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NATIONAL RESEARCH COUNCIL
Division of Medical Sciences

COMMITTEE ON DRUG ADDICTION AND NARCOTICS

Minutes of Fifth Meeting - 5 November 1949
National Research Council Building
Washington, D. C.

ATTENDANCE:

Committee:	Dr. Isaac Starr, Chairman. Hon. Harry J. Anslinger, Drs. Raymond N. Bieter, Dale C. Cameron, Nathan B. Eddy, Erwin E. Nelson, Maurice H. Seevers, and Lyndon F. Small.
U. S. Army:	Lt. Col. F. L. Bauer, M.C., Office of the Surgeon General.
U. S. Navy:	Cdr. J. R. Cavanagh, (MC), Neuropsychiatric Division, Bureau of Medicine and Surgery. Lt. (jg) M. J. Aronson, (MC), U. S. Naval Hospital, Bethesda, Maryland.
Federal Security Agency:	Dr. R. T. Stormont, Food and Drug Administration.
U.S. Public Health Service:	Drs. R. W. Houde and Harris Isbell, Lexington, Kentucky.
Treasury Department:	Mr. Alfred L. Tennyson, Bureau of Narcotics.
Veterans Administration:	Dr. Richard L. Jenkins, Chief, Research in Psychiatry and Neurology.
Drug Manufacturers' Representatives:	Abbott Laboratories, Dr. R. K. Richards. American Drug Manufacturers' Association, Dr. Karl Bambach. E. Bilhuber, Inc., Mr. R. H. Chadwick and Mr. R. O. Houck. Ciba Pharmaceutical Products Company, Dr. Fredrick F. Yonkman. Endo Products, Inc., Mr. D. L. Klein and Dr. M. J. Lewenstein. Hoffman-LaRoche, Inc., Dr. Elmer L. Sevringhaus. Lederle Laboratories, Dr. Raymond W. Cunningham. Eli Lilly and Company, Dr. J. M. Maas. Mallinckrodt Chemical Works, Dr. Melvin A. Thorpe. McNeil Laboratories, Dr. C. J. Kade, Jr.

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Drug Manufacturers' Representatives - continued

Merck and Company, Inc.,
Drs. W. Edwin Clapham and Augustus Gibson.
William S. Merrell Company,
Dr. Robert S. Shelton.
New York Quinine and Chemical Works, Inc.,
Dr. Manuel M. Baizer.
Parke, Davis and Company,
Dr. L. A. Sweet.
S. B. Penick and Company,
Dr. W. G. Bywater.
Schering Corporation,
Dr. Norman Hemingway.
Sharp and Dohme, Inc.,
Dr. J. William Crosson.
E. R. Squibb and Sons,
Mr. R. J. Dahl.
Winthrop-Stearns, Inc.,
Dr. J. B. Rice.

Others: Dr. A. A. James, Medical Liaison Representative, Canada.

National Research Council: Dr. M. C. Winternitz, Miss Anne L. Birch, Miss Wave Elaine Culver, Mr. Herbert N. Gardner, and Dr. Philip S. Owen.

Open Session

The meeting was called to order at 10:15 A.M. by the Chairman, Dr. Isaac Starr.

I. Report on Establishment of Research Fund.

Dr. Starr asked Dr. Eddy to give an informal report on the negotiations for setting up a research fund for studies on analgesia and drug addiction.

Dr. Eddy reported that a meeting was held on 1 July 1949 with representatives of drug manufacturers, the Committee being represented by Dr. Starr, Dr. Small, and himself. Representatives of 17 of the 29 firms invited were present. This meeting was the outgrowth of correspondence following circularization of 74 members of the American Pharmaceutical Manufacturers Association from his office and of about 100 members of the American Drug Manufacturers Association through the courtesy of Mr. Carson P. Frailey.

There have been two major results of this meeting: the plan to invite interested firms to participate in Committee meetings; and a formal request that the Executive Committee of the National Research Council authorize this Committee to invite, accept, and administer funds for support of research on analgesia and addiction. This authorization was given by the Executive Committee on the 26th of July 1949. In September, Dr. Detlev W. Bronk, as Chairman of the Council, wrote to 26 of the drug firms inviting their support of a research fund such as that discussed at the July 1st meeting. So far there have been 14 replies, eight of them saying they had the matter under consideration, two enclosing contributions, and two others making definite promises. Three were not able or not willing to contribute to the fund at this time.

