interest in snake venon is evident from Soviet literature. Ye. N. Pavlovskiy, I. A. Val'tseva, O. A. Malakhov, K. N. Seyfullina, and F. F.

Talyzin,[54-62] Sechenov First Medical Institute, Moscow, compared the physiological effects of the neurotropic serum poisons of the cobras, Bungarus fasciatus and Naja tripudians, and of the viper, Vipera lobetina. The senior author, Dr. Pavlovskiy, is presumably the same person, recently deceased, who served as Lt. General in the Medical Department of the Soviet Army. His early work with venomous animals was done at the Military Medical Academy in Leningrad (formerly known as St. Petersburg). He was a member of the Academy of Sciences and the Academy of Medical Sciences. He served as director of the Zoological Institute in Leningrad from 1944 to 1965.

(U)
21. ~~(S)~~ VENOM AND ANTIVENIN

(U)
a. ~~(S)~~ The Tallinin Pharmaceutical Plant at Uzbek has begun large-scale production of the highly effective drug preparation, Vipraxin (analgesic) obtained from snake venom. This gives the Soviets a capability in the large-scale extraction of snake venom, generally, in the event that this type of poison is utilized as a chemical warfare agent.

b. (U) Antivenin is generally used to treat snake bite. Dr. Ye. N. Pavlovskiy and his associates reported in 1964 that a mixture of propyl gallate, heparin, and hydrocortisone, administered shortly after injection of viper venom (from Vipera lopetina) into mice, acted as a fairly effective antivenom agent; this antidote, however, was not as effective as antivenin.

c. (U) During the period 1954 to 1963, several articles reportedly appeared in the open German literature (probably East German), written by Soviet research scientists, concerning the properties or physiological action of snake venon from the Vipera lobetina, Vipera ammodytes, Ancestrodon halyscaraganus, Bulgarian viper, and sand viper.

(U)
22. ~~(S)~~ EVALUATION

Soviet research appears primarily concerned with the medical aspects of snake venom. Since venoms from various snakes are very toxic, these substances could be useful as CW agents, especially for clandestine antipersonnel operations.

(U)
F. ~~(S)~~ OTHER NATURAL POISONS

(U)
23. ~~(C)~~ INSECT VENOMS

Bee venom has been used for many years as a treatment for rheumatism. M. Artemov, B. N. Orlov, and N. I. Lobachevsky, State University of Gorki, have studied the neurotoxic effects of bee venom.[63] Ye. N. Pavlovskiy, associated with the Military Medical Academy, was concerned with the anatomy of a variety of venomous insects. Later, he investigated the venom apparatus structure of scorpions, mites, spiders, myriapods, beetles, bees, wasps, and caterpillars.

24. (U) FROG AND TOAD TOXINS

F. F. Talyzin and A. A. Pchelkina[64] have reported on the toxicity of venom from the "kokei" frog. (See par. 89.) An article written by Soviet scientists on toad toxins reportedly appeared in open German literature probably East German).

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25. (U) ~~(S)~~ EVALUATION

Research in the U.S.S.R. has not been particularly active in insect venoms and miscellaneous animal poisons; nor are they currently considered as candidates for CW research and development.

Section II. (U) ~~(S/NFD)~~ EAST EUROPEAN COMMUNIST COUNTRIES

A. (U) ~~(S)~~ BULGARIA

26. (U) INTRODUCTION

Natural poisons have not been investigated extensively in Bulgaria. The little interest exhibited appears directed toward a search for new drugs. An ample supply of poison-producing plants is known to grow in Bulgaria.

27. (U) ~~(C)~~ PLANT POISONS

a. (U) ~~(C)~~ Research on plants is done exclusively at the Scientific Research Pharmaceutical Institute in Sofia, where a search for new drugs is emphasized. This research is sponsored and financed by the State. Nivalin (galanthamine), a component of Kahiche, or Snow Drops, was found to be an effective therapeutic agent in treating encephalitis and meningitis. This drug has an anticurare action on neuromuscular linkages and possesses some anticholinesterase activity. In his in vitro study on the inhibitory effects of nivalin derivatives on acetycholinesterase, I. Mikhailova (affiliation unknown), found that any change in the alkaloid molecule, other than quaternization of the nitrogen atom, tended to lower its inhibitory effect.

b. (U) In 1961, P. Prodanov (affiliation unknown), presented his treatise on the "Poison-bearing plants in Bulgaria"[65] reporting that man becomes seriously ill from the honey gathered by bees from the plant, Strandzha evonymus and that the toxins involved are probably arcoline, andromedotoxin, and glycosides. He also mentioned that the cicuta (water hemlock) contains the highly toxic circutoxine--a spasmodic poison--and that ricin from the seeds of castor is also very toxic, but that it is readily destroyed by autoclaving or cooking. The possibility of immunizing animals against the ricin toxin is noted.

28. (U) ~~(S)~~ SNAKE VENOM

The Scientific Institute of Epidemiology and Microbiology (NIEM) in Sofia is under the jurisdiction of the Ministry of Health. It produces an unknown type of antivenin obtained from horses injected with venom from vipers bred at the experimental station west of Sofia.

29. (U) ~~(C)~~ EVALUATION

The Bulgarian contribution of "natural poison" research to an active chemical warfare agent program is evidently minor. Apparently, medical and toxicological aspects of native plant and snake poisons are of primary concern.

B. (U) ~~(S)~~ CZECHOSLOVAKIA

30. (U) INTRODUCTION

Among the Warsaw Pact countries, some of the best research in natural poisons is being conducted in Czechoslovakia. Most of the interest appears to center on LSD-25 and the indole-based alkaloids. The R&D effort on the bacterial toxins apparently stems from the need for producing large quantities of good quality antitoxins. Interest in snake venom is relatively minor.

31. (U) ~~(S)~~ BACTERIAL TOXINS

a. (U) ~~(S)~~ Production of Toxin

Czechoslovak scientists have made persistent complaints about the poor quality and lack of purity of bacterial toxins being produced in their country. The Institute of Epidemiology and Microbiology, Charles University, Prague, has been concerned with this problem and has attempted to develop methods for manufacturing good-quality toxins. The Institute is currently producing streptococcus and staphylococcus toxins with only test quantities of tetanus toxin. Portable equipment, which permits the setting up of a unit for the large-scale cultivation of microorganisms at any location where electricity is available, was purchased by a Prague sera institute. Also, a professor at the Military Medical Academy at Hradec Králové reportedly has been working with experimental quantities of tetanus toxin from Prague. The apparent military interest in the tetanus toxin and the availability of these units for large-scale production of toxin point toward a possible application in a chemical warfare agent program.

b. (U) ~~(C)~~ Staphylococcus Toxin

O. Gulda, Kralova University in Prague and University of Brno in Brno, has studied the physiological effects of staphylococcal toxin for several years, including a study of the influence of the toxin on strychnine-induced convulsions.[66,67]

c. (U) Perfringens Toxins

V. Sobek, Kralova University, Prague, studied the protective effect of chlortetracycline against the toxin produced by the Clostridium perfringens bacterium. The drug was effective when administered 10 minutes prior to intoxication but showed no effect when administered 10 minutes after intoxication.[68]

32. (U) ~~(S)~~ PLANT POISONS

a. (U) ~~(C)~~ General

The quality of research being conducted on natural products derived from plants is excellent -- particularly at the Institute of Organic Chemistry and Biochemistry, Academy of Sciences, Prague. The Soviets depend heavily on the R&D performed here for their basic information. The institute has good laboratory facilities and competent scientists. Professor Frantisek Sorm, director of the Institute, is a leading personality in the natural products field. He has written several papers

on peptide chemistry and alkaloids. Other well-known scientists at the Institute include V. Cerny, who investigated the transformation of plant constituents into compounds similar to human hormones and J. Rudinger, who studied the physiologically active peptides.

b. (U) ~~(S)~~ The Psychotropic Plant Extracts

(1) (U) ~~(S)~~ Czechoslovakia has an excellent climate for ergot cultivation and is a large producer and exporter of ergot alkaloids. M. Semonsky, Research Institute for Pharmacy and Biochemistry, Ministry of Health (VUFB) Prague, is the world leader in the chemistry of the ergot alkaloids. He has worked on the isolation, purification, and separation of these alkaloids.[69-74] The work of J. Roubicěk, Psychiatric Research Institute, Prague, on LSD-25 and psilocybin[75,76] had attracted the attention of Karlheinz Lohs, who is concerned with chemical warfare R&D in the East German military. The most prolific group of researchers dealing with LSD-25, psilocybin, and other hallucinogenic substances in experimental psychoses in man is located in various institutes in and around Prague. This group is composed of M. Vojtěchovsky, V. Vítek, S. Grof, K. Ryšánek, E. Horáčková, and E. Kuhn.[77-87] The data collected include clinical observation, psychological testing, and blood-urine chemistry; it could supply valuable information for assessing the military significance of hallucinogens. Dr. Zdenek Votava, a pharmacologist, apparently directs some of the psychotropic drug research.[88-90] Dr. Votava, a professor at the Medical Faculty of Hygiene, Charles University, Prague, is head of a laboratory in neuropsychopharmacology at the Research Institute for Pharmacy and Biochemistry and is chairman of the Drug Commission of the Czechoslovak Ministry of Health. Worth noting is the fact that Z. Horáková, a pharmacologist employed by Dr. Votava, once worked under Professor E. B. Chain who specialized in producing the ergot alkaloids saprophytically. Dr. Zdenek Fink (Lt. Col.), Head of Defense Against Chemical Warfare Agents at Hradec Králové, has discussed the impracticality of lysergic acid derivatives and other psychochemicals (mescaline and psilocybin) as chemical warfare agents under field conditions.[91,92]

(2) (U) ~~(S)~~ Dr. Miroslav Protiva, Research Institute for Pharmacy and Biochemistry, Ministry of Health (VUFB), has published about 30 articles concerning his work on the derivatives of indole-type compounds, such as tetrahydroharmine and the hypotensive alkaloids, e.g., reserpine.[93-95] J. Trojanek,[96] Research Institute for Natural Drugs, and J. Mokry and I. Kompis,[97,98] Institute of Chemistry, Academy of Sciences, have been attempting to characterize and synthesize the indole-based alkaloids of Vinca minor and Vinca rosea. Dr. F. Sorm also has worked on Vinca alkaloids.

(3) (U) ~~(S)~~ Z. Krejčí at the Institute of Hygiene and Epidemiology, Olomouc, has worked on the chemistry and pharmacology of extracts from the marihuana plant, Cannabis sativa.[99,100]

33. (U) ~~(C)~~ SNAKE VENOM

a. Dr. Frantisch Kornalik, Charles University, Prague, a leading authority on the pharmacological properties of snake venom,[101] has characterized and developed the formulas of two analgesics, one prepared from the adder Vipera berus (Viperalgin) and the other from a cobra venom (Cobratoxin). The Biogens Pharmaceutical Plant in Prague prepares these toxins from the venoms and the products

are sold as remedies for neuritis and arthritis deformans. Dr. Kornalik is currently studying the effect of snake venom on blood coagulation for the treatment of hemophilia and the physicochemical characteristics of venom proteins.

b. Interest in snake poisons appears medically oriented. The U.S.S.R. had expressed an interest in this line of research, particularly in the preparation Viperalgin.

34. (U) ~~(S)~~ MILITARY R&D

a. An extensive R&D program in chemical warfare is evidently conducted under the code name "Iris" at laboratories located in Praha 2 and subordinate to the hospital in Praha-Motol. The extent of interest in the natural poisons is unknown.

b. Hradec Králové is the site of the Military Medicine Research and Postgraduate Institute. Despite Lt. Col. Fink's objection to the natural poisons as potential chemical warfare agents, his statment may be nothing more than a coverup to conceal an actual interest.

c. Dr. K. Lohs, East German expert on CW, visited the Antonin Zapotocky Military Academy at Brno in connection with his work in the field of psychochemicals, probably LSD-25. The Academy, subordinate to the Ministry of Defense, is considered a major center for military research.

