WISCONSIN ALUMNI RESEARCH FOUNDATION

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INTER-OFFICE LETTER

CONFIDENTIAL

TO Professor Wm. H. Young

FROM Ward Ross DATE August 20, 1964

Re: Heidelberger 5-FU Patents

Reference is made to our discussions during the past week regarding the above patents. Following is a summary of recent events, together with a bit of background, regarding this matter.

Early in the week of August 10, 1964, our attention was called to an item in the August 10, 1964, issue of F-D-C Reports (copy attached) indicating that HEW had recently licensed a firm known as International Drug Trading, Inc. under the 5-FU patents. Subsequent telephone conversations with Professor Heidelberger and Mr. Barney of Hoffmann-LaRoche indicated that neither of these gentlemen had been aware of the issuance of this license. Issuance of the license was, however, confirmed in a long distance telephone conversation on August 17, 1964, with Mr. Manuel Hiller, Department Patents Officer, HEW. Mr. Hiller advised that HEW had been approached by International Drug Trading, Inc., that a license under the Heidelberger 5-FU patents had been issued to the firm in accordance with HEW Regulations and that this license was based upon rights in the patents derived by HEW from arrangements with the American Cancer Society and Hoffmann-LaRoche. Mr. Hiller had no information as to the contemplated source of the 5-FU drug to be marketed under its license by International Drug Trading, Inc. and noted that he had made it clear, both in the license agreement and in the letter of transmittal, that in issuing the license HEW was in no way approving any drug proposed to be marketed by the licensee. He carefully advised the licensee that FDA clearance of any such drug to be marketed under the license would have to be obtained.

It was our original intention to communicate our viewpoints regarding this matter to our friends in the American Cancer Society and Hoffmann-LaRoche. On reflection, however, and after discussion of the matter with you, we have decided for the moment to keep our observations "within the family." Note, accordingly, that copies of this memorandum are going only to a limited group in the University and WARF.

It is our considered judgment that this action of the Government - issuance of a license under the 5-FU patents to International Drug Trading, Inc. - is highly significant and from it may be drawn a number

of rather important inferences. Before discussing the impact of the issuance of this license, however, it might be well to review the viewpoints of WARF and the American Cancer Society, on the subject of selection of licensees, back in 1957 when the patenting and licensing of 5-FU were first considered.

In all of these discussions, both the Society and WARF, as its agent, took the strong position that after the exclusive period of Roche's license, additional licenses might be granted, but only to reputable drug manufacturers which would be qualified to handle the very difficult synthesis of 5-FU and the distribution of this highly potent drug through the medical profession. WARF's agency agreement with the Society of February 9, 1957, quite clearly spelled out the understanding between the Society and WARF on this point in Section 3, as follows:

> "It is agreed that the Foundation shall grant licenses under the inventions covered hereby only to firms which in the opinion of the Foundation are financially responsible, which conduct their businesses upon sound scientific lines, which are competent to produce the products embodying any of the inventions and which deal in high quality pharmaceutical products."

From the report of the issuance of a preliminary injunction against International Drug Trading, Inc. by the U. S. District Court in Detroit in patent litigation between Pfizer and International, and from the basis upon which the court issued the injunction, it would seem clear that International Drug Trading, Inc. is not a firm which would have qualified as a licensee under the Cancer Society-WARF agreement of February 9, 1957. We have been able to obtain from patent counsel for Pfizer handling the tetracycline infringement suit against International, copies of affidavits and a deposition submitted by Pfizer and upon the basis of which the court in Detroit issued the preliminary injunction. Copy of affidavits in that case (affidavit and supplemental affidavit of Thomas Lodge and affidavit of defendant Cohen) and of letter from Dick Hutz of the patent firm in Wilmington acting for Pfizer, are attached. We have also had the opportunity to study the deposition of Wineberg, one of the defendants in the Detroit suit.

The following conclusions seem quite obvious from the foregoing and the enclosed:

A. International Drug Trading, Inc. and its President, Norman Cohen, have a very poor financial standing - in fact, almost nil.

B. This firm has no research facilities, manufacturing facilities or scientific personnel and is, thus, obviously in no way qualified to carry on the difficult synthesis of 5-FU.

C. The firm has no force of detail men whatever and, therefore, is obviously wholly incompetent to present this drug to the medical profession.

The clear implication to me from the incident described above is that the particular government agency here involved - HEW - apparently intends in its administration of government patents to license "any and all comers" without regard to the standing, capabilities, reputation, or competence of the applicant. Apparently the government has no criteria or requirements to be met by prospective licensees, does little or no screening of applicants for licenses and evidently has no interest in any of the factors that have always concerned WARF as a patent licensing organization and certainly concerned the Cancer Society when we worked out our agency agreement in 1957.

