25 April 1955

104-55

Chief, [redacted] Office, OO/C

Case [redacted] - Comments on Visit with [redacted]

1. I had dinner with [redacted], 22 April 1955, and he wanted this information sent to you.

2. [redacted], presently on loan to the US Public Health Service in Washington, D. C., where he has a title of Commander, arrived in [redacted] this past week for the purpose of locating a home for his family. [redacted] has been on loan to the US Public Health Service for the past two years and will return to the [redacted] on 1 July 1955, where he will take up his former duties in the Neurology Section.

3. [redacted] has an M. S. degree in Chemistry, an M. D. degree, and is a full-fledged Psychiatrist. [redacted] speaks of him as the best Neurochemist in the field.

4. [redacted] has been working in Washington, D. C. on LSD-25 and gave these findings of his to [redacted]

a. LSD-25 can be detected - it fluoresces under ultra-violet lights. Using the fluorometer, you can make a chemical deduction in the blood and spinal fluid. This detection can be done to .0002 of a gamma in a period of 30 seconds.

b. 40 percent is excreted in the urine.

c. It passes the blood brain barriers.

5. [redacted] feels that [redacted] should be included in the [redacted]. He says, with [redacted], as far as his department is concerned it would be complete because it would furnish him with a Neurochemist. [redacted] has worked with [redacted] in the past and knows his ability and [redacted] upon [redacted] return to [redacted], will work with him again on his problems.

6. Let me know your reaction to this as I feel that Mr. [redacted] should be informed of it. If you haven't any biographic material on [redacted] please let me know.

7. A doctor from a pharmaceutical firm (name illegible) I believe his name is [redacted] who was at the [redacted] when you were there, is sending Dr. [redacted] a new "thorazine" which has never been tried clinically. He has asked Dr. [redacted] to experiment with it which [redacted] has agreed to do.

8. A [redacted] representative was at the [redacted] Dental this past week and has made arrangements with [redacted] whereby all new stuff in [redacted] field will be sent to him for research.

9. The photostats were sent to you by pouch on 23 April 1955.

10. The original four, Mr. [redacted] Doctors [redacted] and [redacted] send their regards. I assure you that their enthusiasm has not lessened in anyway. It will be of real interest to me to see how they will handle any problems that you may send on to them.

11. I am enclosing, herewith, a report on "Pharmacology of KP-207" which was sent to Dr. [redacted] by the [redacted] people [illegible].

PHARMACOLOGY OF NP-207

A. NP-207 with the empirical formula - $C_{20}H_{23}N_2SCl$. HCl - was selected following a comparative pharmacological study on a series of many phenothiazine derivatives.

B. The pharmacological analysis of NP-207 can be summarized as follows:

1. Toxicity:

Mouse LD_{50} i.v.:	Chlorpromazine	41½ 3.3 mg/kg
	NP-207	67½ 5.8 mg/kg
Rabbit LD_{50} i.v.:	Chlorpromazine	30 mg/kg
	NP-207	27 mg/kg

2. One of the most characteristic properties of NP-207 is a broad spectre of activity on isolated smooth muscle organs.

	NP-207
Acetylcholine Antagonism (isolated intestine guinea pig) (Human therapeutic dosage of NP-207	35 X less active than Atropine. -100 X that of Atropine.
Histamine Antagonism (isolated intestine guinea pig) (Human therapeutic dosage of NP-207	1.5-2 X less active than Sandostene - 5 x that of Sandostene
Adrenaline Antagonism (seminal vesicle guinea pig) (Human Therapeutic dosage of NP-207	3.3 X less active than DHE - over 100 times that of DHE)
Basic Antagonism (Isolated intestine guinea pig) (Human therapeutic dosage of NP-207	8 X more active than papaverine - in same range as papaverine)

3. Potentiation of barbiturate anesthesia in mice:

NP-207 potentiates the narco-sedative effect of penthothal.

Drugs used:	% of animals lying for more than 2 minutes on the side (Seitenlage).
a) 20 mg/kg Pentothal i.v.	0%
b) a) + 2 mg/kg NP-207 i.v.	25%
c) a) + 3 mg/kg NP-207 i.v.	37%
d) a) + 5 mg/kg NP-207 i.v.	88%

4. Analgesia potentiation in mice (hot plate test):

A normally ineffective dose of morphine (4 mg/kg) produces partial analgesia in animals pretreated with 6 mg/kg NP-207. Complete analgesia is obtained if the animals are pretreated with 15 mg/kg NP-207. NP-207 alone has no analgesic action.

5. Effect on body temperature:

The body temperature of rabbit and rat is decreased under the action of NP-207. To obtain a temperature drop in the rat of 0.8-1.2° Celsius in normal room temperature, 2 mg/kg NP-207 are needed.

6. Dinitrophenol hyperthermia in rats can be inhibited by NP-207.

7. Inhibition of Nikethamide and Nicotine convulsions in mice:

NP-207 protects the animals against these types of convulsions.

8. Circulatory system of the cat:

NP-207 produces a moderate but fairly long lasting blood pressure fall (10-30 mm Hg) in doses of 0.5 - 2 mg/kg. The effect, however, is not very proportional to the quantity of drug injected. Respiration is not affected. The reflex pressure rise during bilateral clamping of the common carotid artery is inhibited by NP-207, but rarely abolished. Adrenaline pressure rise is also less marked after NP-207, but this "adrenolytic" effect is much weaker than what would correspond to the high adrenaline antagonism in the isolated seminal vesicle of guinea pig.

PRELIMINARY CLINICAL INFORMATION OBTAINED FROM THE TREATMENT OF OVER 100 PATIENTS WITH NP-207

INDICATIONS:	The usual Chlorpromazine indications.
DOSAGE:	75 to 500 mg. per day in units of 25 mg. - 10 patients received 800 mg. per day without side effects.
DURATION:	Up to eight weeks.

SIDE EFFECTS: No effect on liver function, sedimentation of the blood, blood pressure or body weight.

Many of the above patients prior to NP-207 treatment experienced side effects with chlorpromazine such as blood pressure changes, Parkinson-like symptoms, increased sedimentation rate of the blood, edema and increased body weight. These symptoms did disappear when the patients were changed to NP-207. When the dosage of NP-207 exceeded 500 mg. per day some patients complained of lassitude.

Bellergal, 3 times daily, 1-2 tablets can avoid the symptoms of ANS disturbances due to the application of Thorazine-like compounds.