Dr. Eddy said that the response had been a little slower than the Committee had hoped, since a considerable sum of money would be necessary before a research program could be considered. He felt that there would be no lack of worthwhile projects to be considered as soon as it would become known that funds were available for this type of research; several were already known to the Committee. Dr. Beecher's project at Massachusetts General Hospital and that of Dr. Seevers at the University of Michigan were currently being held in abeyance for lack of funds.

II. Safety and Addiction Liability of Dihydrocodeinone (Dicodide, Hycodan). Report by Dr. Harris Isbell. (See Appendix A.)

Dr. Isbell stated that this compound, dicodide, bears the same relationship to codeine as Dilaudid does to morphine. It has been used extensively in Europe. He described the work at Lexington with the drug as that of administration of single doses to addicts to determine signs of euphoria. In doses of 20 to 30 mg very intense and unmistakable signs of euphoria were exhibited. Dr. Isbell explained these signs in detail and stated the euphoric potency of the compound was at least equal to that of morphine and on that score it would definitely be dangerous from the standpoint of addiction liability. A single dose of 40 mg afforded striking relief of symptoms of abstinence from morphine, and the compound also had addiction liability from this standpoint. In an experiment with a former morphine addict, a dose level of 240 mg per day was attained for a total of 31 days. Unfortunately, Dr. Isbell noted, he had not planned to carry the experiment for a sufficient length of time and ran out of the drug before he had completed his studies of tolerance. He reported that the subjects were "on the nod", got in their beds and vegetated. He noted definite partial tolerance of this drug when used as a sedative. Following withdrawal of the drug, he saw a very clean-cut morphine-like picture of abstinence. The intensity of the abstinence syndrome with respect to this compound varied very greatly; the over-all picture is very similar to that of abstinence from codeine. However, he felt that its dependence-liability was much greater than that of codeine. He concluded that the total addiction liability of the compound (dicodide) is considerably greater than that of codeine and perhaps approaches that of morphine.

Dr. Small asked whether there was any local reaction at the site of injection.

Dr. Isbell stated that none had been observed.

Dr. Lewenstein said that this drug was not intended for the control of pain, but only for the relief of coughs.

Dr. Isbell said that their work was not concerned with pain control, but only with addiction liability. The danger from their point of view, was that the drug might afford another and perhaps more easily obtainable addicting agent. Addicts would take it by hypodermic, even if the drug were intended for oral use. He said that he did not think addiction would be very great under conditions of proper therapeutic use, and this opinion applied also to Dilaudid.

Dr. Lewenstein said that he was sorry that they had been unable to finish the experiment. His firm had indicated its willingness to furnish more of the drug at any time. He wished to call attention to the fact that Dr. Isbell had not used doses on a therapeutic level, but had started with a single dose of 20-25 mgm. The recommended dose is only five mgm, with a maximum of 15 mgm.

He pointed out that Dr. Isbell's subjects had all been previously addicted, and added that he thought it important to distinguish between primary and secondary addiction.

He also stated that there is a tremendous difference between the addiction liability of a drug taken by mouth and by parenteral administration. He had not seen one case of primary addiction to dicodide where the drug was taken by mouth, and wished that some more work could be done along these lines.

Dr. Eddy did not believe that making the preparation available only for oral administration and in small doses would be any guarantee against abuse. There is nothing to keep an addict from taking more than one tablet.

Mr. Anslinger held that the secondary addiction established by Dr. Isbell was sufficient evidence that primary addiction would also occur.

Dr. Isbell said that in testing addiction liability they were not dealing with therapeutic doses. An addict takes all he can get; he does not stay down to the therapeutic level of dosage. The number of addictions at a therapeutic level he felt would be very small.

He stated that if a drug relieves abstinence when given parenterally, testing it orally was unimportant. Regarding the question of primary vs. secondary addiction, he pointed out that it is not ethical to determine the addiction liability of drugs in people who have not already been addicted. Former addicts are probably the best subjects in any case, because they are known to be susceptible.

Dr. Shelton felt that it had been indicated here that the drug would be more easily available than morphine. He asked if they were not under the same control.

Dr. Isbell said that was true, but that many doctors will let addicts have prescriptions for codeine, or its derivatives, more readily than morphine. In his experience, he had found that addicts will inject anything. He had even seen them inject crude opium.

