

November 23, 1971

Dr. R. Mechoulam
Laboratory of Natural Products
The School of Pharmacy
The Hebrew University of Jerusalem
Faculty of Medicine
Jerusalem, Israel

Dear Dr. Mechoulam:

Separately I have sent you the import permit of EA 1476.

There is much interest in the antagonists, and particularly in a long acting formulation in this country. I have attended two meetings focused on this problem during the past month. The immediate focus of interest is in naloxone pamoate, which in animal trials releases naloxone for 10-14 days. We will begin an assay of this material in January.

At present, the two best antagonists are naloxone and l-cyclazocine,. Naloxone is enclosed. For l-cyclazocine, samples would have to be obtained from Dr. Sidney Archer, Winthrop Laboratories. It is also probable that M-5050 of Reckitt & Coleman may be useful, but neither l-cyclazocine or M-5050 have received testing in man. Therefore, for the present, naloxone is the drug of choice. Should you believe the chemistry of cyclazocine would be a better choice, I would suggest you write Dr. Archer for a sample of l-cyclazocine to test.

The testing is a problem. I recall that the Israeli pharmacologists were able to assay the duration of action in animal subjects, using morphine challenges. Is that correct? Our facilities permit us to assay the duration of antagonism in man, using heroin challenges. We have not been able to undertake toxicology studies in our laboratories, and have been trying to obtain the funds to study M-5050 under a contract. This is under review. Should you make some samples available that you believe has a long release rate, we will try to assess the animal duration (release) and if interesting, arrange for the other trials.

Dr. R. Mechoulam

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We are grateful for your interest, and Dr. Freedman asks to be remembered to you.

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

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