AIR1 941130 064ca

Ø388

DEPARTMENT OF THE AIR FORCE
DAVID GRANT USAF MEDICAL CENTER (MAC)
TRAVIS AIR FORCE BASE, CALIFORNIA 94535

500

REPLY TO ATTN OF: SGMC

SUBJECT: Proposal for Clinical Investigation. The effects of perhexiline maleate upon regional myocardial perfusion and the extent of transient myocardial ischemia as assessed by potassium-43 myocardial perfusion imaging.

TO: SG

Thru: SGHS
SGE

1. Perhexiline maleate has been demonstrated to be effective in reducing the frequency and severity of exercise induced angina pectoris. The mechanism of action of this agent is unclear. A consideration for mode of action is that the drug reduces myocardial ischemia when a given stress is imposed on the heart, rather than acting by reducing myocardial oxygen demands at a given work load as is the case with currently available agents. Myocardial perfusion scanning with potassium-43 allows identification of myocardial ischemia and measurement of the extent of myocardial ischemia during angina pectoris. The research protocol herein submitted is designed to investigate the effectiveness and mode of action of perhexiline maleate by, (a) positively identifying test subjects as having myocardial ischemia by performing exercise potassium-43 myocardial perfusion scans, (b) assessing the effect of the drug on the subjects exercise capacity by quantitative treadmill exercise testing, and (c) assessing the effect of the drug on the extent of regional myocardial ischemia by potassium-43 myocardial perfusion scans. Perhexiline maleate has been shown to be a safe agent in animal studies and in use in a large number of human subjects during previous Phase II investigations.

2. Bibliography is attached. No previous studies similar to the one here proposed have been accomplished.

3. Technical approach: See attached protocol. Treadmill exercise testing as utilized in this study is a standard test used both for screening large populations for evidence of ischemic heart disease, and for functional evaluation of patients with known coronary heart disease. It has been routinely used in determining the response of patients to therapeutic maneuvers. A physician is always in direct supervision of the exercise test and all required emergency equipment is on hand. The radiation dose received in potassium-43 myocardial scanning is well within acceptable diagnostic limits, even with multiple studies being accomplished.

4. Equipment and supplies: All equipment necessary for completion of this study is on hand. All required expendable supplies related to the conduct of this study will be provided directly by Merrell-National Laboratories, the developers of perhexiline maleate.

5. Investigation Schedule:
   a. Investigation will begin as soon as approval of this protocol is received.
   b. Total duration of the investigation will be approximately nine months.

c. See protocol for individual patient time schedule.
d. Completion is anticipated by June 1974. Delay in approval is the primary factor which may influence completion date.

6. Volunteers for this investigation will be fully informed of the purpose, nature, and possible adverse effects of the study, as per AFR 169-8. "Consent of Volunteer" form is attached.

7. FDA form FD-1572 is attached.

8. Personnel Data:
a. Medical Center Commander: Brigadier General Evan W. Schear, USAF, MC
b. Investigator: Lt Colonel M. D. Flamm, USAF, MC
Associate Investigators: Colonel R. L. McGowan, USAF, MC
Colonel N. D. Martin, USAF, MC
Lt Colonel L. P. Koop, USAF, MC
Major B. L. Zaret, USAF, MC
Major S. L. Savran, USAF, MC
Master Sergeant H. P. Wells, USAF
c. Principal investigators curriculum vitae are attached.

9. Manpower:

1	Lt Colonel	AFSC	T9386C	50 hours off duty time
1	Colonel	AFSC	T9386C	50 hours off duty time
1	Colonel	AFSC	W9386R	30 hours off duty time
1	Major	AFSC	9386C	20 hours off duty time
1	Lt Colonel	AFSC	9386	20 hours off duty time
1	Major	AFSC	9386	50 hours off duty time
1	Master Sgt	AFSC	90970	30 hours duty time, 60 hours off duty time
1	Sergeant	AFSC	91630	60 hours duty time

MELVIN D. FLAMM, JR., LT COL, USAF, MC
Chief, Cardiology Section

5 Atch:
1. Bibliography
2. Protocol
3. Consent of Volunteer form
4. FDA for FD-1572
5. Curriculum Vitae (4)