Dr. Lewenstein stated that insofar as he remembered from the literature, there had never been any case of direct addiction reported, although dicodide had been used for more than 20 years. Morphine may have been more readily available, but the fact remains that much dicodide had been used. He claimed that with dicodide, one does not get tolerance.

Dr. Isbell stated that he had observed tolerance to dicodide.

Dr. Lewenstein stated that his firm was making only the bitartrate.

Dr. Starr asked why the bitartrate could not be injected.

Dr. Lewenstein replied that it would produce unpleasant side reactions.

Mr. Anslinger remarked that this would not be a deterrent to an addict.

III. Safety and Addiction Liability of Dihydrohydroxycodeinone (Eucodal, Nucodan-Endo). Discussion of Proposed Brochure of Endo Products, Inc., Referred to the Committee by the Bureau of Narcotics.

Dr. Eddy informed the Committee that Mr. H. G. Anslinger of the Bureau of Narcotics had referred to it the text of a proposed brochure by Endo Products, Inc., concerning their product Nucodan (Eucodal). The Bureau had requested the advice of the Committee as to whether the descriptive material was appropriate, and as to the addiction liability and relative safety of the drug.

Dr. Seevers noted that in the suggested brochure it was stated that the substance may be more habit-forming than codeine. He said he had not seen enough evidence to establish what position Nucodan occupies between morphine and codeine, or whether it is potentially as habit-forming as morphine.

Dr. Eddy stated that there is published evidence of its relation to morphine experimentally. It is much closer to morphine in its analgesic power, and more depressant to respiration, than codeine. The tone of the brochure is to compare it with codeine. From this comparison the physician would get the impression that this is a codeine-like substance, and he would tend to be less careful with it, and to prescribe it more readily. Dr. Eddy noted that there were several references to addiction to Eucodal in German literature. His feeling was that the comparison from the standpoint of safety to make the physician aware of what he is dealing with, should be with morphine and not with codeine. He felt that Nucodan should be thought of as a poorer morphine rather than as a better codeine.

Dr. Starr noted that the brochure stated that no habituation was found in rabbits after several injections of 0.01 gm. He considered this to be a misleading statement.

Dr. Lewenstein remarked that it had been taken from Dr. Eddy's book.

Dr. Eddy pointed out that the statement, though accurate, was misleading when separated from its context, since rabbits do not readily become addicted, and are thus not suitable animals for experimental studies of addiction.

Dr. Starr mentioned that the manufacturers had been careful to state that Nucodan had addiction liability.

Dr. Eddy felt that in view of the comparisons with codeine, physicians would pay no attention to the warning about addiction.

Dr. Lewenstein stated that he had gone carefully over the literature and had found that in all reported cases of addiction to Eucodal, the drug had been given by injection or there was a history of former drug addiction. There was only one case of primary addiction in the entire literature, and even this case had been treated with morphine in between.

Dr. Lewenstein stated that his firm was willing and wanted to say that Nucodan may be habit-forming, but that the evidence from the literature so far available did not bear out that this drug, when given orally, has great addiction liability. He said that only one case of oral addiction is to be found

in the literature. He pointed out that his firm incorporated certain other products in Nucodan, including a small amount of homatropin. While this was included for other reasons, he thought it would be a strong deterrent to addiction. He summed up his remarks by saying he believed this drug would be a valuable addition to the armamentarium of the doctor; that he did not believe it was as strong an analgesic as morphine, but believed it would be closer to codeine; and that he would be glad to make such changes in the descriptive brochure as would conform to the views of the Committee.

Dr. Small remarked that the deterrent effect of homatropin was not important, since the homatropin could easily be destroyed by dissolving the tablet and boiling the solution.

Dr. Isbell said that even atropin is not too much of a deterrent.

Dr. Starr reminded the Committee that quantities of new substitutes had been introduced with the idea that they were less habit-forming than morphine, and that this sometimes proved not to be the case. He cited the introduction of heroin as an example. He felt that if someone became addicted to one of these newer drugs, he would eventually transfer to the regular type of narcotics sold in the black market.

Mr. Anslinger remarked that the German government had put Eudocal under the same restrictions as morphine, but had not put codeine under those restrictions.

Dr. Lewenstein stated that his firm was willing to say in the brochure that it may be as habit-forming as morphine, but asked whether it would be necessary to state that it is not as good as morphine and just as habit-forming.

Mr. Anslinger asked if the late Dr. O. Anselmino, in his book, "ABC of Narcotics Drugs", had not related the drug to morphine.

