methods show significant differences in dissolution rate are not now available. Until such data are available it is not possible to rule out the usefulness of each method in particular situations or to define the limitations of any method. Once such data is available it is anticipated more stringent dissolution rate requirements will be set. The Commissioner requests that manufacturers who conduct research utilizing the "paddle-water" and "paddle-acid" methods, particularly in comparison with the method in the USP, submit any data obtained using these methods to the Food and Drug Administration pursuant to section 505(j) of the act.

Available evidence shows that digoxin tablets which have a dissolution rate below the compendial requirement (i.e., 55 percent at one hour) when tested by the in vitro method in USP XVIII are not adequately bioavailable when tested by in vivo methods. Correlative in vivo and in vitro data are not now available to predict with certainty the minimum dissolution rate at which biologic availability will be demonstrated. Manufacturers whose digoxin tablets do not now meet the compendial requirements for dissolution may reformulate their product to achieve a dissolution at any rate above the dissolution requirements of the USP, but not more than 95 percent dissolution at one hour or more than 90 percent dissolution at 15 minutes. The Food and Drug Administration recommends that these manufacturers reformulate their products to achieve dissolution of 70 to 90 percent at one hour by all three methods. This recommendation is based on data compiled by the Food and Drug Administration which indicates that when in vitro tests uniformly show dissolution at 70 to 90 percent at one hour by all three methods there is good probability to predict that in vivo tests