at one hour, when tested by the method in the USP, is greater than 95 percent of the assayed amount of digoxin or so that the quantity of digoxin dissolved at 15 minutes is greater than 90 percent of the assayed amount of digoxin are new drugs which may not be marketed without an approved new drug application. Persons intending to market such drugs are required to submit full new drug applications as provided for in § 130.4 (21 CFR 130.4). The application shall include, but not be limited to, clinical studies establishing significantly greater bioavailability than digoxin tablets meeting compendial requirements and dosage recommendations based on clinical studies establishing the safe and effective use of the more bioavailable digoxin product. Marketing of these digoxin products will be allowed only under a proprietary or trade name, established name, and labeling which differs from that used for digoxin tablets that meet all of the requirements in USP XVIII and that are formulated so that the quantity of digoxin dissolved at one hour is not more than 95 percent of the assayed amount of digoxin or that the quantity of digoxin dissolved at 15 minutes is not more than 90 percent of the assayed amount of digoxin.

The Food and Drug Administration is familiar with two in vitro methods ("paddle-water," "paddle-acid"), in addition to that described in the USP, developed to measure digoxin tablet dissolution. These three methods result in data which show significant differences in dissolution in comparative tests on some formulations. Definitive bioavailability data to compare the relative value of each of these methods to predict bioavailability of the few formulations where the