SECRET

29 December 1955

62.

MEMORANDUM FOR: THE RECORD

SUBJECT: Visit with Dr. Isbell at Lexington, Kentucky

1. One purpose of this visit was to introduce (b)(3) to Dr. Isbell and to get the benefit of Dr. Isbell's knowledge and experience in the alcohol problem. This was done and will be covered by D (b)(3) 's report.

2. In the antidote work on LSD, Dr. Isbell reported that he had conducted several more tests with Frenquel under the supervision of Dr. Fabing and under true double blind conditions. He said that although he does not yet have the dose key back from Merrill and Co., none of the doses produced effects which would lead him to believe any antidote effect had been found. He said also that so far the partial blocking effect of chlorpromazine is the only clue in this field.

3. NIH still is pursuing the work on bufotenine and after working up to 1 gram of Cohoba Snuff with no effects in the men but sneezing, Dr. Isbell reports that he has gotten up to quite high doses of bufotenine I.V. with no results as yet. He said that Fabing told him that he had worked up to doses of it that caused the men to turn blue in the face at which point a short-lived psychotic episode was precipitated. In addition to this work, NIH has sent Dr. Isbell a quantity of Rivea seeds for testing in his men. These came from Dr. Kety, who described the effects that were obtained by Dr. Cochin of NIH using a hot 1N HCl extract of the seeds in animal tests on cats, rats, pigeons, and dogs. The chief reactions seemed to be sedation with catatonia and analgesia without producing sleep, dilatation of pupils, and anorexia. There seemed to be a wide margin between effective and lethal dose and effects were obtained with amounts of the order of 50 seeds per dog indicating a relatively high potency. I described our progress in this field to Dr. Isbell and he agreed to give us the results of his tests and to test the gluco-alkaloid which was obtained from Rivea by Dr. Cook when it has been run on animals.

4. In connection with small animal testing, Dr. Isbell said that he felt that the hallucinatory drugs could certainly be screened in such a way. He pointed out that the psychologists at the hospital had produced amphetamine hallucinations in their conditioned rats such that the rats would push an imaginary bar in the Skinner box and eat imaginary food. Also he felt that the loss of wildness and biting reflex in rats, monkeys, etc., as well as other indications, suggested by Dr. Pelikan were valid indicators of hallucinatory activity.

5. I asked Dr. Isbell about the use of 1-dromeran as an alcohol extender and he agreed that this should be effective and quite safe. He noted that Hoffman La Roche has a new derivative, N-phenethyl-1-dromeran which is 3 times as potent as 1-dromeran and should also be orally effective. He agreed to test this. We also discussed the use of this material and/or reserpine and scopolamine in conjunction with chloral in the K material. He recommended that I start some animal work on such materials indicating

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that reserpine should potentiate chloral and alcohol as well as barbiturates and that the potentiation might be in duration and/or depth of sleep.

6. A report on the reserpine plus LSD work will be available soon. There appears to be a potentiation of the LSD effect such that in some cases 6 mg. reserpine given in 3 - 2 mg. portions I.M. during 24 hours preceding 60 Ugm. LSD brought on reactions usually seen at about the 150 Ugm. level of LSD. Dr. Isbell wants to determine whether or not the usual tolerance to LSD can be avoided by combination with reserpine before he finishes his study.

7. A number of other matters were disposed of during the meeting. These included the ordering of another gram of LSD, plans to test the Lilly material as soon as Dr. Pfeiffer has finished with it, and plans to check suspected variations in potency of various batches of Sandoz LSD.

8. Finally, I gave Dr. Isbell a briefing on our relationship and projected plans vis-a-vis Dr. Baldwin and asked him for his opinion on this approach to our problems suggesting at the same time that he might wish to talk to Dr. Wikler about it. He agreed that Dr. Wikler would be able to give us some sound help in arriving at a decision and indicated that his own first feeling about the program was that it would be of value to us in many ways, remembering at the same time that it would be a large and costly undertaking which no doubt would have to run for an extended period in time. He also felt that NIH should be willing to bear considerable of the cost though.

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TSS/Chemical Division

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