(iii) Analytical and statistical techniques used are of sufficient sensitivity to detect those differences in rate and extent to absorption that are not attributable to subject variability.

(3) Each manufacturer of a drug product subject to this section that is selected by the Food and Drug Administration as the reference material, who has not conducted in vivo bioavailability/bioequivalence studies fulfilling the requirements of this section before (the effective date of the final regulation) shall conduct an in vivo bioavailability study in humans comparing its product (i.e., the reference material) with a solution or suspension of an equivalent amount of the sulfonamides contained in the reference material.

(4) Each manufacturer of a drug product subject to this section shall submit the results of the required in vivo testing to the Food and Drug Administration on or before (180 days after the effective date of the final regulation. The Food and Drug Administration may grant, upon request, an extension of up to 180 days when pilot studies are required before the tests are begun. An extension of time necessary for an initial review of a protocol will be granted by the Food and Drug Administration when a protocol is submitted.

(5) Any manufacturer of a drug product subject to this section who has conducted one or more in vivo bioavailability/bioequivalence studies before the effective date of this section may request an evaluation of the studies to determine whether the studies are adequate and conclusive to ensure the bioavailability/bioequivalence of the drug product in light of current scientific knowledge and methodology. Any such request must contain the new drug application number, the established (generic) name of the product, the dosage form and strength of the drug product, and the date(s) of submission of the pertinent study information contained in the new drug application.

(6) Each manufacturer who holds an approved or pending full new drug application for the drug product and who requests an evaluation of a previously conducted study shall submit the request for evaluation to the Division of Anti-Infective Drug Products (HFD–140), Bureau of Drugs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Each manufacturer who holds an approved or pending abbreviated new drug application for the drug product and who requests an evaluation of a previously conducted study shall submit the request for an evaluation to the Division of Generic Drug Monographs (HFD–530), Bureau of Drugs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

(h) *Modifications.* Alternative methods or modifications to the bioequivalence requirement for in vitro testing as set forth in this section may be used if evidence is submitted demonstrating that the modification will assure the bioequivalence of the drug to an extent equal to or greater than the methods set forth in this section. The data should be submitted to the Director, Division of Biopharmaceutics (HFD–520), Bureau of Drugs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, and must be approved before they are used. Any approved modification will be incorporated into the appropriate guidelines for the drug.

(i) *Reference material and guidelines for testing.* (1) The reference materials to be used in the in vivo and in vitro tests are specified in the "Guidelines for In Vivo Bioavailability Studies for Sulfonamides," and "Guidelines for In Vitro Dissolution Testing for Sulfonamides." The same lot or batch of the test drug product used in the in vitro test and the reference lot that has the highest dissolution in the specified time must be used in the in vivo test unless a manufacturer has conducted, before (the effective date of the final regulation), in vivo tests in humans to demonstrate bioavailability/bioequivalence.

(2) Guidelines for in vivo and in vitro tests of sulfonamides are on file in the office of the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, and are available on request to that office.

Interested persons may, on or before December 18, 1979, submit to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, written comments regarding this proposal. Four copies of all comments shall be submitted, except that individuals may submit single copies of comments. The comments are to be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday.

In accordance with Executive Order 12044, the economic effects of this proposal have been carefully analyzed, and it has been determined that the proposed rulemaking does not involve major economic consequences as defined by that order. A copy of the regulatory analysis assessment supporting this determination is on file with the Hearing Clerk, Food and Drug Administration.

Dated: October 12, 1979.

J. Richard Crout,

Director, Bureau of Drugs.

[FR Doc. 79–32216 Filed 10–18–79: 8:45 am]

BILLING CODE 4110–03–M

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21 CFR Part 331

[Docket No. 79N–0152]

Antacid Drug Products for Over-the-Counter Human Use; Proposed Amendment of Monograph

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The agency proposes to amend the antacid monograph to require that antacid drug products containing calcium and magnesium contain a precautionary statement. Current labeling requirements for OTC antacid drug products are that antacids containing aluminum contain the drug interaction precaution "Do not take this product if you are presently taking a prescription antibiotic drug containing any form of tetracycline." This proposed amendment would require that the labeling of antacids containing calcium and magnesium also contain this same drug interaction precaution for concomitant therapy with tetracycline and its derivatives.

DATE: Comments by December 18, 1979.

