epithelium into a ciliated and secretory state (Brenner and Slayden 1995). Progesterone gradually suppresses estrogen-stimulated oviductal differentiation. In contrast to the oviduct and endometrium, the cervix and vagina of different nonhuman primate species vary extensively (Hafez and Jaszczak 1972). For instance, the cervix of women is typically short with a straight canal; baboons display a longer cervix, also with a straight canal. In contrast, macaques possess a large cervix with a striking sigmoidal flexure. The torturous nature of the cervix of macaque complicates transcervical procedures including noninvasive biopsies and hysteroscopy. Also like the oviduct, the cervix of macaques displays ciliated cells that increase in number during the proliferative phase of the menstrual cycle (Jaszczak and Hafez 1973).

2 Use of Artificial Cycles

The menstrual cycle consists of an estrogen-dependent "follicular" or "proliferative phase" and a P_4-dependent "luteal" or "secretory phase." NHPs including macaques (Slayden and Brenner 2004), vervets (Carroll et al. 2007), and baboons (Cox et al. 2000) have been ovariectomized and treated with subcutaneous capsules that release E_2 and P_4 to recreate the pattern and level of serum E_2 and P_4 that occurs during the natural cycle (Slayden and Brenner 2004). A standardized artificial cycle protocol (Slayden and Brenner 2004) has been developed for macaques where ovariectomized animals are treated with a subcutaneous 3–5-cm E_2-filled Silastic capsule for 14 days and then leaving the E_2 capsule in place, a 6-cm subcutaneous P_4-filled capsule is placed for 14 days. Removal of the P_4 capsule results in menstruation and completes the cycle.

The "artificially cycled" animals display endometrial histology that is identical to the natural cycle (Slayden and Brenner 2004). For instance, E_2 during the artificial follicular phase drives epithelial cell proliferation and P_4 during the artificial luteal phase-stimulated glandular secretory differentiation. It is noteworthy that a brief period of glandular cell proliferation occurs in the endometrial basalis zone during the artificial luteal phase (Padykula et al. 1989).

Artificial menstrual cycles appear to be physiologically competent because it is reported that pregnancy can occur in ovariectomized artificially cycled macaques (Hodgen 1983). The artificial cycle protocol produces well-defined levels of E_2 and P_4, and therefore, these animals are useful for pharmacodynamic evaluation of steroid antagonists.

3 Induction of Menstruation

Old World NHPs including baboons and macaques menstruate at the end of each cycle similar to women. During menstruation the upper (luminal) half to two thirds of endometrium is shed. In the macaque, treatment of E_2-primed animals with P_4 (>1 ng/ml in serum), for at least 3 days, is required to prime the endometrium for