AUC_{O-t} should be equivalent at any dosing interval whether or not steady-state is achieved.

29. Page 17, section III.D. Statistical Analysis, second paragraph. The choice of whether to use untransformed data should be made by the sponsor based on whether transformation is necessary to allow for homogeneity of variance. It should not be determined prior to the study because the data should dictate which transformation, if any, is required.

CVM does not agree with this recommendation. The sponsor has the option to use untransformed or log transformed data, but the decision should be made prior to conducting the study.

30. Page 19, section III.D., second from the last paragraph relating to selection of confidence interval. One comment noted that CVM states that in general the confidence interval for untransformed data should be 80 to 120. Firstly, percent should be specified. Secondly, emphasis should be added that these are general rather than the adamant and steadfast specifications of CVM. The opinion of many statisticians with considerable experience in this field is that the ±20 percent interval is entirely too restrictive. In the animal health market, the potential cost to evaluate generics or combinations may be so great as to preclude bringing a useful drug/combination to the market.

CVM has made the requested editorial changes. However, CVM will continue to accept ±20 percent as the acceptable confidence interval for the pivotal parameters. CVM invites sponsors to submit data to justify broadening the confidence interval for a particular drug.

31. Page 20, section IV.B. Statistical Analysis. One comment noted that for pharmacologic endpoint studies as described, it appears that these studies described are evaluating significant differences rather than statistical equivalence. As such, these pharmacological endpoint studies are not as rigorously designed from a statistical standpoint as classic bioequivalence plasma level studies, inasmuch as differences are being evaluated rather than equivalence. The comment suggested that pharmacological endpoint studies should also be evaluating statistical equivalence, rather than significant differences. In fact, a comparable equivalence testing is alluded to on page 22 regarding clinical endpoint studies, studies which would be expected to be less able to prove equivalence than pharmacologic endpoint studies.

CVM agrees with the comment and has modified the guidance to read as follows:

For parameters which can be measured over time, a time *vs* effect profile is generated, and equivalence is determined with the method of statistical analysis essentially the same as for the blood level bioequivalence study.

For pharmacologic effects for which effect vs time curves can not be generated, then alternative procedures for statistical analysis should be discussed with CVM prior to conducting the study.

32. Page 23, section VI. Human Food Safety Considerations. One comment asked if there is a need for determining a full depletion profile for the generic? The sponsor proposed that a single point tissue residue study completed out to the withdrawal time of the pioneer would be sufficient.

The Center does not agree with the use of a single point tissue residue study at the withdrawal time of the pioneer as a general practice.

A traditional tissue residue depletion study has always been required for generic products where bioequivalence is determined with a pharmacological or clinical endpoint study. The need for a traditional tissue residue depletion profile is expanded in the revised guidance to include blood level bioequivalence studies, because the Center has concluded that, with the exception of those examples listed in section VI. of the guidance, the tissue residue depletion of the generic product is not adequately addressed through bioequivalence studies.

The use of the traditional tissue residue depletion study provides the Center with the data needed to compute a withdrawal period for the drug product in question, using our statistical tolerance limit model, whereby the 99th percentile is calculated with 95 percent confidence. Use of a single point tissue residue study ordinarily would not provide the data needed to use our current model, since the single-point study would not contain sufficient information regarding the variability of the residue depletion profile. Additionally, since the analytical methods approved for regulatory purposes can rarely measure the marker residue at the withdrawal time, a single point residue study at the pioneer withdrawal time would be limited by the efficiency of the regulatory analytical method at the drug concentrations typically seen at the pioneer withdrawal time. When the tissue residue values include negative or zero values (i.e., values below the limit of quantitation for the assay), the number of animals needed in the study will depend on the method variance and the number of zero values, and will vary from drug to drug. It is not possible to predict, a priori, the number of animals that will be needed to provide data of sufficient confidence for a single point tissue residue depletion study to obtain the confidence similar to that seen for the pioneer drug using our traditional residue depletion study design.

The Center will consider the use of a single point tissue residue depletion study in those cases where the regulatory analytical method can be validated and demonstrated to measure reliably residues in the treated animals at the pioneer withdrawal time so that a 99th percentile statistical tolerance limit with 95 percent confidence can be calculated.

