as biopsy specimens are taken progressively later during the therapeutic course. Finally, late in the course, the predecidual reaction already referred to occurs and this type of endometrium is usually maintained without breakdown or bleeding for a prolonged period if proper Enovid-E administration is continued.

ACTION ON GONADOTROPIN EXCRETION. It has been clearly demonstrated in animals that Enovid administration reduces the gonadotropin content of and secretion by the anterior pituitary gland; a similar action has been demonstrated[58] in man. Pincus[57], and Kupperman and Epstein[59] report a sharp reduction in gonadotropin excretion by women during Enovid administration. Suppression of gonadotropins readily explains the observed effects of the drug.

Additional details of clinical and laboratory observations are included in Searle Physicians' Product Brochure No. 67.

Essential Information for Physicians on the Clinical Application of Enovid-E

1. PRESCRIBE one tablet daily beginning on day 5 of the cycle and continuing through day 24. Begin medication on day 5 *whether or not* menstrual flow has ceased.

2. Admonish regarding regularity of taking medication as directed. Regularity applies not only to the days of the cycle but also to the time of day that the tablet is taken. A tablet taken in the morning of one day and another in the evening of the next day may result in an interval of thirty-six hours between doses. If a tablet is forgotten, it should be taken when remembered, but the regular tablet for that day also should be taken at the regular time.

3. Instruct the woman to increase the dose for five days if spotting or breakthrough bleeding occurs. If the spotting is very slight, she may ignore it with the expectancy that it will not occur in later cycles.