which was dated March 3, 1988, failed to meet ANDA specifications. KV records also showed that the stability test result KV reported in its annual report was the average of two retests performed by KV on April 19, 1988.

In the June 6, 1989, annual report, KV falsely reported that lot V9133 conformed to U.S.P. specifications in a content uniformity test conducted 6 months after the lot was manufactured. KV's records, however, showed that the first 10 capsules of the lot failed U.S.P. relative standard deviation (RSD) specifications and contained no evidence that KV tested an additional 20 capsules. Without further testing of an additional 20 capsules, the batch failed to meet U.S.P. specifications. Therefore, lot V9133 did not conform to U.S.P. specifications.

In its May 8, 1990, annual report KV reported that lot V9432 passed a 24-month stability test in April 1989. Records at the firm, however, show that the lot failed its stability test on May 15, 1989. During retesting on June 5, 1989, the lot passed stability testing and met assay specifications twice. KV averaged the passing tests and then improperly averaged that resultant average with the failing result. This final average was reported as a passing result in the May 8, 1990, annual report.

KV reported in its May 8, 1990, annual report that lot V9527 met ANDA assay specifications, purportedly in an 18-month stability test of nitroglycerin conducted in February 1989. Records at the firm, however, show that the lot failed the first stability test on May 15, 1989. The lot passed the second and third stability tests, done on June 5, 1989. KV improperly averaged the three test results and reported in the annual report the average as a passing result. Furthermore, the retests were conducted 21 and 22 months after the batch was manufactured, but KV reported in the annual report that the tests were conducted at 18 months.

KV reported in an August 6, 1992, letter to the agency that lot V9991 passed the 24-month content uniformity test and conformed to U.S.P. specifications. Records at the firm, however, showed that the group of capsules tested failed because its RSD was above U.S.P. RSD specifications. In addition, the results of two individual capsules were below U.S.P. specifications. According to U.S.P. specifications, such failing results require testing an additional 20 capsules, which KV did not do. Therefore, this lot did not conform to U.S.P. specifications.

KV reported in an August 1, 1990, supplement that lot V9527 passed a 12-month stability test for nitroglycerin. Records at the firm, however, show that the lot failed a stability test on September 22, 1988, and thus did not meet the ANDA assay specifications. KV then conducted two retests on October 4, 1988. KV selectively reported the result of only one of the passing retests, and also falsely reported the date of the test as August 15, 1988, which was 2 months before the actual test date.

D. Conclusion

On the basis of the foregoing findings, the Director finds that KV submitted untrue statements of material fact in the AADA and two ANDA's listed above, and, therefore, proposes to withdraw the approval of these applications under section 505(e)(5) of the act.

III. Evidence That the Drugs Lack Substantial Evidence of Effectiveness

Sction 505(e)(3) of the act provides that approval of an AADA or an ANDA shall be withdrawn if, on the basis of new information, evaluated together with the evidence available when the application was approved, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have. Because KV submitted untrue statements regarding the stability of its product in annual reports, supplements, and amendments to its applications, the agency cannot be assured of the products' stability. Moreover, the agency can no longer be assured as to the accuracy and validity of any of the data used to support approval and continued approval of these applications. Thus, the discovery of these untrue statements constitutes new information demonstrating that there is a lack of substantial evidence that the drugs will have the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in their labeling.

The reliability of stability data is of particular concern when, as here, the results of multiple stability tests, both reported and unreported, indicate a significant history of stability problems. Without reliable stability data, FDA cannot be assured that a drug will maintain the efficacy upon the basis of which the drug was approved. Similarly, in the case of stability problems with generic drugs, FDA cannot be assured that the drug will continue to be bioequivalent to the innovator drug over a given period of time. In either case, an unstable drug product may be more or less potent than the efficacy parameters that the agency approved.

Because there are no reliable data or information to demonstrate the stability and bioequivalence of these products to the listed drugs, the three products listed above lack substantial evidence of effectiveness.

IV. Proposed Action and Notice of Opportunity For a Hearing

The Director has evaluated the information discussed above concerning the filing of untrue statements of material fact by KV and, on the grounds stated, is proposing to withdraw approval of the following AADA and ANDA's:

1. AADA 62–047, Erythromycin Ethylsuccinate Oral Suspension, 200 and 400 mg;
2. ANDA 71–929, Disopyramide Phosphate Extended Release Capsules, 100 mg; and
3. ANDA 86–538, Nitroglycerin Extended Release Capsules, 2.5 mg.

Notice is hereby given to the holder of the AADA and ANDA's listed above and to all other interested persons that, based upon the information discussed above concerning the filing of untrue statements by KV and, on the grounds stated, the Director proposes to issue an order under section 505(e) of the act withdrawing approvals, including conditional approvals, of the foregoing AADA and ANDA's, and all amendments and supplements thereto. The Director finds that: (1) The applications contain untrue statements of material fact; and (2) on the basis of new information before her with respect to the drugs, evaluated together with the evidence available to her when the applications were approved, there is a lack of substantial evidence that the drugs will have the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in their labeling.

In accordance with section 505(e) of the act and 21 CFR part 314, the applicant is hereby given an opportunity for a hearing to show why approval of the AADA and ANDA's should not be withdrawn.

An applicant who decides to seek a hearing shall file: (1) On or before July 26, 1995, a written notice of appearance and request for a hearing, and (2) on or before August 25, 1995, the data, information, and analyses relied on to demonstrate that there is a genuine issue of material fact to justify a hearing. Any other interested person may also submit comments on this notice. The procedures and requirements governing this notice of opportunity for a hearing, a notice of appearance and request for a hearing, submission of information