U. S. Narcotic Farm, Lexington, Kentucky.

September 30, 1935.

Memorandum to Assistant Surgeon Himmelsbach.

I have read over the article on "Addiction Potentialities of Dihydrodesoxymorphine-D" by Mathan B. Eddy, John G. Reid and Homer A. Howes, and also your comments on the same, with which I am in agreement.

It seems to me that the experiments made by these authors definitely prove that descenorphine has decided addicting properties, but they have unfortunately written this article in such a vein as to give the impression that they feel that it is not addicting or only very slightly so. The experiments on menkeys are especially striking.

It is noted on page 18 that the authors object to the substitution phenomena as proof of addiction potentiality and say that this phenomena is valid only if the previous administration of morphine does not affect the ability of the new substance to cause abstinence symptoms and only if abstinence symptoms after acute withdrawal of the new substance were the same in character and degree whether or not there had been previous morphine administration and addiction in the individual under observation. They do an experiment (3D) designed to prove their contention but which in my opinion does not prove it. They give desomorphine to animals that were previously addicted to morphine. They then withdraw the desomorphine and these animals upon withdrawal suffer as much as they previously suffered when morphine alone was withdrawn and not as much as animals that had been addicted to desomorphine alone.

The difference here is, in my opinion, not due to any mysterious action of morphine and desomorphine due to the fact that they were given to the same animals. It rather proves, especially in the case of No. 5 which is cited, that this animal was more strongly addicted than the animals upon which desomorphine alone had been used because No. 5, counting all of its addiction insults, had been carried on an opiate longer than those animals upon which desomorphine alone had been used. Another thing to be considered here is that desomorphine is necessarily given in smaller doses than morphine because of its high toxicity. It is logical to expect that the larger doses of morphine would cause a higher degree of addiction unless desomorphine, grain for grain, has greater addiction potentialities.

Experiment No. 4 with the rats should be taken to show that one dose daily of desomorphine is not sufficient, when given over a short period of a month or two, to cause marked addiction in animals, probably because the dose is necessarily small, due to the toxicity of the drug and also because the action of this drug is briefer than the action of morphine. It is noted that when the authors gave the drug three times per day an effect (hyper-irritability) was produced comparable to that previously reported by you. I am, however, not prepared to say that this effect is evidence of addiction.

Very truly yours,

Lawrence Kolb, Medical Director, Medical Officer in Charge.