35. (U) ~~(S)~~ EVALUATION

a. The Czechoslovaks have an excellent R&D program on the natural poisons, particularly the hallucinogenic plant alkaloids and the bacterial toxins.

b. Research on plant poisons, especially those substances that are potential incapacitating agents in chemical warfare, is undoubtedly extensive. The Czechoslovaks have conducted much of the Warsaw Pact Countries basic research relating to the effects of LSD-25 and other indole-based alkaloids on the higher nervous system.

c. Interest in the bacterial toxins appears concentrated on the tetanus, staphylococcus, and perfringens toxins, with little or no interest in botulinum toxin. Availability of portable units for the large-scale production of bacterial toxins could give the Czechoslovaks some military capability in the utilization of these toxins as chemical warfare agents. Presently, however, agreement is general that the techniques of toxin production in Czechoslovakia are far behind those of the advanced Western countries.

d. The Czechoslovaks appear more concerned with the medical aspects of the natural poisons than with their possible use as chemical agents in military offensive operations. However, the U.S.S.R. evidently depends on the research efforts of the competent Czechoslovak scientists and can utilize their research data in furthering the Soviet active chemical warfare agent program.

C. (U) (S) EAST GERMANY

36. (U) (C) INTRODUCTION

The "natural poison" research in East Germany has included some work on bacterial toxins, but the principal interest centers on plant alkaloids. Since 1964, some improvement has occurred in the quality of research, particularly in the field of biochemistry.

37. (U) (C) PLANT POISONS

a. Ergot and Other Plant Alkaloids

(1) Because Italy and Switzerland have attained the position of practically monopolizing the ergot field in world markets, the amount of research on ergot production in East Germany has generally slackened; however, research for improving ergot yields still continues at the Institute of Biochemistry of Plants at Halle. Dr. Kurt Mothes, of this Institute, has been attempting to develop a new strain of ergot. Dr. D. Groeger, an assistant to Dr. Mothes, is considered an expert in this field.[102,103] Dr. Groeger also has been conducting studies on plant alkaloids that are derivatives of indole, including the species, Penganum harmale, which has long been known to contain components having psychotropic activity (e.g., harmine). Research information on ergot that is collected here is probably passed on to large-scale producing units located elsewhere in East Germany, because such units are not available at the Institute. Prof. Threnn, Pharmaceutical Plant VEB Arzneimittelwerk, Dresden, also has shown a particular interest in ergot alkaloids.

(2) The Institute at Halle has extensive greenhouses. The work here is generally concerned with the biochemistry and physiology of alkaloids and other plant extractives. Much of the research deals with the formation of alkaloids in plants, using radioactive "tracers" in these studies. The Institute is used as a training facility for plant physiologists and chemists from the U.S.S.R. and Egypt; nevertheless, it does not appear to be military sponsored or financed.

b. Military Interest in Plant Alkaloids

Karlheinz Lohs,[104] military expert in chemical warfare, and K. Stade,[105] an expert in military medicine, have expressed a definite interest in such psychochemicals as LSD-25, mescaline, and psilocybin. K. Stade has pointed out that these substances could be useful as chemical warfare agents after suitable aerosolization. K. Lohs showed a strong interest in the work of the Czechoslovak, Dr. J. Roubiček, on LSD-25. These indications appear to denote a military concern in the psychochemical research being conducted in East Germany.

38. (U) (S) MISCELLANEOUS NATURAL POISONS

Dr. H. Schmoller, Institute of Pharmacology, University of Rostock, made a study of botulinum toxin, as well as toxins found in the bee, scorpion, and spider. The Vaccine Research Institute in Dessau has conducted production research on botulinum toxin and antitoxin, and the Medical Academy, Berlin/Buch, has studied the staphylococcus toxin. A stable solution of a spider toxin was reportedly prepared; when applied externally, it exhibited a central and peripheral neurotropic activity. The bacterial and insect toxins could be useful candidates in a chemical warfare agent program.

(U)
39. ~~(S)~~ EVALUATION

There appears to be a strong interest in the indole-type alkaloids, particularly those having hallucinogenic properties. Although only slight interest is displayed in the bacterial and insect toxins at present, most likely it will accelerate in the future. Some East German "natural poison" research is believed to be military oriented and coordinated with a similar Soviet activity.

(U)
D. ~~(C/NFD)~~ HUNGARY

(U)
40. ~~(C)~~ INTRODUCTION

Ergot is an important Hungarian export item and is the subject of much research and production. Some interest in the bacterial toxins is also evident.

(U)
41. ~~(C/NFD)~~ PLANT POISONS

Ergot is artifically cultivated and there are state-sponsored competitions for highest average yields.[106] The Research Institute for Pharmaceutical Industry, Budapest, has a pilot fermentation plant which may be involved in ergot production research. J. Borsy and M. Fekete, at this Institute, have investigated the antagonism of ergot alkaloids and other lysergic acid derivatives to mescaline stimulation.[107-110] Dr. L. Nemeth and Profs. B. Kellner and Becksi, Research and Production Facilities at the Gedeon Richter Chemical Works, were producing ergot by artificially inoculating rye flour or glume with ergot spores, rather than by the deep fermentation process. Drs. K. Szasz and E. Varga of the Gedeon Richter Chemical Works have been removing indole-based alkaloids from Vinca minor and Vinca rosea with large, fully automatic and controlled extraction units.

(U)
42. ~~(C)~~ BACTERIAL TOXINS

The Hungarian Government claims concern over the possible covert enemy introduction of Clostridium botulinum into the country's foodstuffs. Large amounts of Cl. botulinum and Cl. tetani are being prepared, allegedly for pharmacological evaluation of ganglion-blocking effects. Need for stockpiling the botulinum antitoxins, A,B,C,D, and E had been expressed. The State Serum Institute in Budapest produces the necessary vaccines and antisera.

(U)
43. ~~(C)~~ EVALUATION

It is extremely unlikely that the "natural poisons" research being conducted in Hungary could be linked to a chemical warfare agent program. Rather, the research, particularly the work on bacterial toxins, appears to have a medical orientation. The strong interest in ergot alkloids apparently stems from the historic importance of ergot as a commercial product. Hungary's pharmacological interest in the hallucinogens (LSD-25, mescaline, harmine) may support a Soviet chemical warfare agent program.

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(U)
E. ~~(C)~~ POLAND

(U)
44. ~~(C)~~ BACTERIAL TOXINS

(U)
a. ~~(C)~~ Nonmilitary Research

Aside from bacterial toxin research, little research is conducted in Poland on "natural poisons" valuable to a chemical warfare program.

(U)
(1) ~~(C)~~ Much of the research on the bacterial toxins appears directed toward the toxin associated with Clostridium botulinum.

(U)
(a) ~~(C)~~ Toxicity of botulinum toxin. H. Kowarzyk, L. Czerchawski, and L. Fal, Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wroclaw, studied the effects of the combined action of the botulinum and tetanus toxins in animals. At certain dose ratios, botulinum toxin suppressed the effects of tetanus poisoning; on the other hand, additional experiments indicated that the tetanus toxin potentiated the effects of botulinum poisoning.[111] J. Mierzejewski, Research Center of Veterinary Service (location unknown), found distinct differences in the doses of toxin (type C) required to produce poisoning in laboratory animals depending on the animal species, as well as the route of administration.[112,113]

(U)
(b) ~~(C)~~ Toxin production and stabilization. H. Meisel, H. Albrycht, D. Rymkiewicz, A. Switalska, and P. Tremblower, Department for Testing Sera and Vaccines, Warsaw, isolated from canned fish a strain of Clostridium botulinum (type E) which caused food poisoning in man.[114,115] Immunologically, this toxin was shown to be identical to a type E toxin isolated in France and in the U.S.S.R. The toxin produced had low toxicity, due to the presence of protoxin, but the latter was readily activated with trypsin to the active toxin. H. Meisel, et al, were able to prepare highly stable toxin by precipitating the toxin with ammonium sulfate at pH 7.5. These preparations remained highly active for at least 1 year when stored at 5° C.

(U)
(c) ~~(C)~~ Detection. M. Chajkavski, Research Center of Veterinary Service, has been investigating methods of detecting botulinum toxin (type C) in air. This research indicates an obvious concern with the possible use of aerosolized toxin as a CW agent. K. Wawrzkiewicz and Z. Cygan (affiliation unknown) reported on the use of chick-embryo cell cultures for the quantitative estimation of Clostridium bacilli toxins.[116]

(U)
(d) ~~(C)~~ Detoxification. A report in the Military Doctor, Warsaw, No. 5, 1965, indicated that halazone (which liberates chlorine on contact with water) was ineffective for the detoxification of botulinum toxin in drinking water.

(2) (U) J. Iskiersko, Academy of Medicine, Lublin, conducted several studies on the characterization of diphtheria toxin and toxoid. Tyrosine occupied the N-terminal position in the two polypeptide chains comprising the toxin and toxoid protein. Glycine was found to be the C-terminal amino acid. About 24 epsilon-amino groups of lysine were present on the surface of the toxin molecule and the toxoid contained 10 epsilon-amino groups. Some epsilon-amino groups evidently were fixed by formaldehyde during detoxification procedures.[117-119]

b. (U) Military Research

The Microbiological Laboratory for Food Technology of the Hygiene Department at the Military Institute of Hygiene and Epidemiology conducts research on means to combat cases of poisoning. The laboratory is headed by a Dr. M. Z. Henrich. The laboratory maintains close contact with the Epidemiology-Sanitation Station, which deals frequently with various poisons in its operations. The laboratory also has liaison with similar laboratories in Hungary and Rumania. Within the framework of its CW program, the Polish Army is evidently responsible for the detection, identification, and treatment of toxic bacterial agents.

(U)
45. ~~(C)~~ EVALUATION

Little research on the natural poisons is evident for the purpose of supplying prospective agents in a CW program. The strong interest in the bacterial toxins, particularly botulinum toxin, apparently stems from a desire to defend the populace against possible poisoning. The only military significance of this research, probably, is its defensive nature.

(U)
F. ~~(C)~~ YUGOSLAVIA

(U)
46. ~~(C)~~ BACTERIAL TOXINS

The physiological effects of botulinum toxin and its elimination from the body were studied at the Atomic Research Center at Vinca, by the use of radioactive "tracer" techniques. The botulinum toxin was produced by the Institute for Biological Technology at Belgrade University, probably under the supervision of Prof. R. V. Katic who had published a series of papers on botulinum toxin, toxoid, and antitoxin. According to recent reports, Yugoslav Army officers conducted this research on the botulinum toxin, presumably under Prof. atic. The Military Academy of Medicine also has been sponsoring research on the tetanus toxin.

47. (U) PLANT POISONS

Studies have been undertaken on the ergot alkaloids (e.g., LSD-25),[120,121] on muscarine, and on curare-like compounds which cause paralysis.

(U)
48. ~~(C)~~ EVALUATION

Yugoslavia, like other East European countries, has a strong interest in botulinum toxin. The Yugoslav military probably is only interested in the defensive aspects of botulism poisoning.

Section III. (U) ~~(S/NFD)~~ ASIAN COMMUNIST COUNTRIES

A. (U) ~~(S/NFD)~~ COMMUNIST CHINA

49. (U) ~~(S)~~ INTRODUCTION

Since 1952, Communist China's CBR program has been patterned after that of the U.S.S.R. With Soviet assistance, terminated in 1960 at the beginning of the Sino-Soviet split, and without new ties elsewhere, its scientific development will be retarded for several years. Moreover, Communist China hampers the training of its gifted students by emphasizing political standing and class origin rather than educational qualifications. Despite these handicaps, some quality research is performed in the biochemical field. Rapid advances in industry, due to increased technical manpower, have been reported, but a large gap continues to exist between the country's research and its production capabilities. Research results published in the scientific journals, therefore, are not necessarily being directly applied to production technology. Most research on natural poisons evidently has been influenced by a Chinese desire to find new plant extractives for medicinal purposes. There is a minor interest in bacterial toxins.

