U.S. Food and Drug Administration (FDA) regulations state that “[t]his part (21 CFR 312) does not apply to the use in the practice of medicine for an unlabeled indication of a new drug product approved under part 314 or of a licensed biological product.” 21 CFR 312.2(d). If in the treatment of individual patients, physicians use an approved, marketed product for an indication not in the approved labeling as part of the “practice of medicine,” 21 CFR 312 is not applicable. Because 21 CFR 312 is not applicable, this type of use does not require the submission of an Investigational New Drug application (IND) or review by the Institutional Review Board (IRB).

The investigational use of approved marketed products differs from the situation described above. Clinical investigation means “any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.” 21 CFR 312.3(b). If the activity is a clinical investigation, IRB review and approval is required. Compliance with 21 CFR 312, including submission of an IND, is required unless the criteria for exemption are met. 21 CFR 312.2. Even if the clinical investigation is exempt from 21 CFR 312, the exemption provisions still require compliance with 21 CFR 56 and the informed consent requirements in 21 CFR 50. See the Human Research Protection Program Manual 7-1 “Investigational Drugs and Devices” for further information on INDs.