Dr. Lewenstein replied that he had related it to morphine on its addiction possibilities only. He stated that some reports indicate that Eucodal may be less habit-forming than morphine, although his firm was not insisting on such a statement.

Dr. Starr asked whether an addict interested in taking a drug by mouth would not very soon begin taking it by injection.

Dr. Lewenstein replied that this was why his firm had not proposed to make the drug available in injectable form. He believed that there was a difference in the primary addiction liability of any drug depending upon whether it was taken orally or by injection.

Dr. Eddy stated he still had the feeling that as the brochure is written the physician will get the impression that Nucodan is nearer codeine than morphine. The danger of abuse is not in therapeutic use; the danger is that the physician, when an addict comes to him and asks for a prescription, will write one in the belief that Nucodan is a codeine-like drug and that the addict may be able to get along with it. Dr. Eddy did not believe that the fact that the drug was in oral form would be a deterrent. He suggested revising the order of these statements, and telling the physician about the habit-forming qualities first rather than at the end, where the physician would probably not pay enough attention to it.

Mr. Klein stated that Endo Products, Inc. had been marketing Hycodan since 1942, and had sold some 60 million doses, but had not received a single report of abuse of the drug. Recognizing the possibility of abuse and the force of the argument that physicians might tend to prescribe a product like codeine, he asked whether one should assume right at the outset that there would be abuse, in view of this experience with a similar product.

Dr. Eddy asked in what form Hycodan had been available.

Mr. Klein replied, first in five mg tablets, later in powder, and finally in elixir.

Dr. Isbell asked if it had been advertised.

Dr. Lewenstein replied that it had only been advertised to the medical profession. He stated that this drug was used in a number of tuberculosis institutions. Glenn Dale Sanitorium, Glenn Dale, Maryland, had been using it for about seven years in fairly large quantities, with no case of addiction. He could cite the same record from dozens of other institutions.

Mr. Houck stated that E. Bilhuber, Inc. was marketing this drug under the name Dicodide, for the treatment of cough. The company, however, thinks Dilaudid is better for this purpose.

Mr. Klein, returning to the wording of the brochure, asked whether it would be sufficient to place the statement concerning the addiction liability of Nucodan at the beginning of the text.

Dr. Eddy thought that the physician should be warned to use the same precautions in its administration that he would use in the case of morphine, and that the manufacturers could then feel free to make such scientific comparisons as they wished.

Dr. Lewenstein felt that if the brochure began with such a statement, nine out of ten physicians reading it would decide not to use it. If we really want to stick to the facts, he said, we have to compare it in its therapeutic effects to codeine.

Mr. Anslinger stated that he agreed with Dr. Eddy's views, noting that the United Nations' supervisory body, in reviewing estimates for Eucodal, put it on the same basis as morphine and similar drugs.

IV. Report on a Direct Addiction Experiment with N-methyl-3-hydroxy-morphinan by Dr. Isbell. (Morphinan)

Dr. Isbell presented a report of his experiments, which is reproduced as Appendix B.

Dr. Eddy noted that this drug was used in Germany, and had been tried in Switzerland. He suggested that Dr. Sevringhaus might know something about it.

Dr. Sevringhaus stated that the description Dr. Isbell had given of this drug was entirely consistent with that which Hoffman-LaRoche had had with the compound, except that his company had used only therapeutic doses, and probably for this reason, had not observed the delayed side effects. His firm had not observed the development of addiction to the drug. He felt that the peculiarities of delayed action and delayed side action may be consistent with each other.

V. Tolerance and Addiction to the Barbiturates. Report and Presentation of a Motion Picture by Dr. Isbell.

Dr. Isbell stated that for the past ten years the U. S. Public Health Service has had an increasing number of morphine addicts committed to the Lexington institution who were also taking large amounts of barbiturates. (Appendix C.) The drugs used seemed to be on the order of pentobarbital, seconal, and amytal. The information contained in the case histories as to the dosages of these drugs was entirely unreliable.

From experiments it was found that if barbiturates were abruptly withdrawn or if dosage was suddenly refused, grand mal convulsions developed, and sometimes delirium. This same simple pattern of convulsions and psychosis is reported in German literature (1925), and a monograph has been written giving a very clear description of psychosis following withdrawal of barbiturates. From the clinical material, Dr. Isbell reported, it was very difficult to be certain that the syndrome the observers saw was actually due to barbiturates since it was very difficult to know what these people had been taking and there were various mixed intoxications with morphine, barbiturates, benzedrine, alcohol, and bromides. Many of these addicts were suffering from malnutrition or from various diseases.

