This is a report on the rat reproduction study employing low doses as requested earlier in connection with NDA 11-613 (1/16/64).

Young adult rats, 26 or 27 each sex per group, were administered daily oral doses of 2 and 5 mg/kg during 5-day mating period. Dosing in females was continued through gestation till weaning.

The results showed no difference from controls in most reproduction activities. A slight decrease in conception rate was noted.

| Group (Percent) | Conception rate |
|---|---|
| Control | 55.6 |
| 2 *mg/kg* | 37.0 |
| 5 *mg/kg* | 42.3 |

The effect does not appear dose-related. There were no abnormalities reported in either the parent or the pups.

Comments: The above study seems to indicate that the drug is not teratogenic in the pregnant rat at oral doses of 2 and 5 mg/kg/day, equivalent to 3.3 and 8.3 × human dose of 0.6mg/kg. This is considered adequate to support its use as proposed in the IND.

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MEMORANDUM OF TELEPHONE INTERVIEW

STRASENBURGH LABORATORIES,
*Rochester, N.Y.*
(AF 13-460) *December 8, 1967.*

Between: R. G. Rothwell, M.D.,
Medical Director, Strasenburgh Laboratories, and Robert M. Hodges, M.D.
Director, Office of New Drugs.
Subject: Bionamin—NDA 16-421.

This was a call returned by me at the request of Dr. Rothwell. He wished to inform me that the Bionamin application had recently been amended by 25 volumes of clinical materials and that it had been explained to him that this volume of material constituted grounds for declaring the application withdrawn and resubmitted.

I stated that I had been informed by the reviewing medical officer that Dr. Rothwell made telephone calls at approximately two-week intervals to inquire into the progress of the review of the application and intimated that he was going to continue to call at these intervals presumably with the idea of keeping us on our toes. I stated that I felt that this conduct verged on harassment and was clearly inconsistent with acceptable procedures stated frequently in public by representatives of the FDA, the last occasion being before the Nelson Committee in August by Dr. Goddard. Dr. Rothwell denied that there was any intent of harassment and said that his statement about calling every few weeks was just a little joke. I said that I hoped it was but that this conversation should certainly clear up any misunderstanding. The application would continue to receive expeditious review and if there were any point that required clarification we would be only too pleased to call him. Otherwise, he would hear from us when we had completed our review and the appropriate action had been taken.

ROBERT M. HODGES, M.D.

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FOOD AND DRUG ADMINISTRATION,
*August 28, 1969.*

STRASENBURGH LABORATORIES,
*Rochester, N.Y.*

NDA 16-421

Gentlemen:

1. Reference is made to your new drug application dated June 10, 1966 submitted pursuant to section 505(b) of the Federal Food, Drug and Cosmetic Act for the preparation Bionamin (d-amphetamine, dl-amphetamine and phentermine) capsules.

2. We also acknowledge receipt of your additional communication dated December 20, 1968 addressed to the Acting Director of Bureau of Medicine; his reply of January 9, 1969; and to the meeting held at the FDA on October 2, 1968.

3. On page 2 you state that you were told that what transpired at the May meeting was totally irrelevant. We believe that what was actually stated was that the reviewing medical officer, Dr. Robert Knox, was not present at the May