50. (U) BACTERIAL TOXINS

Han Hung-lin and P'an Jen-chiang, Biological Products Institute of Ministry of Public Health, Peking, reported on the augmentation of toxic activity of botulinus type E toxin by treatment with trypsin. The antigenicity of trypsin-treated toxin was no greater and the immunizing potency was somewhat less than that of untreated toxin.[122]

51. (U) ~~(S/NFD)~~ PLANT POISONS

a. (U) ~~(S)~~ General

The State encourages the use of herb recipes for medicinal purposes. About 1 million such recipes have been collected and tested for their pharmaceutical and clinical value by various university institutes. Plants, containing desirable active principles, are cultivated on large state plantations. These could serve as huge reservoirs from which raw products may be obtained in any future search for natural poisons of CW interest.

b. (U) ~~(S/NFD)~~ Ergot alkaloids[123-126]

(1) (U) ~~(S)~~ As early as 1958, the Chinese Academy of Medical Sciences sponsored a program for developing stable strains of ergot which have a high capability for producing alkaloids. More than 800 strains of ergot fungi have been isolated at the Institute of Materia Medica, Academy of Sciences, Shanghai. Lu Shih-i, Kung Hsien-liang, Yueh Te-ch'ao, and Yang Yun p'eng of the Pharmacological Institute of the Academy of Medical Sciences in Peking, have also studied several strains of fungi for improving the yields of ergot alkaloids.[127-132]

(2) (U) ~~(C/NFD)~~ Three Chinese: Chao Chin-chung, Fang Tzi-cheng, and Shu Lensen, educated at the Medical College of the University of Peking, attended the

Third International Symposium for Biochemistry and Physiology of Alkaloids, held in Halle, East Germany, in 1965. One Chinese (name unknown) presented a paper on the ergot alkaloids. The paper was difficult to assess because of its garbled presentation; later, it was indicated as being "very primitive." The Chinese were escorted through Dr. D. Groeger's (East German ergot expert) laboratory at the Institute for Biochemistry of Plants, in Halle. The questions posed by the Chinese revealed their ignorance of ergot alkaloid research. They appeared more interested in the physical facilities and equipment.

(U)
(3) ~~(S)~~ Some studies on LSD-25 are also conducted at the Institute of Organic Chemistry, Shanghai. A laboratory, subordinate to this Institute, is believed to be working on chemical warfare agents and using monkeys as experimental animals.

(U)
c. ~~(S)~~ Other Toxic Plant Extractives

(1) (U) Chu Jen-hung and Fang Sheng-ting, Institute of Materia Medica, have isolated several toxic alkaloids from the Chinese drug Aconitum bullatifolium.[133-136]

(U)
(2) ~~(S)~~ The Pharmaceutical Toxicological Laboratory of Zoology, Institute of Drug Plants, has been interested in toxic alkaloids and related substances. The Institute of Organic Chemistry, Shanghai, is generally concerned with the natural organic compounds. The research on toxic alkaloids at this Institute is probably extensive; possibly, some of these compounds have been synthesized. No evidence indicates that new or radically different toxic substances are being developed as possible chemical warfare agents.

(U)
(3) ~~(S)~~ There is a growing interest in ricin, the highly toxic protein found in castor seeds. This substance was obtained as a white powder by extraction. It can be easily used clandestinely for sabotage purposes.

(U)
d. ~~(S)~~ Military Interest in Plant Poisons

(1) The Chinese Academy of Military Medical Sciences, with its departments in biochemistry, pharmacology, and physiology, could readily orient its research toward the application of natural poisons to a chemical warfare agent program.

(2) The suspicion is that some research with LSD-25 is conducted by the Chemical Defense Institute at Te Sheng Gate in Peking. Monkeys are known to be used as experimental animals. Similar studies are apparently going on at the Research Station, Chemical Warfare School, in Ch'ang-p'ing.

(3) The Agricultural cientific Research Institute, Hainan Island, reportedly under direct command of the Academy of Military Sciences of the Peoples Liberation Army (PLA), is considered one of the most important research centers in Communist China. Monkeys, as well as other animals, are used for testing purposes. Security measures are enforced here. Reportedly, experiments are being conducted on Hainan Island for the dissemination of unidentified chemicals over large areas by low-flying aircraft. Li T'ing, Director of Bacteriological Research Laboratory of Chung-shan Medical Institute, participated in these experiments. The possibilities cannot be overlooked that an extensive chemical warfare "natural poison" agent program is in progress on Hainan Island.

(U)
52. ~~(S/NFD)~~ EVALUATION

There is little evidence of Chinese Communist research being done on snake, insect, and marine poisons, but there appears to be some interest in type E botulinum toxin. The Chinese Communists have a strong interest in the physiologically active plant extractives. The military is apparently associated with some of the R&D on the plant poisons and a safe assumption is that this effort can be applied to a chemical warfare agent program. The large plantations belonging to the State could serve as a rich source of toxic substances for such purposes. Of the plant extracts investigated (ergot, ricin, and miscellaneous toxic alkaloids), only those dealing with the ergot alkaloids appear military oriented.

(U)
B. ~~(C)~~ VIETNAM

(U)
53. ~~(C)~~ "KBANG" POISON

The Communist rebels in South Vietnam (Vietcong) reportedly are using the poisonous extract from the plant, Laportia urentissima Gagnepain, in their military operations. The plant is indigenous to South Vietnam, and the poison is apparently known as Kbang, Kpung, La Doc, Cay Doc, or Man voi. It is a nettlelike plant whose toxic extract causes rapid partial paralysis of extremities. Prolonged contact may cause death.

(U)
54. ~~(C)~~ "ANTIARIN" POISON

The plant Antiaris toxicaria Lesch, which grows throughout South Asia, is used by East Indian natives as an arrow poison. It has been employed by Vietcong guerrillas in South Vietnam on "arrow traps" and is probably also being used on poison-tipped bamboo stakes that pierce a victim's feet. The poison is known as antiarin. Gian, an extract of unfurled leaves, is considered a good antidote for antiarin.

(U)
55. ~~(C)~~ EVALUATION

North Vietnam and Communist China possibly prepare these toxic extracts for the Vietcong, although the latter are probably capable of preparing their own supply of crude extracts.

(U)
Section IV. ~~(S/NFD)~~ FREE-WORLD COUNTRIES

(U)
A. ~~(C/NFD)~~ FRANCE

(U)
56. ~~(C/NFD)~~ INTRODUCTION

The French have shown an interest in natural poisons as possible CW agents; substances of specific interest to the military are botulinum toxin and LSD-25.

(U)
57. ~~(C/NFD)~~ BACTERIAL TOXINS

(U)
a. ~~(C/NFD)~~ Active French research and development on botulinum toxin goes back to the beginning of World War II. Numerous scientific articles on the

physiological, clinical, toxicological, and immunological aspects of botulinum research have appeared in French periodicals. French Army officials responsible for this research have stated that they have completed their study on botulinum toxin. The toxin has been used at the Army CBR Research and Development Center at Le Bouchet for testing the protective mask, ANP51M53. Botulinum toxin is also being used in the cloud chambers at this Center to obtain animal toxicity data. In addition, a room set aside for the preparation of toxin contains a 6-foot by 5-foot walk-in incubator where large bottles (minimum 5 liters) of inoculated Clostridium botulinum media are incubated to produce maximum yields of toxin. In a study carried out at the Research Institute of Biological and Veterinary Services of the Armed Forces, Alfort, a method was devised to detect botulinum toxin in water.

b. (U) R. Richou, P. Lallouette, H. Richou, and N. Mantel studied the effect of heat on the hemolytic, fibrinolytic, and antigenic activities of α -staphylococcus toxin.[137]

(U)
58. ~~(C/NFD)~~ PLANT POISONS

In the animal-holding area of the Army CBR Research and Development Center at Le Bouchet, monkeys have been used to test the effects of psychotropic candidate CW agents, such as LSD-25.

59. (U) SNAKE VENOM

Drs. J. Cheymol, F. Bourillet, and M. Roch-Arveiller, École Médecine, Paris, investigated the pharmacological action of the venom from the cobra Naja naja, which was found to depress neuromuscular transmission.[138] Dr. Paul Boquet, Pasteur Institute, Paris, prepared a comprehensive treatise on serpent venoms, containing a listing of Vietnam's poisonous snakes. Of special interest was his estimate of the mortality rate of persons bitten annually by these snakes.

(U)
60. ~~(C/NFD)~~ DISSEMINATION OF POISONS

The French are interested in developing a spray tank for use with jet aircraft capable of spraying either chemical or biological agents by changing the jets or orifices on the tank. They have also been interested in the possibility of using drone aircraft to disseminate chemical and biological agents. Dissemination of aerosolized natural poisons from such spray tanks or drones is a distinct possibility.

(U)
61. ~~(C/NFD)~~ EVALUATION

The use of botulinum toxin for testing a protective mask indicates a capability in the dissemination of the toxin, presumably without loss of activity. However, there is no evidence that the toxin has been standardized for military use and no detailed information has been received regarding French research on dissemination systems for this agent. The only other substance derived from natural products and of apparent interest to the military is LSD-25.

(U)
B. ~~(S/NFD)~~ ISRAEL

(U)
62. ~~(C/NFD)~~ INTRODUCTION

The generally high level of scientific research conducted in Israel appears well-integrated; much of this research is in support of government planning. Research on the natural poisons is devoted extensively to plant, marine, snake, and insect poisons. A relatively strong interest in hallucinogenic substances is evident.

(U)
63. ~~(S/NFD)~~ BACTERIAL TOXINS

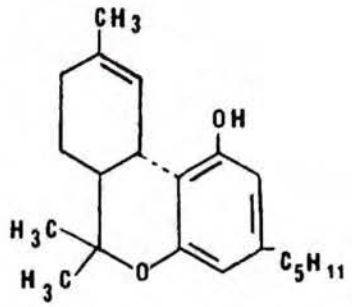
a. The Israel Institute for Biological Research, in Ness-Ziona, engages in high-quality research on bacterial infections, as well as in the development and testing of new drugs. The Institute is nominally under control of the Prime Minister and is not subordinate to the National Council for Research and Development which regulates scientific facilities in Israel. Prof. R. Goldwasser, Scientific Director, admitted that some classified research is done for the Ministry of Defense. Dr. Goldwasser has demonstrated an interest in the fluorescent antibody staining techniques, which could be useful for detecting high-molecular-weight poisons.

b. Israeli R&D is evidently concerned with pathogenic organisms rather than their toxins. However, some classified research performed here for the Ministry of Defense may involve the bacterial toxins.

(U)
64. ~~(S/NFD)~~ PLANT POISONS

(U)
a. ~~(S/NFD)~~ M. Edery, of the Israel Institute for Biological Research is searching for pharmacologically active plant substances. He appears interested in the pharmacology of the psychotropic drugs and plant extractives. Dr. M. Ben-Tov, of the same Institute, is investigating the hallucinogens.