A person may follow the guidance or may choose to follow alternate procedures or practices. If a person chooses to use alternate procedures or practices, that person may wish to discuss the matter further with the agency to prevent an expenditure of money and effort on activities that may later be determined to be unacceptable to FDA. Although this guidance document does not bind the agency or the public, and it does not create or confer any rights, privileges, or benefits for or on any person, it represents FDA's current thinking on bioequivalence testing for animal drugs. When a guidance document states a requirement imposed by statute or regulation, the requirement is law and its force and effect are not changed in any way by virtue of its inclusion in the guidance.

Interested persons may, at any time, submit to the Dockets Management Branch (address above) written comments on the document. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The documents and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 17, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–13106 Filed 5–23–96; 8:45 am]

BILLING CODE 4160–01–F

[Docket No. 95N–0212]

Epitope, Inc.; Premarket Approval of OraSure® HIV–1 Oral Specimen Collection Device

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Epitope, Inc., Beaverton, OR, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the OraSure® HIV–1 Oral Specimen Collection Device. FDA's Center for Biologics Evaluation and Research (CBER) notified the applicant, by letter of December 23, 1994, of the approval of the application. A revised approval letter was issued on October 18, 1995.

DATES: Petitions for administrative review by June 24, 1996.

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Sukza Hwangbo, Center for Biologics Evaluation and Research (HFM–380), 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–3524.

SUPPLEMENTARY INFORMATION: On May 9, 1991, Epitope, Inc., Beaverton, OR 97008, submitted to CBER an application for premarket approval of the OraSure® HIV–1 Oral Specimen Collection Device. The device is intended for use in the collection of oral fluid specimens by properly trained individuals for the purpose of testing for the presence of antibodies to human immunodeficiency virus Type 1 (HIV–1). The OraSure® HIV–1 Oral Specimen Collection Device consists of both an absorbent cotton fiber pad treated with a proprietary salt solution and gelatin affixed to a plastic stick, and a preservative solution supplied in a plastic container. OraSure® HIV–1 oral fluid specimens are intended to be used only with the Oral Fluid Vironostika HIV–1 Microelisa System screening test manufactured by Organon Teknika Corp. The device is intended for use with subjects 13 years of age or older.

On December 19, 1992, the premarket approval application (PMA) was referred to the Blood Products Advisory Committee, an FDA advisory committee, for review and recommendation. On June 22, 1994, the PMA was referred to the same advisory committee for discussion of post-approval requirements for surveillance studies.

On December 23, 1994, CBER approved the application by a letter to the applicant from the Acting Director, Office of Blood Research and Review, CBER. In response to additional discussions between the manufacturer and FDA, a revised approval letter was issued on October 18, 1995.

FDA has determined that, to ensure safe and effective use, the device is restricted within the meaning of section 520(e) of the act (21 U.S.C. 360j(e)) under the authority of section 515(d)(1)(B)(ii) of the act (21 U.S.C. 360e(d)(1)(B)(ii)) insofar as: (1) Before shipping the device to any customer, Epitope, Inc., must have on file a ''Letter of Agreement for Physician'' signed by the physician who agrees to assume the outlined responsibilities on behalf of the customer; (2) the administration of the device is restricted to individuals who have been trained in the use of the device according to approved labeling; (3) testing of OraSure® samples for HIV–1 antibodies is restricted to the Oral Fluid Vironostika HIV–1 Microelisa System screening test manufactured by Organon Teknika Corp.; (4) the device is not to be provided to subjects for home use; (5) the device is not to be used to screen blood donors; and (6) prior to specimen collection, a test subject must receive a copy of the subject information sheet. The sale, distribution, and use of the device must not violate sections 502(q) and (r) of the act (21 U.S.C. 352(q) and 352(r)).

A summary of the safety and effectiveness data on which CBER based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CBER's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and procedures regulations or a review of the application and CBER's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under § 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the Federal Register. If FDA grants the petition, the notice will state the issue to be reviewed, the form of review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before June 24, 1996, file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h) (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Biologics Evaluation and Research (21 CFR 5.53).

Dated: May 17, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–13176 Filed 5–23–96; 8:45 am]

BILLING CODE 4160–01–F

Food and Drug Administration

Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). This notice also summarizes the procedures for the meeting and methods by which interested persons may participate in open public hearings before FDA's advisory committees.

FDA has established an Advisory Committee Information Hotline (the hotline) using a voice-mail telephone system. The hotline provides the public with access to the most current information on FDA advisory committee meetings. The advisory committee hotline, which will disseminate current