

INFORMATION SHEETS

Guidance for Institutional Review Boards and Clinical Investigators 1998 Update

"Off-Label" and Investigational Use Of Marketed Drugs, Biologics, and Medical Devices

"Off-Label" Use of Marketed Drugs, Biologics and Medical Devices

Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgement. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. Use of a marketed product in this manner when the intent is the "practice of medicine" does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by an Institutional Review Board (IRB). However, the institution at which the product will be used may, under its own authority, require IRB review or other institutional oversight.

Investigational Use of Marketed Drugs, Biologics and Medical Devices

The investigational use of approved, marketed products differs from the situation described above. "Investigational use" suggests the use of an approved product in the context of a clinical study protocol [see 21 CFR 312.3(b)]. When the principal intent of the investigational use of a test article is to develop information about the product's safety or efficacy, submission of an IND or IDE may be required. However, according to 21 CFR 312.2(b)(1), the clinical investigation of a marketed drug or biologic does not require submission of an IND if all six of the following conditions are met:

- (i) it is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
- (ii) it is not intended to support a significant change in the advertising for the product;
- (iii) it does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- (iv) it is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
- (v) it is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and

(vi) it does not intend to invoke 21 CFR 50.24.

For additional information on whether or not an IND or IDE is required in a specific situation, contact:

For DRUG PRODUCTS contact:
Drug Information Branch (HFD-210)
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
301-827-4573

For a BIOLOGICAL BLOOD product, contact:
Office of Blood Research and Review (HFM-300)
Center for Biologic Evaluation and Research
Food and Drug Administration
1401 Rockville Pike
Rockville, Maryland 20852
301-827-3518

For a BIOLOGICAL VACCINE product, contact:
Office of Vaccines Research and Review (HFM-400)
Food and Drug Administration
8800 Rockville Pike
Bethesda, Maryland 20892-0001
301-827-0648

For a BIOLOGICAL THERAPEUTIC product, contact:
Office of Therapeutics Research and Review (HFM-500)
Food and Drug Administration
1451 Rockville Pike
Rockville, Maryland 20852-1420
301-594-2860

For a MEDICAL DEVICE product, contact:
Program Operations Staff (HFZ-403)
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850
301-594-1190