(U)
b. ~~(C/NFD)~~ Dr. D. Lavie, Department of Chemistry, Weizmann Institute of Science, Rehovoth, is conducting a systematic collection of plants (and other natural products) with the view of extracting pharmacologically active constituents. Promising substances are studied in the laboratory for possible modification of the molecule to enhance a desired activity or to minimize the side effects. Dr. Lavie recently became interested in hallucinogens and other toxic natural products with a desire to cooperate with the United States along these lines. He is presently under contract to Bristol-Meyers Co., United States, to furnish constituents of natural products having useful pharmacological activity. Drs. R. Mechoulam and Y. Gaoni, of this Institute, helped to elucidate the structure and stereochemistry of the active components of marihuana.[139] A new component of marihuana has been isolated (cannabigerol). A tentative structure for this compound has been postulated and its synthesis undertaken. These researchers are attempting to isolate hitherto unknown constituents of marihuana and to elucidate their structures. They have recently synthesized the active component, dl - Δ^1 - 3, 4-trans tetrahydrocannabinol:[140]



(U)
c. ~~(C/NFD)~~ Dr. E. Menczel, Hebrew University, Jerusalem, is studying the hallucinogenic and pharmacodynamic effects of indigenous plants, especially those possessing psychotropic effects -- specifically, Psilocybe mexicans fungus (peyote, or mescal buttons) and flowering heads of Lophophera williamsi. Dr. A. Z. Joffe, same university, is in charge of a research project involving the fungus Aspergillus flavus Link, and its toxin. He is attempting to relate its infectivity to plants with its harmfulness to animals. He has been studying the fungal toxins for many years, having once conducted such research for the U.S.S.R. Prof F. Bergmann has studied the lethal and nonlethal plant poisons, including the psychochemicals derived from ergot alkaloids and from desert vegetation.

d. (U) O. Peczenik, I. L. Fisher, and M. Librus, Hebrew University, Abu Kabir, have reported on the mechanism of poisoning by Amanita phalloides and Amanita verna, utilizing alcohol extracts of the toadstools.[141]

(U)
e. ~~(S/NFD)~~ Some nongovernmental R&D on plant poisons appears to be in support of pharmaceutical companies in the United States. In addition, other investigators have expressed interest in coordinating some aspects of their work with the United States Government's "natural products" R&D program.

(U)
65. ~~(S/NFD)~~ MARINE POISONS

a. (U) Prof. F. Bergmann is interested in the poisonous action of stinging fish, food poisoning by marine animals, the biological, chemical, and immunological properties of marine poisons, and their mechanisms of action. The animals chosen for study were obtained from the Red Sea and the Indian Ocean. Prof. Bergmann has collaborated with Profs. K. Reich, M. Kidron, and I. Parnas in investigating the dinoflagellate toxin found in the Prymnesium parvum Carter, which is responsible for the death of fish and has more recently been reported to cause hemolysis of rabbit erythrocytes and inhibit acetylcholine-induced contractions of the small intestine of the guinea pig.[142,143]

(U)
b. ~~(S/NFD)~~ R&D on the marine poisons is relatively small at present but a continued investigation may uncover substances that could be potentially useful as CW agents.

(U)
66. ~~(S/NFD)~~ SNAKE VENOM

(U)
a. ~~(C/NFD)~~ Dr. Eleanor Condrea, Rogoff Medical Research Institute, Beilinson Hospital, is investigating the enzyme action of snake venom[144] One enzyme

phospholipase A, has a high degree of specificity. Cobra venom also contains a basic protein called DLF (direct lytic factor). The phospholipase and DLF apparently are both necessary to induce lysis of erythocytes by the splitting of the phospholipids. Dr. Simon Gitter, deputy head of the Institute and associated with the Department of Pharmacology, Hebrew University, Jerusalem, had isolated the dried venom of the domestic snake, Vipera palestinae, and found that the LD_{50} of the venom, when injected intravenously into mice, was 10 µg/20 gm mouse. In collaboration with Drs. H. I. Bicher and M. Rosen, University of Tel-Aviv, he reported on the pharmacodynamic mechanism of the neurotoxic and hemorrhagic fractions of the Vipera palestinae venom.[145] With C. Klibansky, Drs. Gitter and Bicher isolated three different neurotoxins from the Indian cobra (Naja naja) venom and studied the relation of their action to phospholipase A.[146] Dr. Gitter was formerly a staff member of the Israel Institute for Biological Research, Ness-Ziona.

(U)

b. ~~(S/NFD)~~ Snake venon R&D is of interest to a CW program. Israeli researchers are developing an expertise in investigating such poisons.

(U)

67. ~~(S/NFD)~~ INSECT POISONS

(U)

a. ~~(C/NFD)~~ A potent polyvalent antiserum against the deadly yellow scorpion, Leiurus (Buthusi) quinquestriatus was prepared by Prof. Aharon Shulov of the Hebrew University, Jerusalem. So potent is the new antiserum that its activity is several times higher than the product manufactured at the Lister Institute in London, previously the world's strongest antiserum against scorpion bites. Prof. Shulov's breakthrough came when he started to use pure, fresh, natural venom, and direct bites from scorpions into animals, mainly donkeys, used for the experiments. The donkeys were first immunized for at least a year with injections of small doses of dried scorpion venom and only in the last stage of the process was the direct sting of the scorpion administered. Prof. Emeritus Saul Adler and Prof. Natan Goldblum of the Hebrew University, and Dr. Haim Gerichter, in charge of the Central Laboratories in the Ministry of Health, assisted Prof. Shulov in this project.

(U)

b. ~~(S/NFD)~~ The work dealing with the production of scorpion antitoxin indicates a competency in R&D on insect poisons and a capability of applying such knowledge to an appropriate CW agent program.

(U)

68. ~~(S/NFD)~~ EVALUATION

There is no evidence that bacterial toxins, including the botulinum toxin, are under study. Plant, marine, insect, and snake poisons have been investigated by research institutions in varying degrees. The strongest interest appears to be in the study of hallucinogens. Although the studies on the natural poisons seem medically oriented, such studies could lead to the discovery of substances that are potential CW agents.

(U)

C. ~~(S/NFD)~~ ITALY

(U)

69. ~~(S/NFD)~~ INTRODUCTION

A rather extensive R&D program on the natural poisons prevails in Italy. Much research has been devoted to the plant, marine, snake, and insect poisons. A

small corps of competent Italian scientists in the research institutions and in nonmilitary government facilities has been working in this field.

(U)
70. ~~(S/NFD)~~ PLANT POISONS

(U)
a. ~~(C/NFD)~~ Arrow Poison

Prof. M. Pavan, University of Pavia, Institute of Comparative Anatomy and Institute of Agrarian Entomology, Pavia, indicated an interest in the plant poisons, specifically in the mixture of dried toxic components consisting of yagueli, mogouga, and mokoula -- used as an arrow poison for many years by African natives. This mixture is of possible interest as a lethal CW agent.

(U)
b. ~~(S/NFD)~~ Ergot Alkaloids

(U)
(1) ~~(S/NFD)~~ Dr. Ernest B. Chain, Higher Institute of Health, Rome, developed a large-scale production method for ergot by submerged cultures, using the strain Claviceps paspali. In 1962, he accepted a position at the Imperial College of Science and Technology University of London. Dr. D. Bovet, director of therapeutic chemistry in a laboratory associated with a medical school on the island of Sardinia, had been interested in the constituents of ergot and other alkaloids. Dr. Bovet is a wiss-born Nobel Prizewinner noted for his work on antihistamines.

(U)
(2) ~~(C/NFD)~~ Prof. Dr. B. Camerino of the Farmitalia Pharmaceutical Company, Milan, claims his company's improved fermentation process, involving the culture of Claviceps (species unknown) in a medium containing mannitol, could supply exceedingly large quantities of lysergic acid. This may permit lysergic acid to be produced at a considerably lower cost than theretofore possible and would probably accelerate adoption of LSD-25 by many countries as a standard incapacitating CW agent.

(U)
c. ~~(C/NFD)~~ Research on Other Psychotropic Substances

Studies on bufotenine and psilocybin have been made at the Institute of Pharmaceutical Chemistry and Toxicology, University of Genoa.

(U)
71. ~~(C/NFD)~~ MARINE POISONS

Dr. F. Ghiretti, University of Bari, Italy (formerly with the Zoological Station in Naples), performed studies on toxins of marine origin, such as the poisonous saliva of octopi and morays. He recently investigated the toxicity of the blood sera from marine animals. He found that the blood serum of the tuna fish caused complete paralysis of laboratory mice or rats within 10 to 15 minutes when 0.1 ml serum per kilogram animal body weight was injected; on the other hand, the blood serum of the more primitive skate produced only transitory effects on injection of 2 to 4 ml per kilogram body weight. This finding is contrary to the belief of some researchers that the more primitive the animal from which the blood serum is drawn, the more toxic the serum is for a given highly developed animal, the degree of toxicity being dependent on differences in position between the two animals on the biological scale. Dr. Ghiretti also isolated and purified the neurotoxic factor (apparently a protein) in the blood of the moray eel and related species. Dosage of 0.01 ml to 0.02 ml of "moray eel" serum per kilogram weight of rabbit was sufficient to cause death by heart failure after violent convulsions.

(U)
72. ~~(C/NFD)~~ INSECT POISONS

(U)
a. ~~(C/NFD)~~ Prof. M. Pavan has for many years been interested in toxins from such insects as the butterfly, beetle, bedbug, water bug, weevils, ants, and spiders. He has isolated and characterized two toxic components (pederine and pseudopederine) from the toxin isolated from the beetle, Paederus fuscipes. As little as 1 μg of the toxin causes necrosis of human flesh. It is more toxic than cantharidin and is reportedly more than 15 times as toxic as cobra venom. The sores produced by the toxin heal rapidly without resulting scars, and the toxin is therefore suitable as a potential CW incapacitating agent. Prof. Pavan's studies on the mothlike butterfly, of the genus Anaphe, showed the presence of an irritating substance in the very small barbed hairs, which presumably are used by the insect for defensive purposes. When striking human flesh, this toxin causes irritation and swelling, sometimes associated with high fever.

b. (U) Studies on the spider venoms have been made at the Institute of Pharmaceutical Chemistry and Toxicology, University of Genoa. L. Neri, S. Bettini, and M. Frank, Higher Institute of Health in Rome, investigated the pharmacological effects of venom from the black widow spider, Latrodectus mactans tredecimguttatus.[147]

(U)
73. ~~(S/NFD)~~ EVALUATION

Although Italian scientists have studied the natural poisons obtained from various insects, marine organisms, and plants, they have little interest in bacterial toxins. Impressive results are seen in the large-scale production of the ergot alkaloids by an improved fermentation technique. Possibly, some products being studied could prove useful as either lethal or incapacitating chemical warfare agents; however, none of the work on natural poisons appears sponsored by military organizations.

(U)
D. ~~(C/NFD)~~ JAPAN

74. (U) INTRODUCTION

Japanese investigations are extremely active in the chemistry of natural poisons. Much of their R&D is devoted to the pharmacological properties of plant extracts, bacterial toxins, marine poisons, snake venoms, and toad poisons. The Japanese appear technically capable of applying research principles to production.

(U)
75. ~~(C/NFD)~~ BACTERIAL TOXINS

G. Sakaguchi and his coworkers have conducted several studies on the toxin production of Clostridium botulinum, type E. They noted that the production of active toxin could be increased by treatment with trypsin. In 1959, they characterized the inactive toxin precursor or protoxin.

76. (U) ~~(C/NFD)~~ PLANT POISONS

a. (U) The use of medicinal plants has had a long history in Japan. Some of the more important plants being cultivated include the Lycoris squamigera (galanthamine), Securinega flueggeoides (securinine), Artemisia nurramensis (santonin), and Indian rauwolfia (reserpine).

b. (U) ~~(C/NFD)~~ S. Tanda and Y. Malsunami classified four types of parasitic races of Claviceps purpurea found in Japan. They studied the effects of the host plant on the size of the ergot. Dr. N. Abe, an expert on the ergot fungus, has done extensive work on ergot alkaloids. His findings are said to be highly reproducible in other laboratories. Ergot alkaloids, of course, are a rich source of lysergic acid for producing the hallucinogen LSD-25. In 1935, Drs. T. Hoshino and K. Shemodaira synthesized bufotenine, another hallucinogenic agent. This substance is found naturally in the seeds of certain leguminous shrubs and in the Amanita fungi (Amanita mappa, Amanita pantherina, and Amanita musaria).

c. (U) ~~(C/NFD)~~ Prof. T. Tsunematsu, Pharmaceutical Dept., Tohoku University, wrote a treatise on mushrooms and mushroom poisons which was published in the October 1962 edition of Yakuji Nippo (Pharmaceutical News).