In our discussions of this matter, attention has been called to Section 6.3 of Part 6, "Inventions and Patents (General)" of the HEW Regulations adopted in September 14, 1955, and amended December 4, 1957. That section reads as follows:

> "6.3 Government-owned patents; licensing; dedication to the public. All licenses under patents and pending patent applications for the administration of which the Department is responsible shall be issued by the Secretary. Licenses will be royalty-free, revocable and nonexclusive. Except in unusual cases when determined upon recommendation of the head of the constituent organization that unconditional licensing would be contrary to the public interest, licenses will be issued to all applicants and will contain no limitations or standards relating to the quality of the products to be manufactured, sold, or distributed thereunder. To reduce the need for individual license applications, patents held for unconditional licensing shall be dedicated to the public as may be feasible."
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> (NOTE: Underscoring added).

It has been pointed out that in the absence of a determination in this case by the head of the constituent organization (presumably NIH) "that unconditional licensing would be contrary to the public interest," Mr. Hiller and associates in HEW presumably had no discretion under their own Regulation and had no alternative except to license International Drug Trading, Inc. under the 5-FU patents. It seems to me that the answer to this is twofold, (a) that the head of NIH has been

derelict in failing to rule that in the case of these important 5-FU patents, "unconditional licensing" is contrary to the public interest; and secondly, if in requiring the licensing of "all applicants" this is a bad regulation, then it should be changed.

A final word with reference to the impact of this 5-FU situation on the University and WARF in regard to their future dealings with HEW in invention matters. Two questions should be examined and, hopefully, discussed in the future with HEW. In the first place, would any patent management organization such as WARF, should it be permitted to administer a government developed invention, be subject to Section 6.3 of the Regulations? From WARF's viewpoint, if WARF is going to be required to license "all applicants," it is very doubtful whether WARF will choose to participate in this venture in any manner.

The second question relates to whether HEW has given or is giving any consideration to amending Section 6.3 of the Regulations so that the government itself, in licensing under patents owned by it, will be in a position to exercise at least some discretion in insisting that applicants for licenses be, as a minimum, of decent reputation and competent to properly use the invention.

W. R.

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cc: President Fred H. Harrington

(T&G) **TETRACYCLINE PRELIMINARY INJUNCTION** granted Pfizer by Mich. Federal Judge Thornton against International Drug Trading Inc., Seneca Laboratories Ltd., Norman S. Cohen, Leonard Frank Wineberg, and TMCO Pharmaceuticals, defendants in patent infringement suit filed in Aug. 1963. On July 1, the court ordered defendants to post $100,000 bond within 20 days, or a preliminary injunction would be issued. Judge Thornton found: "The only business of the defendant International is the importation of Tetracycline Hcl capsules, purchased from Seneca, and the sale of such capsules throughout the U. S. International has practically no assets within this district or within the jurisdiction of any other U. S. District Court with which to respond to a judgement of this court, and the financial condition of defendant Cohen is precarious."

¶ In the meantime, at Washington, International Drug Trading's President Norman Cohen disclosed that he has obtained a royalty-free, non-exclusive license from the H-E-W Dept. under the 5-FU patents the govt. took away from the Wis. Alumni Research Foundation and the American Cancer Society last year. Roche, which participated in the development of 5-FU, markets the cancer drug. Cohen said he's aware that no one can make a profit at Roche's current prices for 5-FU, but he's interested in establishing a name as a mfr. He's also working on a dexamethasone IND filing, and he is hunting financing to locate a plant in the Washington area.

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(T&G) **PHA--HOPEFUL APLASTIC ANEMIA DRUG** has touched off a quiet research race in industry. Phytohemagglutinin (PHA), known for some time to cause lymphocytes in vitro to form plasma cells, was administered to humans recently and found promising in treatment of usually fatal aplastic anemia. PHA, believed to act on cell wall to stimulate generalized immune response, would be potentially useful in treatment of hypgammaglobulinemia, leukemia, any condition in which resistance to disease is usually lowered.

¶ A seed extract containing mucoproteins, PHA has been used by immunologists since 1908, so there is no patent possibility on the crude substance. Difco supplies PHA in the U. S., Burroughs-Wellcome in England. Several firms are attempting the chemical characterization of PHA. Abbott, as part of its intensified immunology program, is in the process of closing an agreement for a noted New York researcher to do the biological screening of chemical compounds coming out of the company's work on PHA.

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(T&G) **AMPHETAMINE-BARBITURATE-PSYCHOTOXIC** drug bill hearing, arranged for Aug. 3 to help Sen. Dodd's (D-Conn) re-election campaign, caught the senator uninformed on the opposition. "I don't know anyone who is against it," Dodd said as he finished his prepared statement. Sen. Yarborough (D-Texas), conducting the hearing, read into the record a short filing from the American Medical Assn. (AMA) which opposed the bill on the grounds that "education and appropriate local and state laws supply the answer." The situation is "critical," Dodd commented. "Everyone who knows anything about the problem is of one mind. . . that the law needs to be tightened up."

¶ PMA press released its support of the original Dodd bill, but noted that it may file a statement later on the amended version which added controls over psychotoxic drugs. FDA would classify "some of the tranquilizers which are already causing problems" as "psychotoxic drugs," FDA Com. Larrick told the subcmte. The FDA head objected to a section of the Dodd bill requiring a rule-making hearing before a drug could be added to the "dangerous drug" list. He contended that Federal Register publication of proposals, plus conferences, would prevent delays.