Appendix 2

Report of the Task Force on Carcinogenic Potential

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The available prevalence and incidence rates of cancer of the uterine cervix, cancer of the endometrium, and cancer of the breast were reviewed in order to establish, as near as possible, the expected normal rates for these cancers in the human female.

All of the published and submitted data on patients who have received any of the estrogen-progestogen combinations for contraceptive purposes over a period of time were reviewed.

The animal experiments, published and some unpublished, using these hormonal agents, or similar agents, as they relate to the production of malignancy or the influence on an existing malignancy, were studied.

The following observations and conclusions were made:

Cancer of the Uterine Cervix

Dysplasia, carcinoma in situ, and invasive cancer were considered. The importance of the geographic location and of the socioeconomic level of the population sample were very evident: for example, the prevalence of carcinoma in situ and invasive cancer in Puerto Rico was almost six times that of a Metropolitan New York group composed of women, for the most part, from a higher socioeconomic level. Another important factor was the average age of women showing these changes: roughly 35 years for dysplasia, 40 years for carcinoma in situ, and 47 years for invasive cancer (tables 1–7).

The data from the various study groups using contraceptive pills were difficult to analyze for the following reasons:

1. Initial cytological status was not given in many instances and in others patients with suspicious or positive Papanicolaou cytology were admitted to the study.
2. The various methods of collecting cytological specimens and the personal equation in reading and reporting any changes make standardization of data difficult.
3. The frequent absence of histopathology after cytologic suspicion was found.
4. The preponderance of patients in the age group before 35.
5. The relatively small number of patients followed regularly and thoroughly for 4 years or more.

In the data submitted there is no evidence of any increased incidence of premalignant or malignant changes in the uterine cervix which could be attributed to the use of the contraceptive pills in this relatively short time interval (tables 8–13). Any valid conclusion must await accurate data on a much larger group of women studies for at least 10 years. Also, in the data, there is no evidence to support the statement which has been made—that the use of the contraceptive pills may have a protective effect against the development of malignancy of the uterine cervix.

One study, in need of supporting evidence from other investigators, may be significant. This study showed an appreciable increase of coccoid bacteria, Trichomonads, and fungi in women using contraceptive pills for a year or more compared to a matched control group. This alteration in the microbiological content of the genital tract might be related to the use of the pills and could account for some increase in such cytological reports as atypical cells or class 2 Papanicolaou.

Uterine Endometrial Malignancy

Endometrial carcinoma is primarily a disease of the postmenopausal years and only 5 to 8 percent of these occur before the age of 40.

In the data submitted the paucity of endometrial biopsies as a routine followup procedure, the limited number of women more than 40 years of age, and the short duration do not permit drawing any conclusions relative to the effect, either