77. (U) ~~(C/NFD)~~ MARINE POISONS

a. Dr. Yakoo has investigated the puffer fish toxin, tetrodotoxin and formulated a tentative chemical structure. The tetrodotoxin is exceedingly toxic and may be potentially useful as a CW agent.

b. Drs. T. Okaschi and Y. Hasmimoto have studied the physiological effects of a neurotoxin, nereistoxin, isolated from a marine annelid. The concentrations of nereistoxin in live worms are 60 to 106 mg/100 gm. The MLD for killifish is about 0.3 mg/kg; LD_{50} for mice is about 33.6 mg/kg.

78. (U) ~~(C/NFD)~~ SNAKE VENOM

a. Japanese workers have isolated L-amino oxidase from snake venoms of the Japanese "Mamushi" (Agkistrodon halys Blomhoffi) and "Habu" (Trimeresurus okinavensis). The two enzymes were stronger than that obtained from cobra venom and were especially effective in oxidizing arginine and isoleucine. "Mamushi" snake venom causes regional lymphedemapathy, with swelling of extremities. Fatalities are rare if antivenin is injected in time. The "Habu" snake venom causes local severe necrosis and infrequently causes death by circulatory failure or shock. Freeze-dried antivenins, effective against "Mamushi" and "Habu," have been produced.

b. The venoms of the "Mamushi" and "Habu" may become useful as physical incapacitants or lethal agents.

79. (U) TOAD POISONS

a. M. Okoda and T. Ishihara, Department of Pharmacology, Tokyo Medical and Dental University, have isolated toxic components from Senso, the dried venom of the Chinese toad.[148] One of these components, bufotenidine, aappears to have some

hallucinogenic properties. Another toxic component is bufalin, which reportedly has an anesthetic potency 90 times greater than cocaine. Other toxin components isolated were resibufogenin and cincobufagin. Drs. Ohtake, Kondo, Ohno, Vocke, and other scientists have isolated and characterized some of the toxic components from the domestic toadskin of Bufo vulgaris Japonicus including bufotalin, bufothionine, bufogenin, and resibufogenin. The hallucinogen, bufotenine, was found in the toad, Bufo vulgaris Lauer.

b. Bufotenidine and bufotenine may prove to be useful incapacitants.

(U)
80. ~~(C/NFD)~~ EVALUATION

Japan's interest in the plant extractives appears to stem from the needs of the medical profession in its search for new drugs and herbs. The military is also interested in the therapeutic aspects of the natural poisons, but the high caliber of investigations in the ergot alkaloids, marine poisons, snake venoms, and toad poisons, could provide potential candidates for a chemical warfare agent program.

(U)
E. ~~(S/NFD)~~ NETHERLANDS

(U)
81. ~~(S/NFD)~~ INTRODUCTION

The Netherlands appears to have a strong R&D interest in the natural poisons, particularly those derived from bacteria, plants, and insects.

(U)
82. ~~(S/NFD)~~ BACTERIAL TOXINS

(U)
a. ~~(C/NFD)~~ Dr. W. Berends has isolated and cultured the bacterium that develops during the preparation of "bongkrek," a coconut product. The organism produces an extremely toxic substance. The active component, bongkrekic acid, was isolated from cultures on moist, defatted copra. Partially purified bongkrekic acid was toxic for rats in doses of 20 mg/kg. Death resulted after 2 to 5 hours and while a dose of 10 mg/kg was tolerated, a repeated dose after 48 hours, was fatal. For mice, intraperitoneally, the LD50 of the partially purified bongkrekic acid was 3.5 mg/kg. The mice experiments were carried out collaboratively at the U.S. Army Biological Center, Ft. Detrick, Md. Dr. Berends studied the toxic metabolites of the bacterium and found its toxicity due, at least in part, to its inhibition of the oxidation process in the citric acid cycle.

(U)
b. ~~(S/NFD)~~ Dr. H. C. Bartlema, Chief of Microbiology Research Department of the Medical-Biological Laboratory, National Defense Research Organization, TNO, conducted preliminary studies of mass immunization against infectious diseases by means of aerosolized toxoids. Aerosols of tetanus toxoids, generated by a Collison-type nebulizer, were applied to mice. A single dose, far in excess of the amount required to confer immunity by subcutaneous injection, must have been inhaled; yet, immunity was not conferred. In association with Dr. H. Kohne, Dr. Bartlema also investigated the toxicity of bacterial endotoxin and its application to inhalation immunization experiments for protection against disease.

(U)
c. ~~(C/NFD)~~ The work at TNO is obviously directed at offensive CW measures and the Dutch admit this. The tetanus toxoid was probably chosen for aerosol immunization experiments because of its similarity to the botulinum toxoid. These studies may eventually provide some agent development potential for the Dutch.

(U)
83. ~~(C/NFD)~~ PLANT POISONS

a. Capt. M.C.W. Elskamp, National Defense Research Organization, TNO, has studied the toxicity of the poison, manchineal, from the tree, Hippomane macinella L. The tree is considered very toxic and is found chiefly in Southern Florida, Central America, and the West Indies. The fruit resembles crab apples, and its consumption results in death. Early Indians used the tree extract as one ingredient for arrow poison. When dew from the tree falls on human flesh, it causes blistering and burning of the skin. When it falls into the eye, irreversible blindness occurs. There are at least two toxic principles: one affects the eye, but not the skin; the other affects the skin, but not the eye.

b. Dr. C. A. Salemink, Organic Chemistry Department, University of Utrecht, has studied the biological pathways of muscarine synthesis and its occurrence in marihuana (Cannabis indica L). F. Kogl, former professor at Utrecht, has isolated, characterized, and synthesized muscarine.

c. These plant poisons, particularly manchineal, are potential incapacitants.

(U)
84. ~~(S/NFD)~~ INSECT POISONS

a. Prof. Van der Meer, Pharmacological Laboratory, University of Amsterdam, has been conducting research on the isolation, purification, and identification of the paralyzing poisons produced by ticks, predatory wasps, and spiders. The wasp venom causes paralysis in caterpillars, the normal prey of wasps, by producing a neuromuscular block. Prof. Van der Meer also was interested in the toxin of sea anemones.

b. The insect toxins may be of interest in a chemical warfare agent program.

(U)
85. ~~(S/NFD)~~ EVALUATION

The Netherlands scientists are cognizant of the interest in bacterial toxins existing at the U.S. Army Biological Center, Ft. Detrick, Md. This U.S. laboratory conducted biological experiments on bongkrekic acid supplied by Prof. Berends of the Netherlands in a cooperative effort between the two countries. There is some evidence of a desire on the part of the Netherlands military to build an R&D capability in the natural poisons.

(U)
F. ~~(S/NFD)~~ SWEDEN

(U)
86. ~~(C/NFD)~~ INTRODUCTION

There appears to be a military interest in this country in the plant, bacterial, and toad poisons, some of which is apparently related to CW R&D.

(U)
87. ~~(S/NFD)~~ BACTERIAL TOXINS

Some scientists in the Department of Bacteriology at the Karolinska Institute, Stockholm, are directly associated with the Research Institute of Swedish National Defense (FOA). Dr. Bangt Zacharias is working on continuous culture and large-scale culturing of tetanus toxin. Prof. C. G. Heden is interested in the mass culture of organisms and in various biotechnical problems. He has developed a system combining a diffusion chamber with a cellophane diffusion membrane in a two-phase polymer system for producing large quantities of a very potent tetanus toxin. M. Puziss and Prof. Heden reported on the production of toxin from the Clostridium tetanus in biphasic liquid cultures,[149] It is interesting to note that little has been reported on botulinum toxin;[150] however, Dr. Henry Markkula of FOA has a comprehensive understanding of world research on this toxin.

(U)
88. ~~(C/NFD)~~ PLANT POISONS

Much research is conducted on the pharmacologically active principles extracted from plants at the Royal Pharmaceutical Institute in Stockholm. Prof. Dr. Finn Sandberg is studying the alkaloids of the maize ergot and other plants and travels frequently to Africa and South America to collect plants of possible pharmacological interest. High-caliber research is conducted by Dr. Sandberg in laboratories equipped with modern analytical equipment and instrumentation. Dr. Gunner Samuelsson is investigating the toxic peptides from the mistletoe. Stig Agurell and Martin Johansson are interested in the biosynthesis and analysis of ergot alkaloids.[151,152]

(U)
89. ~~(S/NFD)~~ MISCELLANEOUS POISONS

Dr. Bo Holmstedt, Director of Toxicology, Karolinska Institute, had indicated an interest in the venom produced on the skin of the Columbian "kokei" frog (Phyllobates bicolor). He recently carried on some of his research at Baylor University, Waco, Texas, U.S.A. The toxin from the frog, known as batrachotoxin, has a lethality (0.5 µg/mouse, when injected subcutaneously, produces death) comparable to that of VX nerve agent. Indian natives of Colombia used the toxin in blowguns and on arrowheads. Ten times as toxic as the venom of puffer fish, batrachotoxin has no known antidote.

(U)
90. ~~(S/NFD)~~ DISSEMINATION OF NATURAL POISONS

A classified Swedish patent concerns an invention that deals with needlelike particles propelled by explosive loaded in hand grenades, small-arms ammunition, artillery projectiles, bombs, or landmines. When impregnated with a narcotic or toxic agent, the needles can be used against human and animal targets.

(U)
91. ~~(S/NFD)~~ EVALUATION

The Swedes are extremely capable in developing new analytical techniques and equipment. Their research on the natural poisons, particularly the toxin of the Colombian frog and poisons derived from plants, could lead to the development of an extremely potent CW agent.

G. (S/NFD) UNITED KINGDOM

92. (S/NFD) INTRODUCTION

The British have an excellent, but relatively small, R&D program on natural poisons. British scientists have been reviewing and studying the literature on animal poisons, specific enzyme inhibitors, psychochemical substances, cardioactive compounds, and other classes of plant poisons. Frequent visits to pharmaceutical firms and organizations have been useful in providing leads to new toxic substances.

93. (S/NFD) PLANT POISONS

a. Natural products of high pharmacological activity are being isolated and examined at Nancekuke. This military facility is continuing a batch-scale extraction of leaves from Rhododendron ponticum in an attempt to obtain quantities of the toxic component, andromedotoxin. This toxin appears to be one of the most active compounds demonstrating behavioral effects in rats; it is lethal for rabbits after an intravenous dose of 60 µg/kg.

b. The Chemical Defense Experimental Establishment (CDEE) at Porton has been testing natural products derived from plants. Vain attempts have been made to break down the molecule of ricin into smaller fragments and still retain toxicity. Ricin is being characterized by the determination of its amino acid sequence. Peptides, related to phalloidin, and extracts of powdered wood of Spirostachys africanus are also being investigated. The latter was found to produce eye irritation.

c. Research at Exeter University, under the direction of Prof. H. N. Rydon, has concentrated on the purification of ricin. The most recent product was obtained by fractional precipitation with ammonium sulfate, but this material was shown to be nonhomogeneous. Studies on the mode of action of ricin in vivo have shown that it decreases the phagocytic activity of the reticulo-endothelial system in rats. Ricin was shown to adsorb on surfaces of red blood cells. This action was evident when either cells or plasma from "donor" rabbits, which were given 200 µg/kg of a purified ricin preparation, were administered to "recipient" rabbits. In all cases, the rabbits receiving the red cells died in 20 to 65 hours after injection, while none of those receiving plasma died. Post-mortem examination of the animals showed typical signs of ricin poisoning. Some efforts to degrade the ricin molecule, without destroying its toxicity, were unsuccessful.

d. Researchers at the Tropical Products Institute, London, have investigated islanditoxin and patulin from poisoned rice, aflatoxin from infected peanuts, and psoralens from celery pink rot. Islanditoxin was found to damage the pancreas and liver. Its three active components: luteokyrin, regulosin, and citrinin, when injected subcutaneously in mice, gave LD_{50} of 2.21 mg/kg, 10.7 mg/kg, and 0.35 mg/kg, respectively.

