

The hearings undertaken by the Monopoly Subcommittee of the Select Committee on Small Business have helped delineate many of the issues identified in this report, and we appreciate your interest in these important and difficult topics.

Sincerely,

BOB FINCH, *Secretary*.

Enclosure.

RESEARCH ON THE MEDICAL EFFECTS OF ORAL CONTRACEPTIVES

A wide variety of medical effects of oral contraceptives have been identified and have received attention in the medical and general literature. In spite of the large number of publications on these subjects, it still is not known if the changes which have been observed signify actual harm to the health of women and their children. The only exception is thromboembolism which is now thought to increase with oral contraceptive use.

A great deal of new information is required and has been delineated in two reports of the Advisory Committee on Obstetrics and Gynecology of the Food and Drug Administration, and at hearings before the Monopoly Subcommittee of the Select Committee on Small Business. The important questions which have been asked include the following: First. Do the various functional and tissue changes which have been observed signify actual harm to women, or to children conceived after discontinuing oral contraceptives? Second. What specific formulations and dose levels provide the best balance between safety and efficacy? Third. What prescribing practices do physicians employ for oral contraceptives and what aftercare is provided?

This report was prepared at the request of Senator Gaylord Nelson by scientists at the National Institutes of Health and reviewed by several experts outside NIH who are also concerned with these issues. The report begins with a review of research now supported by the Department of Health, Education, and Welfare, and by private non-profit agencies. The report notes that research on oral contraceptives is related to the broader and potentially more important field of contraceptive development, and concludes with a detailed outline of a research plan on oral contraceptives for the coming years which is consistent with the ability of the scientific community to expand investigations in these fields. The report does not examine organizational issues and is limited to the presentation of types of research underway and what is required.

DIFFICULTIES IN RESEARCH ON ORAL CONTRACEPTIVES

It is important to recognize that research on these topics is unusually difficult and that the interpretation of the data is often controversial. Indeed, there are some questions which may be impossible to answer. For instance, the constituents of oral contraceptives and their doses change with time, and it may be impossible to ascertain with certainty the effects of some of the agents now in use since in several years they may no longer be employed.

One reason research on oral contraceptives is difficult is the extended lapse of time required to answer some of the questions asked. An example is the possible relationship between oral contraceptive use and the development of cancer. It is well known that most agents proven to cause cancer in humans have a latent period of approximately ten years. For this reason, it has been necessary to wait until now to initiate studies of the possible effects of oral contraceptives on breast cancer. The initiation of such studies earlier would probably have produced negative results. Another difficulty relates to the large number of patients required to answer some questions. For example, in order to establish if oral contraceptives cause a doubling in the incidence of breast cancer, two groups of women must be followed, one on oral contraceptives and one as control, and each group must number about 25,000. Comparable studies of carcinoma of the endometrium would require 85,000 women in each group.

A third reason such studies are difficult is the simple fact that there are a large number of effects, many of which are interrelated and deal with fundamental biological processes which are often incompletely understood. The relationship between oral contraceptives and sugar metabolism is an example. It has been observed that oral contraceptives appear to alter the way the body handles sugar but the changes which have been observed are subject to different interpretations by different experts. Indeed, there is controversy concerning the proper definition of diabetes which some have suggested may be induced by the use of oral contraceptives.