Appendix 7

Pilot Study To Test Feasibility of Obtaining Valid Case and Control Data in Idiopathic Thromboembolic Disease

P. E. SARTWELL, M.D., A. T. MASI, M.D., AND J. W. LONG, M.D.

An epidemiologic pilot study was designed and conducted under contract with the Food and Drug Administration at the Johns Hopkins School of Hygiene and Public Health, Department of Epidemiology. A report of the completed pilot study and specific recommendations for the major study follows.

The primary objectives of the pilot study were:

(*a*) To define the problems inherent in testing the hypothesis that oral contraceptives serve as a causative factor in thromboembolic diseases in women not otherwise predisposed to these diseases.

(*b*) To develop the methods and procedures that could best meet the needs of the study performance.

(*c*) To test the validity and practicality of these methods, and to coordinate them for maximum yield of pertinent data.

(*d*) To evaluate the feasibility of the study design in its entirety.

(*e*) To interpret the results of the pilot phase and form conclusions upon which appropriate recommendations can be based for a definitive study if indicated.

Copies of the clinical record abstraction form and interview questionnaire which were developed during the pilot study and tabulations of the results follow.

Design of the Study

A. Final diagnosis of all patients discharged alive from the Johns Hopkins Hospital from 1963–65 were obtained.

B. After careful review, cases of idiopathic thromboembolism in married women were selected.

C. These were controlled with twice the number of carefully matched patients selected from a group whose discharge diagnoses would not remotely be related to thromboembolic disease.

D. Each of the selected patients was extensively interviewed with the objective to obtain in a casual but accurate fashion data regarding oral contraceptives.

Summary and Conclusions

This pilot study has demonstrated that the study design is feasible and can be expected to furnish valid case and control data necessary to achieve an acceptable answer to the hypothesis stated in the study proposal, and to do so within practicable limits of time and cost. It was possible to obtain satisfactory completion of interview questionnaires on all cases and controls selected.

It is desirable that the initial case selection for analysis be somewhat broader than the limited few that would be designated restrictively as "purely idiopathic"; the final case selection should be the result of deliberate and searching appraisal under supervision of the principal investigators. It is desirable to consider the opinions of an advisory group regarding the criteria to be used to define "idiopathic." Such a group should include experts in the fields of cardiovascular disease, peripheral vascular disease, hematology, endocrinology, and metabolic disease.

It is presently considered that if a main study is to be done it should draw cases and controls from approximately 20 large hospitals (the size of Johns Hopkins Hospital or larger), which it is estimated should yield about 200 cases and an equal number of controls. Such a study could possibly be completed in 2 years. The basis for this estimate is that the Johns Hopkins Hospital yielded 10 idiopathic cases, constituting about 1 case per 10,000 discharges for all cases, or 10 percent of the