94. (S/NFD) SNAKE VENOM

The Chemical Defense Experimental Establishment at Porton (CDEE) investigated the phospholipases found in snake venom. They reported that cell lysis caused by snake venom is associated with the presence of phospholipase A which hydrolyzes

lecithin with the formation of free fatty acid and lysolecithin. The venoms of the sea snake, cobra, and cottonmouth were found to promote the release of intracellular glutamic-oxaloacetate transaminase from red blood cells. Cells require this enzyme for protein metabolism and synthesis. Toxic components of snake venom may prove useful as potential CW agents.

(U)
95. ~~(S/NFD)~~ MISCELLANEOUS POISONS

a. Tropical Products Institute investigated the bacterial toxin, bongkrekic acid. CDEE has been testing a simple tetrapeptide, derived from insulin, for toxicity. Exeter University has attempted to isolate and characterize the toxic peptides derived from partial degradation of toxic proteins. Prof. Roughton, Department of Colloid Science, Cambridge University, investigated the effects of psychotropic drugs.

b. The discovery of new, simple toxic molecules may lead to large-scale synthesis of substances having toxic properties suitable for inclusion in a CW agent program.

(U)
96. ~~(S/NFD)~~ EVALUATION

The British show great interest in the natural poisons derived from plant and animal products. They have a good research capability in this field; evidently, it is directed toward developing sophisticated CW agents. Little work is reported on bacterial toxins.

(U)
H. ~~(S/NFD)~~ WEST GERMANY

(U)
97. ~~(S/NFD)~~ INTRODUCTION

The West Germans appear to show a major interest in botulinum toxin and only a minor interest in other natural poisons.

(U)
98. ~~(S/NFD)~~ BACTERIAL TOXINS

Six strains of botulinum toxin were studied. These were identified as types A, B,C,D,E, and F and found to have varying degrees of human toxicity. An aerosolized dose of the toxin was reported to be up to 1000 times more toxic than an orally-administered dose. It has also been reported that the first symptoms of botulism occur 18 to 36 hours after exposure to the toxin by the oral route and about 9.5 hours by the respiratory route. Tests on sheep showed that an aerosolized colloidal suspension of the toxin was far more toxic than an aerosolized solution of pure toxin. This condition exists apparently because aerosols of toxin in distilled water or in physiological saline result in loss of toxic activity, whereas colloidal solvents, such as horse (or cattle) serum, 0.75% gelatin, and skimmed milk, with additions of 7.5% glucose, provide the best protection against degradative mechanical forces.[153] In experiments with washed botulinum spores, intraperitoneal injections of these spores failed to produce intoxication. However, when combined with salt or sterile earth and introduced into a macerated or necrotized wound, the spores germinated, reproduced, and produced toxin. Dr. Vierling, Institutes of Animal Hygiene, Ludwig Maximilian University, Munich, studied methods of producing botulinum toxins, types A and B,

and attempted to characterize these toxins. The alleged objective of this research was to develop a defense against possible attack by stabilized botulinum toxins. Dr. Vierling entered the West German Army in 1963 as a commissioned officer. He has shown an interest in mass immunization by aerosolized toxoid or antitoxin. Von E. Holzer, Municipal Munchen Schwabing, Munchen, found that penicillin caused quite a considerable increase in toxicity of Ci. botulinum.[155] The toxin, a component part of the bacterial cell, is reportedly released as the penicillin destroys the cell. He also reported that of the five types (A through E) of botulinum toxin, only type A can be prepared in a crystalline form. This toxin is said to be a homogeneous protein with a molecular weight of 900,000 and is composed of 19 amino acids.

(U)
99. ~~(C/NFD)~~ PLANT POISONS

a. Prof. T. Wieland is noted for his excellent research on the mushroom amanita toxins, some of which was done in collaboration with other scientists. One study was on the cyclopeptides of the phalloidin toxin from Amanita phalloides, considered Europe's most poisonous mushroom.

b. There is some general interest in the production of ergot alkaloids by a semicontinuous process.

c. Sometime prior to 1945, while in Turkey, Prof. Paul Pulewka learned of cases of intoxication by ingestion of honey from bees which gathered the nectar of the rhododendron plant. The toxin, andromedotoxin, constricted the bronchi of experimental mice. Now associated with the Toxicological Institute of University of Tubingen, Prof. Pulewka is attempting to isolate and identify the toxic fractions using the rhododendron blossoms brought in from Turkey. Analysis of the minute quantities of toxic materials already isolated indicates an absence of nitrogen.

(U)
100. ~~(S/NFD)~~ EVALUATION

The excellent caliber of the West German research on the properties of botulinum toxin has potential for developing a CW agent of this type. Interest in the fairly toxic plant poison, andromedotoxin, may be oriented toward a CW agent program.

(U)
I. ~~(S/NFD)~~ MISCELLANEOUS FREE-WORLD COUNTRIES

(U)
101. ~~(S)~~ INTRODUCTION

Although some interest in natural product R&D is found in Austria, Nationalist China, United Arab Republic, Switzerland, India, and Canada, there is no evidence of any immediate application of natural poissons to chemical warfare.

(U)
102. ~~(C)~~ AUSTRIA

Drs. H. Michl and E. Kaiser, University of Vienna, Austria, published a report on the poison of the Brazilian snake, Bothrops jararaca, and on the chemistry and biochemistry of amphibian venoms. Dr. Michl specifically studied the venom of "unks," the orange-speckled toad (Bombina). This venom irritates the mucous

membranes, hemolyzes cells, paralyzes muscles, aand causes systolic arrest of the heart. The venom was shown to contain several biologically active polypeptides. Dr. Michl is currently attempting to isolate these peptides, elucidate their chemical structure, and determine that portion of the molecule responsible for the toxic effects. Drs. Michl and Kaiser co-authored a book, published in 1958, entitled, "The Biochemistry of Animal Poisons."[155]

(U)
103. ~~(C/NFD)~~ NATIONALIST CHINA

In Nationalist China, R&D on natural products is conducted at the Central Research Laboratory, National Taiwan University, College of Medicine. Dr. Hang Wen-hai investigated the highly toxic plant toxalbumins, including ricin from the castor bean, crotin from croton, and abrin from abrus. Their properties, toxicities, and antigenic activities were determined by biological and physicochemical methods. Yang Chen-chung, Medical College, Kaohsiung, purified a toxic protein from the Formosan cobra venom by salt precipitation and column chromatography. The crystallized toxin, cobratoxin, was found to bee homogeneous and had a molecular weight of 11,000. It was quite stable to heat and lost its toxicity after tryptic digestion. The toxicity of the purified cobratoxin was 6.7 times that of the original venom and had an LD_{50} to mice of 1.1 µg/mouse.[156-158]

(U)
104. ~~(S/NFD)~~ UNITED ARAB REPUBLIC

The CBR facility in the Army of the United Arab Republic (U.A.R.) negotiated with the U.S.S.R. for the establishment of a test laboratory for unconventional warfare studies. Since the latter part of 1965, Army personnel have been taking extensive BW training, reportedly on poisons, in a laboratory on the outskirts of Moscow. The Institute for the Biochemistry of Plants in East Germany is a training facility for U.A.R. plant physiologists and chemists. Such activities could possibly be associated with a desire, on the part of the Arabs, to develop a chemical warfare agent program involving the natural poisons.

(U)
105. ~~(C/NFD)~~ SWITZERLAND

Capt. R. Dolder, Swiss ABC officer, has reported that types A and B botulinum toxins resemble a globulin protein with about 14 different amino acids. The molecular weight ranged from 900,000 to 1,130,000. He believed that the aerosol method is militarily the most effective form of botulinum toxin utilization. Hans Fey, Bacteriological Institute, University of Bern, has reported that the different types of botulinum toxin are different antigenically. The botulinum antitoxin protects only against homologous toxins, but not against heterologous toxins. Man is susceptible to types A,B, and E. Muscle, paralyzed by toxin, may become sensitive again by applying electrical impulses or acetylcholine. During wartime, Fey claims, preventive measures of mass vaccination against botulinum toxin are the only recourse, but he is extremely doubtful that mass immunization can be done at the proper time.

(U)
106. ~~(C/NFD)~~ INDIA

Profs. D. K. Banerji, B. H. Iyer, and Sarma, Indian Institute of Science, India, are working on the structures of natural products. The quality of their work is

not impressive. P. R. Saxena, M. C. Pant, K. Kishor, and K. P. Bhargava, King George's Medical College in Lucknow, have attempted to identify the pharmacologically active substances in the Indian stinging nettle, Urtica parviflora. P. C. Dandiya and M. K. Menon, S. M. S. Medical College in Jaipur, reported that asarone, obtained from the volatile oil of Acorus calamus, antagonized the hallucinogenic effects of mescaline.

107. (U) CANADA

In Canada, work on natural poisons includes the ergot alkaloids and bacterial toxins. Dr. R. M. Baxter, University of Toronto, is concerned with the production of ergot alkaloids by a species of Clitocybe found in Florida. He is studying, specifically, the biosynthesis of the ergot alkaloids. Drs. J. Gerwing, C. E. Dolman, and A. Ko, University of British Columbia, Vancouver, have been studing the mechanism of tryptic activation of botulinum toxin, type E; they have isolated and characterized a toxic moiety of low molecular weight (12,200) in botulinum toxin, type A. Dr. L. A. Robb, Connaught Medical Research Laboratory, University of Toronto, Toronto, has purified diphtheria and tetanus toxoids by using Sephadex Gel.

108. (U) ~~(S/NFD)~~ EVALUATION

Venom from the orange-speckled toad, ricin, and other highly toxic toxalbumins, cobratoxin, ergot alkaloids, and botulinum toxin are among the potential CW agent candidates being studied. Only the U.A.R. and Switzerland apparently show a military interest in "natural poison" R&D. Other countries in the world community have not been represented in this study because of the lack of available information concerning their capabilities in this field.

APPENDIX I. ~~(S)~~

TOXICITY DATA ON SIGNIFICANT NATURAL POISONS (U)

~~(S)~~ Toxicity data on many natural poisons covered in this report and potentially useful as CW agents are listed below. These types of data are approximate at best, because they are often difficult to evaluate for the following reasons: (1) The routes of administration and the experimental animals used tend to vary among the different investigators, so that a rigorous comparison of potency data becomes difficult; (2) to equate toxicity data found in experimental animals to man[163,164] is not quite valid; (3) a precise characterization of the toxic substance often is complicated by the lack of uniformity, purity, and stability; (4) the toxicity of samples of poison taken from the same species, or even from the same animal, varies widely; (5) the response to a given dose of toxic material sometimes shows wide variation even among animals of the same species; and finally, (6) the data may be derived from too few tests because of the low supply of available toxic material.

Toxin	Toxicity Data	Remarks
Plant and fungal poisons		
Antiarin	LD_{50} cat I.V. 94 µg/kg	Formula $C_{29}H_{42}O_{11}$
Psilocybin	Incapacitant (hallucinogen) oral dose 7 to 14 mg/man	Formula $C_{12}H_{17}N_2O_4P$
Strophanthin	LD_{50} cat I.V. 130 µg/kg	Formula $C_{36}H_{54}O_{15}$ component of "Yagueli"
Curare (as d-tubocurarine hydrochloride)	LD_{50} rabbit I.V. 190 µg/kg	Formula $C_{38}H_{44}O_6N_2C_{12}$
Ricin	LD_{50} mouse I.V. 2.2 µg/kg	Glycoprotein, obtained from castor bean
Mescaline	Incapacitant (hallucinogen) oral dose -- 350 to 700 mg/man	Formula $C_{11}H_{17}NO_3$
Andromedotoxin	MLD rabbit I.V. 60 µg/kg	Found in rhododendron

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(U)
APPENDIX I. ~~(S)~~ (Continued)

Toxin	Toxicity Data	Remarks
Plant and fungal poisons		
Tetrahydrocannibinol	Incapacitant (hallucinogen) oral I.D. 4 mg/ 70 kg man ICt_{50} 500-840 mg min/cu m.	Formula $C_{21}H_{29}O_2$ Toxin may be ingested or inhaled. Doses greater than 2.8 mg result in some form of incapacitation
Aconite	MDL rats, subcutaneously 175 µg/kg	Formula $C_{34}H_{47}NO_{11}$
LSD-25	Incapacitant (hallucinogen) oral dose - 50 to 100 µg/man I.V. - 140 µg/man	Synthesized from lysergic acid, obtained from ergot
	Respiratory route - 60 µg/man	Formula $C_{20}H_{25}N_3O$
α -Amanitine	10 µg/kg in mice*	---
Bacterial poisons		
Diphtheria toxin	LD_{50} guinea pig, 0.3 µg/kg*	---
Tetanus toxin	MLD white mouse, intramuscularly 0.004 µg/kg	---
Botulinum toxin, type B	LD_{50} guinea pig, intraperitonealy 0.0007 µg/kg	---
Staphylococcus enterotoxin	Incapacitant, infectious dose is less than 10 µg/man via respiratory route	---
Marine poisons		
Tetrodotoxin	LD_{50} cat I.V., 5 µg/kg	Formula $C_{10}H_{15}N_3O_8$
Shellfish toxin (saxitoxin) hydrochloride	LD_{50} cat or rabbit, I.V. 3.5 µg/kg	Formula $C_{10}H_{19}N_7O_4Cl_2$. Found in Alaskan clams and in California mussels

*Route of administration not known.

