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New FDA Authority to Require Postmarketing Studies and Clinical Trials

The recently enacted Food and Drug Administration Amendments Act of 2007 adds new section 505(o) to the Federal Food, Drug and Cosmetic Act, authorizing the Secretary (hereinafter "FDA") to require postmarketing studies and clinical trials of drugs and biologics under certain circumstances.¹ While the legislation pertains to both "studies" and "clinical trials," these terms are not defined.

Subject to certain limitations described below, these provisions permit FDA to require a sponsor to conduct either postapproval study(s) or clinical trial(s) based on scientific data, including information regarding chemically-related or pharmacologically-related drugs. Required studies or clinical trials must be for one of three specified purposes:

- (1) To assess a known serious risk related to the use of the drug (a "serious risk" is a risk of a serious adverse drug experience, *i.e.*, one that results in death, inpatient hospitalization or prolongation of hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly or birth defect; one that places the patient at immediate risk of death; or one that may jeopardize the patient and may require a medical or surgical intervention to prevent any of the preceding outcomes).
- (2) To assess signals of serious risk related to the use of the drug (a "signal of a serious risk" is information related to a serious adverse drug experience associated with use of a drug and derived from a variety of sources, including clinical trials, adverse event reports, postapproval studies, peer-reviewed literature, etc).
- (3) To identify an unexpected serious risk when available data indicates the potential for a serious risk (an "unexpected serious risk" is a serious adverse drug experience that is not listed in the labeling for the drug, or that may be symptomatically and pathophysiologically related

¹ Previously, FDA's authority to require postmarketing studies was more limited (e.g., products approved in accordance with the accelerated approval provisions (21 U.S.C. § 356(b)(2)(A); 21 C.F.R. §§ 314.510, 601.41); products approved on the basis of animal efficacy data because human efficacy studies are not ethical or feasible (21 C.F.R. §§ 314.610(b)(1), 601.91(b)(1)); and pediatric studies under the Pediatric Research Equity Act of 2003).



to an adverse drug experience listed in the labeling, but that differs in terms of severity, specificity, or prevalence).

FDA may not require a postapproval study unless the Agency first determines that neither the existing postmarketing reports submitted under Section 505(k)(1) (*i.e.*, adverse experience reports and annual reports) nor the postmarket risk identification and analysis system that the Agency will create under new Section 505(k)(3)² will be sufficient to satisfy the purpose of the proposed study (*i.e.*, purposes (1) through (3) noted above). Similarly, FDA may not require a postapproval clinical trial unless FDA determines that a postapproval study or studies will not be sufficient to satisfy the purpose of the proposed clinical trial.

FDA may require such studies or clinical trials for already-approved drugs only if FDA becomes aware of new safety information. “New safety information” is a broadly defined term encompassing information derived from a variety of sources, including a clinical trial, an adverse event report, a postapproval study, peer-reviewed literature, or “other scientific data deemed appropriate” by FDA that pertains to either: (a) a serious risk or unexpected serious risk (as defined above) associated with use of the drug that FDA has become aware of since the drug was approved, since the risk evaluation and mitigation strategy³ was required, or since the last assessment of the approved risk evaluation and mitigation strategy, or (b) the effectiveness of the approved risk evaluation and mitigation strategy obtained since the last assessment of the strategy.

Sponsors may appeal a requirement to conduct a study or clinical trial using “dispute resolution procedures established by the Secretary in regulation or guidance.” It is unclear whether existing dispute resolution mechanisms may be employed or whether new procedures specific to this new authority are to be developed.

Sponsors must submit a timetable for completion of required studies and clinical trials and must periodically report to FDA on the status of such studies or clinical trials.

² The legislation requires FDA to develop, in consultation with experts over the course of several years, a new system of postmarket risk identification and analysis that links and analyzes safety data from multiple, disparate sources (*e.g.*, adverse experience reports, electronic data maintained by the Federal Government under the Medicare and VA health care systems, electronic data maintained by the private sector).

³ Other provisions of the Food and Drug Administration Amendments Act of 2007 add to the Federal Food, Drug and Cosmetic Act new section 505-1 authorizing FDA to require risk evaluation and mitigation strategies (commonly referred to in the past as risk management plans or risk minimization action plans) when such is necessary to ensure that the benefits of the drug outweigh the risks.



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Violations of new Section 505(o) are subject to civil monetary penalties of up to \$250,000 per violation (limited to \$1,000,000 for all violations adjudicated in a single proceeding). Enhanced penalties (up to \$10,000,000 total) are available in cases of violations continuing after FDA has provided written notice of the violation.