He stated that the moving picture shown was based on an experiment with five former morphine addicts who had used barbiturates, with no history of epilepsy and no psychotic history except that one patient had had delirium tremens. Encephalograms were done on all five of the patients. The drugs used were pentobarbital, seconal, and amytal; the dosage was raised until the men reached levels of intoxication as great as the observers could permit.

The motion picture was then shown, depicting the actions of the subjects while under the influence and after the withdrawal of barbiturates, particularly the convulsions and irrational behaviour.

Dr. Isbell said that the men had symptoms similar to those resulting from alcohol in large amounts, except that there was no gastric irritation, and no vomiting. They could eat well, and the men actually gained weight. The hallucinations appeared to be visual. The men sometimes became disoriented, but could maintain their own identity. There was some degree of tolerance. Whether there is as great an emotional disturbance as with morphine, is not known.

Dr. Small asked if these men had loss of memory.

Dr. Isbell said that those who had sexual hallucinations could not remember them, but those having other types of hallucinations could describe them later. They had no memory of the convulsions themselves.

Dr. Richards asked whether these men could be put to sleep with barbiturates during their recovery.

Dr. Isbell said that it took eleven seconal tablets to put one man into a deep sleep, and remarked that an apprehensive person requires a large dose of a barbiturate. He had thought that they would sleep all the time; but even though there is little to do in the hospital, and the men become accustomed to taking naps, these men wanted to stay up and enjoy being "drunk".

Dr. Seevers reported that his group had carried out an experiment on a dog in which sodium barbital was given six days a week for three years. The dog had convulsions regularly every Monday morning. The neuropathologist had found evidence of permanent damage to the brain.

Dr. Starr referred to Mr. Anslinger a question as to the extent of abusive use of barbiturates throughout the country.

Mr. Anslinger stated that field offices of his Bureau received many reports of alleged barbiturate abuses. From these, and from newspaper reports, there was evidence of considerable abusive use. The Food and Drug Administration had reports of a number of cases of illegal sales of the barbiturates, although it was assumed that the facilities of the Food and Drug Administration for this type of enforcement were limited. Mr. Anslinger further pointed out that there had been a movement to have the barbiturates placed under the narcotic law, and two bills had been introduced in Congress seeking to accomplish this purpose. The Bureau, through the Treasury Department, had made unfavorable recommendations on these bills as it was believed that the best solution would be for the states to provide adequate control laws and enforce them. There was at present no evidence of a bootleg interstate traffic in barbiturates.

Lt. Aronson said that in his Navy practice he had come in contact with several cases of attempted suicide by barbiturates. He asked what had become of the proposal to compound an emetic with the barbiturate in order to prevent suicide.

Dr. Nelson replied that the Food and Drug Administration had concluded that this plan would not work. The barbiturate acted more quickly than the ipecac, and parlayzed the emetic center so that the barbiturate could get in its effect without the ipecac taking effect.

Dr. Maas agreed. He reported that there had been about 180 attempted suicides in one month, in an area in California, of which five or ten were successful. He felt that as long as pharmacies sell barbiturates over the counter, this condition would continue

Dr. Isbell questioned the number of actual suicides from barbiturates. He thought that some may have been involuntary suicides, as the drug impairs their judgment.

Dr. Jenkins thought this was true also, and cited a case of such a suicide from his experience.

The meeting recessed for lunch at 12:25 and reconvened at 1:20 P.M.

VI. Definition of Drug Addiction.

Dr. Eddy stated that the Expert Committee on Habit Forming Drugs of the World Health Organization, of which he is a member, expected to meet in January 1950, and that the Narcotics Commission had assigned it the task of drafting a definition of drug addiction for international use. He thought that this Committee would be able to help in supplying a definition for his guidance at that meeting.

Dr. Starr asked for suggestions.

Dr. Eddy submitted his own proposal, which was as follows:

> "Drug addiction is a state produced by the repeated administration of a drug, and characterized by the development of physical and/or psychic dependence, as a result of which the individual experiences intense physical and/or mental suffering when the drug is withdrawn. It is characterized also by the individual's motivation becoming mainly or solely maintenance of his drug supply, to the detriment of himself and society."