APPENDIX I. (U) ~~(S)~~ (Continued)

Toxin	Toxicity Data	Remarks
Miscellaneous natural poisons		
Formosan Sea Snake	MLD 50 µg/kg, rabbit*	Paralytic poison
Cobra venom (Naja flava)	MLD 50 rabbit, I.V. 0.14 µg/kg	---
Vipera palestinae venom	LD_{50} mouse, I.V. 10 µg/kg	---
Colombian "kokei" frog poison (batrachotoxin)	LD_{50} mouse, I.V. 2.7 µg/kg	---
Bufotenine	Incapacitant (hallucinogen) oral dose: 8 to 16 mg/man	Formula $C_{12}H_{16}N_{20}$
Bulbocapnine	Incapacitant (mental sluggishness), 200 to 500 mg/man; LD_{50} mouse subcutaneously 195 mg/kg	Formula $C_{19}H_{19}NO_4$
Pederine	Incapacitant (necrotic). Amounts greater than 1 µg causes necrosis of skin	Formula $C_{25}H_{45}O_9N$

*Route of administration not known.

APPENDIX II. (U) ~~(S/NFD)~~

PERSONNEL, RESEARCH INTERESTS, AND AFFILIATIONS - U.S.S.R., CZECHOSLOVAKIA, AND ISRAEL (U)

(U) ~~(S)~~ U.S.S.R.

(Superscripts opposite names indicate authorship references in Bibliography. Abbreviations asterisked in third column are identified at end of this appendix.)

Scientists	Research Interests	Affiliations
Ado, A. D.	Bacterial neurotoxins	---
Aleksandrov, N. I.[6]	Pasteurella pestis toxin. Aerosol immunizations.	Military Medical Academy imeni S. M. Kirov (VMA), Leningrad
Apanashchenko, N. I.	Diphtheria toxin	---
Arbuzov, S. Ya.	Psychochemicals	Military Medical Academy imeni S. M. Kirov (VMA), Leningrad
Artemov, M.[63]	Bee venoms	State University of Gorki
Babkina, G. T.[182]	Snake venoms	Institute of Organic Chemistry, Novosibirsk
Ban'kovskaya, A. N.[165,173,174]	Ergot alkaloids	VILAR*
Ban'kovskiy, A. I.	Ergot alkaloids	VILAR*
Barshteyn, Yu. A.[25]	Diphtheria toxin	Kiev Epidemiology & Microbiology Institute
Basova, N. N.	Pasteurella pestis toxin	Rostov-on-Don Scientific Research Antiplague Institute
Brisker, A. D.[21]	Staphylococcus toxin	Medical Institute, Chelyabinsk
Bulatova, T. I.[3,7,12]	Botulinum toxin	IEM-AMN*
Burgasov, P. N.	Botulinum toxin	---

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Bychenko, B. D.	Perfringens toxin	IEM-AMN*
Chentsov, B. V.	Shellfish tissue constituents	Murmansk Marine Biological Institute
Chertkova, F. A.[166]	Botulinum toxin	Institute of Vaccine and Sera imeni Mechnikov, Kharkov
Dalin, M. V.	Snake venom	MOLMI*
Dashev, U.	Alkaloids	Institute of Chemistry of Plant Substances, Uzbek.
Davlyatov, Ya. V.[16]	Snake venom	Institute Regional and Experimental Medicine, Academy of Sciences, Uzbek, U.S.S.R., Tashkent.
Derkach, V. B.[16]	Bacterial toxins	Kishinev Medical Institute of Microbiology, Kishinev
Donets, Yu. I.[171]	Cl. perfringens toxins	Odessa Medical Institute imeni Pirogov
Drugov, Yu. V.[28,29]	Military toxicology	Main Military Admin., Ministry of Defense, Moscow
Emanuel, N. M.[56]	Snake venoms	MOLMI*
Fedorov, V.[32,33]	Incapacitating agents	Military-oriented writer
Gavrilenkova, V. Yu.[26]	Pastuerella pestis toxin	--- (Moscow)
Ivanova, L. G.[167]	Perfringens and botulinum toxins	IEM-AMN*
Ivanova, R. A.[41,43,44]	Ergot alkaloids (LSD-25)	Military Medical Acad. imeni Kirov, Moscow
Ivanov, V. I.[26]	Pasteurella pestis toxin	--- (Moscow)
Kabanova, Ye. A.	Botulinum toxin	IEM-AMN*
Kanchukh, A. A.	Pasteurella pestis toxin	Rostov-on-Don Scientific Research Antiplague Institute

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Karnitskaya, N. V.[20]	Staphylococcus toxin	Institute of Epidemiology, Microbiology, and Hygiene, Rostov-on-Don
Khavkin, Yu. A.[23]	Diphtheria toxin	Scientific Research Institute of Vaccines and Serum, Tashkent.
Khil'ko, V. M.	Botulinum toxin	Perm Medical Institute, Perm
Kirilenko, O. A.	Tetanus toxin	Odessa Medical Institute imeni Pirogov
Knunyants, I. L.	Military CW	Maj. General, Red Army
Kochetkov, N. K.	Alkaloids, glycosides	Institute of Chemistry of Natural Compounds, Academy of Sciences, U.S.S.R., Moscow.
Kondratenko, P.	Alkaloids	VILAR*
Konikova, R. Ye.[15]	Botulinum toxin	Military Medical Academy, Leningrad.
Kristallinskaya, N. S.[23]	Diphtheria toxin	Scientific Research Institute of Vaccines and Serum, Tashkent.
Krupenina, V. I.[27]	Plague toxin	Irkutsk Scientific Research Antiplague Institute of Siberia and Far East
Kryzhanovskei, G. N.	Tetanus toxin	Institute of Normal and Pathological Physiology, Academy of Medical Sciences, Moscow
Kuzovkov, A. D.[34-38,47]	Alkaloids, aconite, harmine	VILAR*
Lapin, I. P.	Psychopharmacology	State Science Research Psychoneurological Institute imeni Bekhterev, Leningrad

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Laricheva, K. A.	Experimental psychosis	Military Medical Acad. imeni Kirov, Moscow
Leibova, I. M.[9]	Botulinum toxin	---
Leonova, A. G.	Diphtheria toxin	---
Lobachevsky, N. I.[63]	Bee venom	State University, Gorki
Loseva, N. L.	Pasteurella pestis toxin	Rostov-on-Don Scientific Research Antiplague Institute
Malakhov, O. A.[62]	Snake venom	MOLMI*
Markaryan, M. K.	Botulinum toxin	Military Medical Academy, Order of Lenin, Leningrad
Mashkovskiy, M. D.[168]	Psychodysleptics, curare-compounds	VNIKhFI*
Meshalov, A. S.	Snake venom	MOLMI*
Mikhaylov, V. V.[1]	Bacterial neurotoxins	Saratov Medical Institute, Saratov
Mikhaylova, I. M.[2,169]	Botulinum toxin	Moscow Institute of Vaccines & Sera
Mil'shteyn, G. I.[41-45]	Experimental psychosis (LSD-25)	Military Medical Academy imeni Kirov, Moscow
Minervin, S. M.[170-171]	Cl. perfringens and tetanus toxins	Odessa Medical Institute imeni Pirogov
Mndzhoyan, A. L.[46]	Harmine alkaloids	Institute Fine Organic Chemicals, AN Armen Yerevan
Morgunov, I. N.[25]	Tetanus and diphtheria toxin	Kiev Epidemiology and Microbiological Institute, Kiev Medical Institute
Morozova, M. A.[23]	Diphtheria toxin	Scientific Research Institute of Vaccines and Serum, Tashkent

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Moskvicheva, I. V.[24]	Diphtheria toxin	Research Institute of Vaccines and Serum, Leningrad
Nekhotenova, Ye. I.	Diphtheria toxin	---
Nikol'skaya, I. I.[172]	Snake venom	Institute Chem. Natural Compounds M. V. Lomonosov State University, Moscow
Nikonov, G. K.	Alkaloids analysis	VILAR*
Novosel'Tsev, N. N.	Pasteurella pestis toxin	Rostov-on-Don Scientific Research Antiplague Institute
Orlov, B. N.[63]	Bee venom	State University, Gorki
Ostrovskiy, N. I.[165,173-174]	Ergot culturing	VILAR*
Ovchinnikov, Yu. A.	Cyclodepsipeptides (Biologically active)	Institute of Chemistry of Natural Compounds, Academy of Sciences, U.S.S.R., Moscow.
Pak, Z. P.[3]	Botulinum toxin	IEM-AMN*
Patrikeev, G. T.[17]	Perfringens toxin	---
Pavlov, P. V.[22]	Diphtheria toxin	---
Pavlovskiy, Ye. N.[54,56-62]	Snake venom	MOLMI*
Pchelkina, A. A.	Animal toxins	MOLMI*
Platanova, T. F.[36,38,47]	Aconite alkaloids	VILAR*
Ploskirev, N. V.	Perfringens toxin	IEM-AMN*
Pochinok, V. Ya.[175]	Staphylococcus toxin	Medical Institute, Kiev
Polteva, A. G.[176]	Diphtheria toxin	Irkutsk Scientific Research Institute of Epidemiology and Microbiology.
Pomyankevich, A. N.	Diphtheria toxin	---

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Preobrazhenskiy, N. A.[177-180]	Indoles, curare	Institute for Fine Chemical Technology imeni M. V. Lomonosov, Moscow
Prosvirov, Y. S.	Fish toxins	Atlantic Scientific Research Institute Marine Fisheries and Oceanography, Kaliningrad
Rezepov, F. F.	Botulinum toxin	---
Rozanov, A. Ya.	Tetanus toxin	Odessa Medical Institute imeni Pirogov
Rubtsov, M. V.	Harmine, curare-type compounds	VNIKhFI*
Ryshov, N. V.	Botulinum toxin	Military Medical Academy, Order of Lenin, Leningrad
Sadykov, A. S.	Alkaloids	Tashkent State University imeni V. I. Lenin
Salyamon, L. S.	Military medicine	Institute of Oncology, AMNSSSR Leningrad; Soviet Naval Medical Academy
Samorodov L. M.	Perfringens toxin	IEM-AMN*
Schredov, L. M.	Botulinum toxin	---
Semenov, Ye.[32,33]	Incapacitating agents	Military-oriented writer
Sergeyev, V. M.	Botulinum toxin	---
Sergeyeva, T. I.[167]	Botulinum toxin	IEM-AMN*
Seyfullina, K. N.[62]	Snake venom	MOLMI*
Shalagina, A. I.[165,174]	Ergot alkaloids	VILAR*
Shapiro, N. I.[24]	Diphtheria toxin	Research Institute Vaccines and Serum, Leningrad
Shemyakin, M. M.	Chemistry of Natural Products	Institute of Chemistry of Natural Compounds, Academy of Sciences, U.S.S.R., Moscow

