uniformity of all digoxin products. In addition to inaugurating additional in vivo studies under the extramural contract program, the agency, in its own laboratories, adapted, modified, and validated several dissolution procedures in both acid and water media based on the method originally developed by Dr. Wagner. Samples of digoxin tablets produced by all known manufacturers were obtained for laboratory analysis. A dissolution profile was obtained on all the tablets which met compendial requirements for potency and content uniformity. A satisfactory correlation existed with the available in vivo data.

The USP in conjunction with the FDA have initiated studies to determine the correlation between bioavailability in vivo and the dissolution rate of digoxin tablets in vitro. As a result of the available data from all such studies showing a satisfactory correlation between bioavailability and dissolution, the USP monograph for digoxin tablets has been revised to include a requirement for dissolution. This revision is included in the USP XVIII Sixth Interim Revision Announcement which became effective on November 15, 1973. The dissolution method described in the revision involves the use of a rotating basket in an acid dissolution medium.

The Commissioner has determined that the solution to the problem of the bioavailability of digoxin products will involve three separate but related actions. As a first step, immediate action will be taken to remove from the market those digoxin products which, on the basis of dissolution test results, are not adequately bioavailable. The second action will include procedures to assure that manufacturers conduct the in vivo tests needed to demonstrate the bioavailability of those digoxin