CPG Sec. 470.100 Orders for Post-Approval Record Reviews

BACKGROUND:

This document states the Food and Drug Administration's policy and procedures for the issuance of orders to conduct record reviews for approved new drug products for human and animal use.

During the generic drug investigations the agency encountered some problems that could not be addressed with traditional legal tools. One such problem involved situations where omissions, inconsistencies, untrue statements of material facts, or outright fraud were found in records (e.g., biobatch manufacturing records) submitted as part of some ANDAs (for human use). Another problem involved departures from approved manufacturing procedures. In these instances, where only a few applications are implicated, FDA can readily initiate action against specific products found to have been approved on the basis of false or incomplete information, or which are not made in accordance with approved procedures. However, where many applications are implicated, the sheer volume of records which must be reviewed makes it difficult to determine how many products are involved.

In the 1989 generic drug cases, the affected firms cooperated by engaging qualified outside consultants to review all records, and report results to FDA. Absent such voluntary cooperation, the agency may have to issue orders requiring firms to conduct such reviews.

The agency has concluded that it has a legal basis for requiring drug manufacturers to conduct and report post-approval record reviews under authority of Sections 505(k), 505(e), 512(e), 512(l), 512(m)(4), 512(m)(5), 701(a), 704(a) of the Federal Food, Drug, and Cosmetic Act (the Act) and the Current Good Manufacturing Practice Regulations for drugs that are enforceable under Section 501(a)(2)(B) of the Act. Sections 505(k), 512(l), and 512(m) of the Act sanction such orders on the basis of a finding that such records and reports are necessary in order to determine, or facilitate a determination, whether there is or may be ground for invoking Sections 505(e), 512(e), and/or 512(m)(4).

POLICY:

The FDA may issue an order, requiring a records review and report, where there are questions about the safety or effectiveness of an approved drug, or about the truth or falsity of information submitted in support of the original application, in order to determine whether or not such questions are serious enough to warrant withdrawal of the application approval. Such questions may arise, for example, from findings of noncompliance with approved manufacturing procedures, untrue statements of material facts, fraud, or application omissions and inconsistencies. Such orders shall afford the applicant an opportunity to respond informally to the basis for the order.

REGULATORY ACTION GUIDANCE:

Recommendations for a post-approval record review order may be made by field offices in the appropriate division of the Office of Pharmaceutical Quality Operations (OPQO) or scientific review divisions in accordance with the above policy.

Recommendations initiated by field offices in the appropriate division of OPQO should be forwarded to the CDER or CVM compliance office. Recommendations initiated by review divisions within the CDER Office of Generic Drugs, the Office(s) of Drug Evaluation (I or II), or the CVM Office of New Animal Drug Evaluation shall be made in consultation with their respective compliance office and forwarded to the director of the office which approved the application.

The proposed order for post-approval record review should include the following paragraphs (substitute Section 512(l) or 512(m)(5); and 512(e) and/or 512(m)(4) as required):
In accordance with Section 505(k) of the Act, this order requiring a post-approval record review is based on a finding that such records and reports are necessary to determine, or facilitate a determination, whether there is or may be ground to withdraw approval of the drug application(s) covered by this order.

Noncompliance with this order would be ground to withdraw approval of the application(s) under Section 505(e).

The order for a records review and report shall afford the applicant an opportunity to respond informally to the basis for the order and may permit the applicant to engage outside consultants to perform all, or part of, the review. The order shall issue over the signature of the director of the office which approved the application. A copy of the order should be sent to the program division director of the field office in the appropriate division of OPQO.

Where the applicant fails to comply with the order for records review, or where the results of such a review indicate that withdrawal of application approval may be warranted, existing procedures for initiating withdrawal of application approval apply.

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