ADDRESS: Written comments to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Bureau of Drugs (HFD–510), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301–443–4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 4, 1974 (39 FR 19862), the Food and Drug Administration (FDA) published the final order for OTC antacid drug products generally recognized as safe and effective and not misbranded (21 CFR Part 331). Section 331.30(c)(i) (21 CFR 331.30(c)(i)) requires OTC antacid drug products containing aluminum to bear the drug interaction precaution "Do not take this product if you are presently taking a prescription antibiotic drug containing any form of tetracycline."

This precautionary statement is not the same as the statement presently used for orally prescribed tetracycline drug products. Prescription package insert labeling currently approved for

tetracycline and its derivatives provides the following statement for concomitant therapy with antacids containing aluminum, calcium, or magnesium: "Concomitant therapy: Antacids containing aluminum, calcium, or magnesium impair absorption and should not be given to patients taking oral tetracycline," (Refs. *1* through *4*.) FDA has determined that both OTC and prescription drug labeling should be similar in respect to this drug interaction statement. Therefore, in accordance with § 330.10(a)(12), FDA proposes to amend the antacid monograph to require that antacid drug products containing calcium and magnesium also contain the OTC drug interaction precaution set forth in § 331.30(c)(i).

Available evidence indicates that the most rapid absorption of tetracycline and its derivatives takes place by passive diffusion from the duodenum and ileum (Refs. *5, 6,* and *7*). Many studies have determined that this absorption may be altered as the result of two interdependent factors: first, the chelation of tetracycline with polyvalent metallic cations contained in certain drugs or food (Refs. *8,* through *11*); and second, an increase in gastric pH which in turn augments chelation (Refs. *12* and *13*).

The tetracycline molecule contains numerous sites at which chelation with polyvalent metallic cations can occur. This chelation increases with an increase in the concentration of metallic cations. In in vitro studies of three such polyvalent metallic cations, aluminum, calcium, and magnesium, which are present in OTC antacid preparations, all have exhibited an affinity for the tetracycline molecule (Refs. *7, 12, 14, 15,* and *16*).

More specifically, aluminum forms a chelate through the ionized tricarbonyl methane functional group; magnesium and calcium each form a chelate with tetracycline through its phenolic diketone function (Refs. *5* and *12*). Of the three cations, aluminum has been shown to form the most stable complex, while magnesium and calcium form much weaker ones. When such a chelate is formed, the diffusion rate of tetracycline in solution is depressed, even if the chelate formed is water soluble (Refs. *8, 12, 14, 15,* and *16*).

Evidence suggests that chelation is dependent upon the pH of the system. At a low pH there is little chelate formation, while significant chelate formation occurs at high pH levels (Ref. *12*).

Increased gastric pH may also act independently of chelate formation to decrease the absorption of tetracycline. A study by W. H. Barr, et al., (Ref. *13*) showed a 50 percent reduction in tetracycline absorption when gastric pH was increased by administration of sodium bicarbonate as compared to the absorption recorded by the use of tetracycline alone. Sodium is a monovalent cation and cannot form chelates with tetracycline. Information is not available as to the mechanism by which sodium bicarbonate decreased tetracycline absorption, and the question as to whether antacids, in general, interfere with tetracycline absorption warrants further investigation.

Chelation and an increase in gastric pH act concomitantly and apparently reduce the absorption of tetracycline and its derivatives, thereby decreasing the effectiveness of the antibiotic. With antacids containing aluminum, magnesium, and calcium, this reduction is magnified. Not only do the antacids provide the material for chelation (namely, polyvalent metallic cations), but they also facilitate the process by raising the gastric pH.

A number of clinical studies involving products containing these metallic cations demonstrate the results of concomitant therapy with tetracycline. One double-blind study involved giving 15 milliliters (mL) of an antacid product containing aluminum hydroxide to four subjects at the same time as a single 100 milligram (mg) dosage of doxycycline, and to four other subjects at the same time as a single 300-mg dosage of demeclocycline. This study demonstrated that each group of four patients showed significant reductions in antibiotic serum levels compared to controls (Ref. *9*). In each study group, three of the four subjects showed essentially no measurable plasma levels of antibiotic, and one subject in each group had very low levels.

