Dated: May 20, 1975.

By order of the Assistant Secretary for Maritime Affairs.

JAMES S. DAWSON, Jr.,
Secretary.

[FR Doc.75-13634 Filed 5-22-75;8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Part 331]

ANTACID PRODUCTS FOR OVER-THE-COUNTER (OTC) HUMAN USE

Testing Procedures for Antacid Products Generally Recognized as Safe and Effective and Not Misbranded

In the FEDERAL REGISTER of June 4, 1974 (39 FR 19862), the Commissioner of Food and Drugs promulgated a final regulation for antacid products generally recognized as safe and effective and not misbranded (21 CFR Part 331).

The Commissioner determined that an over-the-counter (OTC) antacid product in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions identified in Part 331 and each of the general conditions established in § 330.1 (21 CFR 330.1).

In the FEDERAL REGISTER of May 11, 1972 (37 FR 9464), the Commissioner of Foods and Drugs promulgated procedures governing the review and classification of OTC drug products, under § 330.10 (21 CFR 330.10). The Commissioner may propose on his own initiative to amend or repeal any monograph, or any interested person may petition the Commissioner for such proposal, pursuant to § 330.10(a)(12). A number of drug manufacturers have petitioned that the antacid in vitro testing procedures identified in Subpart C of Part 331 be amended.

One drug manufacturer has commented that the requirement that distilled water identified in § 331.20(p) be used in the antacid in vitro testing procedure is unnecessarily restrictive. Many laboratories use deionized water for analytical purposes. The manufacturer stated that it would be more realistic to specify the use of United States Pharmacopeia (U.S.P.) Purified Water since it may be prepared by either distillation or ion exchange. The manufacturer further indicated that U.S.P. Purified Water has recognized, defined properties that should assist in obtaining uniform results and would avoid problems that could arise if distilled water were used.

It is the Commissioner's intent to require the simplest test that will yield uniform results and not to place unnecessary restrictions on testing procedures unless there is a reasonable basis for such limitations. The Commissioner concurs that use of U.S.P. Purified Water rather than distilled water is a more appropriate requirement, and therefore proposes to amend § 331.20(p) to provide for use of U.S.P. Purified Water.

Other drug manufacturers have petitioned that the temperature requirements in the antacid in vitro test of 25° C±3° be revised to 37° C±3°. The designation of 37° C has been proposed because that is the temperature of the human body and is also used in numerous U.S.P. tests, including disintegration and dissolution rates and the acid consuming capacity for a number of the antacids listed in the U.S.P. The petitioners have submitted data for the ingredient aluminum hydroxide gel showing that the higher temperature produces higher acid neutralizing capacities. However, the data show that the difference in the acid neutralizing capacity of the final product when tested at 25° C and 37° C is not significant.

All the data submitted relate to products containing aluminum hydroxide gel, which has been used for years as an antacid. The OTC Antacid Panel had recognized aluminum hydroxide gel as a slow reacting antacid. Data have now been submitted to show that the percent of aluminum hydroxide gel neutralized when tested at 25° C and 37° C is sufficiently different that a final product which clearly passes the acid neutralizing test does not contain a sufficient amount of aluminum hydroxide gel at 25° C to meet the requirement that each active ingredient must contribute at least 25 percent of the acid neutralizing capacity. At 37° C this requirement of contribution is met.

One manufacturer of aluminum hydroxide gel stated that the pharmaceutical industry is attempting to respond to the monograph requirement by increasing the dosage levels of the active aluminum ingredient and/or to increase the ratio by weight of the nonaluminum alkali moiety to the aluminum hydroxide in a given formula. The manufacturer suggested that this could possibly lead to the inclusion of unnecessary amounts of certain ions such as sodium, magnesium and/or calcium compounds in an effort to "bolster" the initial reaction velocity of a given antacid combination in order to overcome the inhibition of the neutralizing reaction caused by the lower temperature restriction. The manufacturer further stated that consideration should be given to such formulation changes because some consumers of antacid products are restricted in terms of their intake of such ions as calcium, sodium, magnesium and bicarbonates.

The Commissioner recognizes that there may be a benefit from using an effective amount of a slow reacting aluminum hydroxide gel in an antacid, and does not believe that the proposed test should contain a technical restriction which inadvertently precludes such use. The Commissioner, in paragraph 32 of the preamble to the final order establishing an OTC antacid monograph, published in the FEDERAL REGISTER of June 4, 1974 (39 FR 19866), stated:

> The Commissioner agrees that this [temperature] is a variable that can be eliminated and yet not complicate the test. However, during testing, the Food and Drug Administration has shown that there is no difference between 25° C and 37° C. It is more appropriate to use room temperatures since it requires less equipment. The Commissioner has, therefore, concluded that the temperature will be designated at 25° C±3° in the final order.

On further consideration, the Commissioner believes that designating 25° C as the sole test temperature would result in reformulations and product changes which would not benefit the consumer or result in safer or more effective products. Testing by the Food and Drug Administration and that provided by the industry have shown that the difference between 25° C and 37° C of the final products is not significant.

The Commissioner has evaluated the new data submitted and proposes to amend the monograph to provide for the use of 25 or 37° C ±3°, as the test temperature. Data have been provided and reasons shown why it is reasonable to amend the monograph to provide for testing at 37° C as well as 25° C.

Therefore, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 201, 502, 505, 701, 52 Stat. 1040–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948; (21 U.S.C. 321, 352, 355, 371) and under authority delegated to him (21 CFR 2.120), the Commissioner proposes to amend 21 CFR Part 331 by revising §§ 331.20(p) and 331.23 to read as follows:

§ 331.20 Apparatus and reagents.

* * * * *

(p) Purified Water U.S.P.

§ 331.23 Temperature standardization.

All tests shall be conducted at 25° C ±3°, or 37° C ±3°.

Interested persons may, on or before June 23, 1975, file with the Hearing Clerk Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20852, written comments (preferably in quintuplicate) regarding this proposal. Received comments may be seen in the above office during working hours, Monday through Friday.

Dated: May 19, 1975.

SAM D. FINE,
Associate Commissioner, for Compliance.

[FR Doc.75-13577 Filed 5-22-75;8:45 am]

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

[14 CFR Part 75]

[Airspace Docket No. 75-SO-37]

JET ROUTES

Proposed Alteration and Designation

Correction

In FR Doc. 75-11891 appearing on page 19834 of the issue for Wednesday, May 7, 1975, the second line of numbered paragraph 4, pertaining to J-145, reading "Jet