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Shishkin, B. A.	Bees	Zoology, Buryat Pedagogical Institute, imeni D. Banzarov
Shredov, L. M.	Botulinum toxin	---
Shtannikov, Ye. V.[10]	Botulinum toxin	Military Medical Academy imeni S. M. Kirov, Leningrad and Perm Medical Institute, Perm
Sinitsyn, V. A.[13,14]	Botulinum toxin	Major in Army Medical Corps
Suvorov, N. N.	Indoles	VNIKhFI*
Sverdlov, J. S.	Tetanus toxin	Second Medical Institute, Moscow
Talyzin, F. F.[54,56-60,62,64]	Snake venom; animal poisons	MOLMI*
Tolkachev, O. N.[177-180]	Curare	Institute of Fine Chem. Technology imeni M. V. Lomonosov, Moscow
Torban, M. A.[19]	Tetanus toxin	---
Unusov, S.	Alkaloids	Institute of Chemistry of Plant Substances, Uzbek
Utkin, L. M.	Vinca alkaloids	VNIKhFI*
Val'tzeva, I. A.[54,55,57,58,62]	Snake venom	MOLMI*
Vasilenko, S. K.[181,182]	Snake venom	Institute of Organic Chem., Novosibirsk
Vladimerov, Yu. A.[11]	Fluorescent antibody staining technique	State University imeni M. V. Lomonosov, Moscow
Volkova, Z. M.	Perfringens toxin	IEM-AMN*
Yagud, S. I.[25]	Diphtheria toxin	Kiev Epidemiology & Microbiology Institute
Yakhontov, L. N.	Harmine	VNIKhFI*

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Yakovlev, A. M.[4,5]	Botulinum toxin	Military Medical Order of Lenin Academy imeni S. M. Kirov, Moscow
Yunusov, S. Yu.[50,51]	Alkaloids	Institute Regional and Experimental Medicine, Academy of Sciences, Uzbek, Tashkent.
Yurkova, I. B.[56]	Snake venom	MOLMI*
Zagorevskiy, V. A.	Indoles, curare	Institute of Pharmacology and Chemotherapy
Zanchevskaya, T. A.[18]	Perfringens toxin	Odessa Medical Institute imeni N. I. Pirogov
Zhidkova, F. T.[176]	Diphtheria toxin	Irkutsk Scientific Research Institute of Epidemiology and Microbiology.
Zhuraylev, V. A.[10]	Botulinum toxin	Perm Medical Institute, Perm

*VILAR = All-Union Scientific Research Institute for Medicinal and Aromatic Plants, Ministry of Health, Moscow.

MOLMI = Sechenov First Medical Institute, Moscow.

VNIKhFI = All-Union Scientific Research Chemo-Pharmaceutical Institute imeni S. Ordzhonikidze, Academy of Medical Sciences, Moscow.

IEM-AMN = Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, Academy of Medical Science, Moscow.

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APPENDIX II. ~~(S/NFD)~~ (Continued)

(S) CZECHOSLOVAKIA

Scientists	Research Interests	Affiliations
Cekan, Z.	Ergot and vinca alkaloids	Research Institute for Medicinal Plants, Prague
Cerny, A.[70,72,74]	Ergot alkaloids	VUFB*
Cerny, V.	Plant constituents	Institute of Organic Chemistry and Biochemistry, Academy of Sciences, Prague
Drvota, S.[76]	Psychochemicals	Psychiatric Clinic, Charles University, Prague
Fink, Z.[91,92]	Military toxicology	J. Ev. Purkyne Mil. Med. Res. and Postgrad. Inst., Hradec Králové
Grof, S.[77-80,85]	Experimental psychoses	Psychiatric Research Institute, Kosmonosy
Gulda, O.[66,67]	Staphylococcus toxin	Karlova University, Prague, and University of Brno, Brno.
Horácková, E.[78,79,83]	LSD-25	Research Institute Human Nutrition, Prague
Horáková, Z.	Lysergic acid derivatives	VUFB*
Kabelik, J.	Cannabis constituents	Institute of Hygiene and Epidemiology, Palacky Univ., Olomouc
Knobloch, F.	LSD-25	Psychiatric Clinic, Charles University
Kompis, I.[97,98]	Vinca alkaloids	Institute of Chemistry, Prague
Kornalik, F.[101]	Snake venom	Charles University, Prague
Krejčí, Z.[99,100]	Cannabis constituents	Institute of Hygiene and Epidemiology, Olomouc
Mokry, J.[97,98]	Vinca alkaloids	Institute of Chemistry, Slovak Acad. of Sci., Bratislava

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APPENDIX II. ~~(S/NFD)~~ (Continued)

Scientists	Research Interests	Affiliations
Protiva, Miroslav[93-95]	Indole alkaloids	VUFB*
Roubiček, J.[75-76]	Psychochemicals	Psychiatric Clinic, Charles Univ., Prague
Rudinger, J.	Physiologically-active peptides	Institute of Organic Chemistry and Biochemistry, Academy of Sciences, Prague
Ryšánek, K.[79,81,82,84,86,87]	Experimental psychoses	Postgrad. Medical Institute for Experimental Therapy, Prague
Semonsky, M.[69-74]	Ergot alkaloids	VUFB*
Sobek, V.[68]	Cl. perfringens toxin	Karlova University, Prague
Sorm, F.	Alkaloids	Institute of Organic Chemistry and Biochemistry, Academy of Sciences, Prague
Trojanek, J.[96]	Vinca alkaloids	Research Institute for Natural Drugs
Vejdelek, Z. J.[94]	Reserpine	VUFB*
Vinar, O.	Psychochemicals, indoles	PPsychiatric Research Institute, Prague
Vítek, V.[77,79,81,82,84-87]	Experimental psychoses	Postgrad. Med. Res. Inst. of Exptl. Therapy
Vojtěchovskiy, M.[77-80;82-86]	Psychochemicals, LSD-25	Research Institute Human Nutrition
Votava, Z.[71,88-90]	Psychochemicals	VUFB*
Zikan, V.[70,71,73]	Ergot alkaloids	VUFB*

*VUFB = Research Institute for Pharmacy and Biochemistry, Ministry of Health (VUFB), Prague.

APPENDIX III. (U)

GLOSSARY OF TERMS (U)

Active immunization	Production of antibodies by individual's own body cells under stimulus of antigens introduced into body.
Aerosol	Colloidal system in which air is the continuous phase; maximum size of particles in 50 μ.
Anatoxin	See "toxoid."
Antibiotic	Chemical substance antagonistic to a form of life, such as bacteria.
Antibody	Specific substance produced in the body as a reaction to the presence of an antigen; it reacts with the producing antigen in some observable way, such as flocculation, lysis, and inactivation.
Anticholinesterase	Substance which inhibits action of the enzyme cholinesterase.
Antidote	Remedy for counteracting a poison.
Antigen	Any substance, which when introduced into the blood or tissues, incites, to a greater or less degree, the formation of antibody. When mixed with the antibody, reacts with it in some observable way, such as flocculation, lysis, and inactivation.
Antiserum	Serum that contains antibody or antibodies. Obtained from animal subjected to the action of antigen, either by injection into the tissues or blood, or by infection.
Antitoxin	Antibody found in antiserum or other body fluid which is specifically antagonistic to some particular toxin.
Antivenin	Antitoxic serum against snake venom.
Antivenom	Substances, other than antivenin, antitoxic against snake venom.
Alkaloid	One of a large group of organic, basic, physiologically active substances derived from plants.

APPENDIX III. (U) (Continued)

Biosynthesis	Building up of a chemical compound in a living organism.
Biotoxin	Toxin from a biological organism.
Cardioinhibitory	Restraining or inhibiting the movements of the heart.
Dialysis	Process of separating crystalloids from colloidal substances in solution by diffusion of the former through a semipermeable membrane.
Ecology	Branch of bioscience of living organisms as affected by the factors of their environment.
Extractive	Any substance present in an organized tissue and requiring extraction by some special method.
Fibrinolytic	Hydrolyzing or liquefying fibrin (clotting substance in blood).
Fluorescence antibody staining	Binding of a substance, exhibiting fluorescence, to an antibody protein for specific detection of an antigen-antibody reaction.
Fungus	Any one of a class in the plant kingdom of a low order of development, including ergot, mushroom, and toadstool.
Ganglion-blocking	Substance that blocks the nerve impulses passing through the ganglion. The latter is a mass of nerve cells serving as a center of nervous influence.
Hallucinogen	Substance that produces a sense perception not founded on objective reality, i.e., hallucination.
Helebore	Violent gastrointestinal poison.
Hemolytic	Causing destruction of the red blood corpuscles with the liberation of hemoglobin.
Histotoxic	Poisonous to tissue.
Hypotensive	Characterized by low blood pressure.
Hypoxic	Producing a deficiency of oxygen in inspired air or low oxygen tension.

APPENDIX III. (U) (Continued)

Ichthyotoxin	Poisonous principle found in some types of fish.
Immunity	Power which the body of an individual acquires to resist an infection or toxin intoxication.
Inactivate	Destroy the activity of.
Indirect (passive) hemagglutination	Serological test for detection of antigen (e.g. toxin). Red blood corpuscles, on which specific antibody was previously adsorbed, agglutinates in the presence of antigen as the result of an antigen-antibody reaction.
Intoxication	State of being poisoned.
LD_{50}	Amount (dose) which kills 50% of a group of test animals.
Lymphedemapathy	Disease of subcutaneous tissues due to presence of excessive lymph fluid.
Lysis	Destruction of cells by specific substance.
Mass immunization	Immunization of a group of animals or humans simultaneously.
MLD	Minimum lethal dose.
Necrosis	Death of a cell or group of cells in contact with living tissue, e.g., destruction of epidermal cells.
Neurotoxin	Toxin that affects nerve tissue.
Neurotropic	Having an affinity or predilection for nervous tissue.
Passive hemagglutination	See indirect hemagglutination.
Passive immunization	Introduction into body of an antiserum (containing antibodies) formed in the body of another individual or animal.
Phagocytic	Pertaining to cells that ingest microorganisms or other cells and substances.
Pharmacodynamics	Study of the action of drugs on living organisms.

APPENDIX III. (U) (Continued)

Pharmacological	Pertaining to the effects of drugs on living things.
Phospholipase	Enzyme that splits the phospholipids to phosphoric acid and free lipid.
Phospholipid	Substances that are highly active intermediates in lipid biosynthesis.
Physiological saline	Solution approximately isotonic to body fluids, usually an 0.85 to 0.90% NaCl solution.
Phytochemistry	Study of the chemical processes in plants.
Polyvalent	Heterogeneous mixture containing more than one type of toxin, toxoid, or antitoxin.
Potentiate	Render more active physiologically.
Ppm	Parts per million (μg/gm)
Protease	Enzyme that digests proteins.
Proteinase	Any enzyme which splits native proteins.
Protoxin	Inactive precursor of a toxin, formed by certain bacteria in the course of producing the toxin.
Psychochemical	Chemical substances affecting psychological functions.
Psychopharmacology	Study of action drugs on psychological functions.
Psychosis	Mental disorder; specifically, the deeper, more far-reaching and prolonged behavior disorders.
Psychotropic	Causing a change in the mental processes in response to a stimulus.
Spasmolytic	Checking spasms; antispasmodic.
Sublethal	Not fatal, i.e., below lethal levels.
Tincture	Alcoholic solution of a substance.

APPENDIX III. (U) (Continued)

Toxin	Poison formed as a specific secretion product in the metabolism of a plant or animal organism. Toxins are colloidal and chemically related to proteins.
Toxoid	Toxin treated in order to destroy its toxicity but still capable of inducing the formation of antibodies on injection.
Toxophoric	Chemical group or site in the molecule of toxin responsible for its toxicity.
Tracer (radioactive)	Radioactive isotope of a chemical element which can be introduced into the body and followed in its metabolism and distribution.

APPENDIX IV. (U)

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