There exists within the Agency a continuing requirement from the Operating Divisions for a substance or substances that will render an individual or animal helpless and immobile, either consciously or unconsciously, until definite control measures can be instituted. The instances and situations where such an advantage can be utilized are too numerous to be mentioned. Within TSS/CD this problem has been designated the "K" (Knockout) Problem.

From various sources (scientific literature, TSS/CD projects, etc.) numerous bits of disjointed information have been accumulated in this area. Many provocative suggestions were raised that warrant further investigation. To date, there are no active projects or individuals specifically established by TSS/CD for the investigation of this problem. Therefore, this project was designed for the purposes of centralizing all efforts in this field, consolidating the existing data, and initiating active research on some of the many existing provocative suggestions.

The project will be established within the first and the f

The Experimental Evaluation of Sedative Agents

## A. Tick Paralysis

Certain species of ticks (genus Dermacentor) have been incriminated in a clinical syndrome commonly referred to as "tick paralysis". This syndrome occurs in both man and animals. It results from a tick bite, and is characterized by ascending flaccid paralysis of the musculature. Removal of the tick is usually followed by complete and rapid spontaneous recovery. The etiology of tick paralysis remains obscure. The disease is believed to result from the inoculation of some unidentified tick-generated, toxic substance which appears to be neurotropic.

As a by-product of Project Naomi, a sizeable amount of this neurotropic toxic substance is being isolated. The development and experimental evaluation of this substance as a sedative agent will be carried out within the scope of this "K" Problem project.

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Narcotic Effect of Fatty Acids

As a result of preliminary investigations carried out within MKULTRA Subproject 57 (terminated 31 May 1957), it was found that the parenteral administration of fatty acids induced a state of unconsciousness in small animals which when examined by electroencephalogram techniques turned out to be similar to ordinary sleep. The length of narcosis varied with the dose of the fatty acid administered. Of extreme interest is the fact that fatty acids, unlike other narcotic agents, are normal constituents of the diet and body tissues.

Investigation will be carried out on:

- 1. Mechanism of fatty acid narcosis,
- Effective modes of administration other than parenteral, i.e. oral, respiratory,
  - Additional fatty acids short or long chain, saturated and unsaturated.

## C. Assay of New Sedative Agents

The methods usually employed for the assay of sedative drugs are not specifically directed toward the evaluation of sedative activity although all methods utilize one or another of the characteristics of "sleep" as the criterion of effect. In the absence of a pharmacological definition of sleep, evaluation of sedative action has been conducted at different levels of this state, ranging from sleep itself to hypnosis, and even to general anesthesia. It is apparent that the criteria or endpoints employed in such evaluations have either overshot the target of sedation or have not bracketed it adequately. This then leads to a state of general confusion in the evaluation of the newer sedative agents.

To utilize effectively the sedative agents available, both tested and untested, requires the development of a systematic method of testing and systematic method of characterizing the drug, both in terms of the symptomatology produced and in terms of describing potency in producing given effects by means of standardized and valid statistical procedures. An objective report will be designed that will attempt to standardize the reporting procedure for all TSS/CD research

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projects employing animal experimental procedures.

II. Incapacitating Agents

As a result of animal testing procedures, a number of centrally acting skeletal muscle relaxants have been found. Several are or have been evaluated clinically in man with varying results. Occasionally, clinical reports appear claiming that certain pharmacological agents that have minimal muscle relaxant effects in some experimental animal preparations produce dramatic relief of spasticity in man. Clinical impressions are the usual criteria of effectiveness.

There exists within the the comportunity for clinical evaluations of some centrally acting skeletal muscle relaxants on the therapeutic relief of spasticity in man.

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