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RESEARCH**

APPLICATION NUMBER:

60-666

MICROBIOLOGY REVIEW

March 17, 1970

MICROBIOLOGIST REVIEW OF FORM 6# 60-666
(Amendment Submitted February 19, 1970)
(Re: Human Blood Level Studies)

Sponsor: Beecham Pharmaceuticals
65 Industrial South
Clifton, New Jersey

Product: Totacillin (ampicillin trihydrate) for Oral Suspension,
125 and 250 mg./5 ml.

- 1) Two studies are reported. Study 1 tested the product at a concentration of 125 mg./5 ml., and Study 2 tested it at 250 mg./5 ml. The same single dose, 500 mg., was used in each study, e.g., 20 ml. (125 mg./5 ml.) in Study 1, 10 ml. (250 mg./5 ml.) in Study 2.
- 2) Each study employed 12 male volunteers in a two-way, crossover. The reference product was Bristol's Polycillin (ampicillin trihydrate) suspension, 125 mg./5 ml. in Study 1 and 250 mg./5 ml. in Study 2.
- 3) Study 1, 125 mg./5 ml.: The following average blood concentrations (ug./ml.) were obtained:

	<u>0.5 hour</u>	<u>1 hour</u>	<u>2 hours</u>	<u>3 hours</u>	<u>6 hours</u>
Beecham	_____				
Reference	_____				

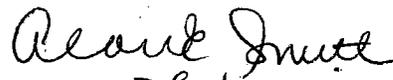
- 4) Study 2, 250 mg./5 ml.: The following average blood concentrations (ug./ml.) were obtained:

	<u>0.5 hour</u>	<u>1 hour</u>	<u>2 hours</u>	<u>3 hours</u>	<u>6 hours</u>
Beecham	_____				
Reference	_____				

- 5) In both studies, blood concentrations obtained with the test product were as high or higher than those obtained with the reference product. Thus adequate bioavailability has been established for the two dosage forms of Totacillin tested.
- 6) It is recommended that this application be approved as submitted.


Edward Kravitz, D.Sc.

cc Orig Form 6 (BD-240)
Dup Form 6 (BD-240) DCS (BD-240)
OND (BD-100) DAD (BD-140)
BD-140/EKravitz/cbs 03/17/70
R/D endorsed by: AESmith-03/17/70


3/19/70

Alan E. Smith, M.D.

October 23, 1969

Deputy Director

Division of Anti-infective Drugs (MD-140)

E. Kravitz, D.Sc.

Division of Anti-infective Drugs (MD-140)

Re: Beecham Pharmaceuticals

Clifton, New Jersey

Form 6: NDA 60-666

IND: 5536

Evaluation of blood level data re: Form 6
(146a.118), Doc. ONS 18782, IND 5536, NDA 60-666,
Beecham Totacillin (ampicillin trihydrate) for oral
suspension.

1. Two studies were performed in children. Serum samples were frozen and airmailed to Beecham for assay. No studies in adults are reported.
2. Study I utilized 24 children. Twelve were 3-5 years old, and twelve were 8-12 years old. Each subject received a single dose of 250 mg. (10 ml.) Totacillin p.o. Blood samples were obtained immediately prior to and at 0.5, 2, and 6 hours after medication in the younger group and at 0, 0.5, 1, 2, 3, and 6 hours in the older group of children.
3. Study II was identical to Study I, except that each child received the 250-mg. dose in 5 ml. There were twelve subjects 2-6 years old and twelve 8-12 years old.
4. The following were among the deficiencies noted: The blood level values obtained varied considerably among the groups of subjects studied. The "fasting state" consisted of only a two-hour minimum of preparative fasting, and food was supplied after the 0.5-hour or 1-hour sample was taken. No crossover comparison with a reference product was done.

Nevertheless, in our judgment, the blood concentrations obtained with this antibiotic preparation were adequate for therapeutic purposes.
5. It is recommended that this application be approved as submitted.

Edward Kravitz, D.Sc.

cc:

Orig. Form 6 (CC-100)

Dup. Form 6 (CC-100)

CC-100

Orig. IND

Dup. IND

Trip. IND

MD-100

MD-140

MD-14; EKravitz/MD-140/mhl 10-7-69

Typed: 10-23-69

R/D init. by AESmith 10-8-69