Dr. Isbell stated that drug addiction, to him meant a state of chronic intoxication brought about by compulsive, willful use of a drug and carried on to such an extent that harm is caused to the individual himself.

Dr. Starr stated his definition did not have anything to add to those previously given. It was that drug addiction is a condition produced by taking a habit-forming drug over a considerable period of time.

Dr. Isbell thought Dr. Eddy's definition put too much emphasis on dependence and not enough on what was going on while taking the drug.

Mr. Anslinger pointed out that the question of a definition occupied several hours of discussion at the last meeting of the Commission on Narcotic Drugs of the United Nations, and that the Commission had wisely referred the question to the World Health Organization.

Dr. Eddy and Dr. Isbell had considerable discussion as to whether the definition would include so-called addiction to marihuana and cocaine. Dr. Eddy thought that it would, since these drugs produce psychic dependence, but he suggested the elimination of the sentence reading "as a result of which the individual experiences intense physical and/or mental suffering when the drug is withdrawn".

After further discussion, the following tentative draft was formulated:

> "Addiction is a state of harmful and chronic intoxication produced by the repeated administration of a drug, characterized by the development of a compulsion to continue to take and a tendency to increase the dose of the drug, to the detriment of himself and society, and of psychic and/or physical dependence. Addiction is also characterized by the individual's motivation which becomes mainly or solely concerned with maintenance of his drug supply."

Dr. Lewenstein felt that "mainly or solely" was too strong, and that it would be more accurate to say that the maintenance of the drug supply becomes an important motivation. He also suggested that the phrase "detriment of himself and society" be amended to read only "detriment of himself".

It was agreed that the draft quoted above would be sent to the members by mail for further consideration. This was done by Dr. Eddy, and after considerable correspondence, the following definition was agreed upon by a majority of the members:

> ADDICTION IS A STATE OF PERIODIC OR CHRONIC INTOXICATION DETRIMENTAL TO THE INDIVIDUAL AND TO SOCIETY, PRODUCED BY THE REPEATED ADMINISTRATION OF A DRUG. ITS CHARACTERISTICS ARE A COMPULSION TO CONTINUE TAKING THE DRUG AND TO INCREASE THE DOSE, WITH THE DEVELOPMENT OF PSYCHIC AND, SOMETIMES, PHYSICAL DEPENDENCE ON THE DRUG'S EFFECTS. FINALLY THE DEVELOPMENT OF MEANS TO CONTINUE THE ADMINISTRATION OF THE DRUG BECOMES AN IMPORTANT MOTIVE IN THE ADDICT'S EXISTENCE.

VII. Algesimetry. Report by Dr. Raymond Houde.

Dr. Houde discussed the results of experimental work (Appendix D) which he had done with small animals, and which was directed toward establishing a method for measuring and charting intensity of pain. Certain narcotic drugs were used in the experiments.

VIII. Review of the Addiction Liability of NU-1196 (Nisentil) and Recommendation with Respect to Further Work at Lexington..

Dr. Isbell reported that he had carried out single dose tests for addiction liability of Nisentil, a drug of the Piperidine series. He had administered 50 mg of the drug at the 30th hour of abstinence from morphine, and found definite response. He said that the manufacturers, Hoffman-LaRoche, Inc., had questioned the validity of this procedure, and he asked whether the Committee felt that Nisentil should be subjected to direct addiction liability procedure.

Dr. Sevringhaus stated that he had entered this technical objection on the basis of the particular type of drug in question. He said that it does not produce euphoria and is not a hypnotic. His company was not convinced that it would be of significant use for chronic pain. It was being used as a means of relief from acute pain, as in obstetrics. His company felt that it should be considered in a separate category from other drugs including Demerol. He would recommend further drug addiction tests to settle the dispute as to its status.

Dr. Isbell replied that tests had been run on Demerol and on five others of the series, Bemidone, Keto-Bemidone, 1196, 1932, and 1772, but by the acute single dose method only. Nisentil belongs in the Demerol series; his personal feeling was that it is about like Demerol.

Dr. Starr asked Dr. Isbell if he were pressed with testing work at Lexington, and whether the facilities were becoming too taxed.

Dr. Isbell replied that he was not pressed with respect to the new drugs, but that he was quite fully occupied with his work on Mescaline and other undertakings.

The Committee recessed briefly at 3:00 P.M., while the representatives of the drug manufacturers left the meeting, before reconvening in executive session.