Michel, et al., (Ref. *17*) gave five adults 1 gram (g) of oxytetracycline each morning for 4 days. On the third and fourth days, in addition to the oxytetracycline each subject received either 30 mL of an aluminum gel antacid or a full breakfast. In another treatment the same five subjects received an additional treatment of 1 g chlortetracycline for 4 days and food or 30 mL of an aluminum gel antacid on the second and fourth days. Blood samples were taken 3 hours after administration. Results of the testing showed that simultaneous ingestion of the antacid with either chlortetracycline and oxytetracycline resulted in a marked depression in antibiotic blood levels, compared to antibiotic blood levels without antacid. The simultaneous ingestion of the antibiotics with food caused no significant alteration in blood levels.

In another study, chlortetracycline was administered to five hospitalized patients and six normal male subjects at an oral dosage of 500 mg every 6 hours for 6 consecutive days (Ref. *18*). On the fourth, fifth, and sixth days, all subjects were given 30 mL of aluminum hydroxide suspension immediately following each dose of chlortetracycline. Results showed that in four of the hospitalized patients, there was a decrease in serum levels of chlortetracycline within 24 hours following administration of the aluminum hydroxide solution, compared to chlortetracycline levels recorded in the first 3 days. After 48 hours, four patients had serum levels of antibiotic below 1 microgram/milliliter (μg/mL); the fifth patient maintained a serum level of 5 μg/mL. On the third day of the combined therapy, one patient suffered a recurrence of her urinary tract infection, which promptly subsided when the aluminum hydroxide was discontinued. The six normal males averaged serum levels of 4.2 μg/mL of chlortetracycline after the 3-day administration, but serum levels dropped to 0.49 μg/mL with concurrent administration of the aluminum hydroxide.

Tetracycline was administered to 10 patients in oral doses of 500 to 1,000 mg alone, or concomitantly with 30 mL of a 50-percent magnesium sulfate solution. Results of the testing showed that when the magnesium sulfate was administered concomitantly with tetracycline, the blood level of tetracycline was reduced fourfold, when compared to the blood level produced by the tetracycline used alone (Ref. *19*).

In a comparison of blood serum levels of tetracycline, 12 patients received 4 tetracycline preparations (250 mg tetracycline base with citric acid, 250 mg tetracycline with lactose, 250 mg tetracycline phosphate complex with 22 mg calcium, and 250 mg tetracycline hydrochloride with 40 mg dicalcium phosphate) in a Latin-square pattern as follows: On each of 4 days at 4-day intervals, three patients received a single oral dose of one of the four preparations so that upon completion of the study each patient had received each of the four medications. At the end of the study, it was found that the two tetracycline preparations containing calcium measured 1, 3, 6, and 8 hours after administration resulted in serum levels only half of those found with the tetracycline administered with lactose or citric acid (Ref. *30*).

Sweeney, et al., (Ref. *21*) recorded serum and urine levels of tetracycline

from 31 healthy subjects after the administration of 3 separate treatments of tetracycline (250 mg tetracycline base with citric acid, 250 mg tetracycline base with lactose, or 250 mg tetracycline phosphate complex containing the equivalent of 22 mg calcium in each dose). A comparison of the serum and urine levels showed that the tetracycline phosphate complex resulted in significantly lower readings at all measurements. The investigators then measured serum and urine levels of tetracycline in 12 healthy patients, each of whom received, in separate tests, samples of 250 mg tetracycline base, 250 mg tetracycline base with sodium hexametaphosphate, or tetracycline hydrochloride with dicalcium phosphate. Results of the study showed that in all 12 patients, serum and urine tetracycline levels recorded after administration of the tetracycline hydrochloride with dicalcium phosphate were significantly lower than after administration of any of the other two preparations.

Research with dairy products has produced similar findings. Dairy products contain a considerable amount of calcium and magnesium. Although the amounts of calcium and magnesium vary with the source of the dairy product, such products generally contain between 118 and 120 mg/100 g calcium and between 13 and 14 mg/100 g magnesium (Refs. *8, 22,* and *23*). When 12 volunteers reviewed 300 mg demeclocycline simultaneously with milk or buttermilk (240 mL) or cottage cheese (240 g), serum antibiotic levels were reduced by as much as 80 percent, when compared with a control group of four, who received 300 mg demeclocycline with water (Ref. *11*).

References

(*1*) "Physicians' Desk Reference," 32d Ed., Medical Economics Company, Oradell, NJ, p. 723, 1979.

(*2*) "Physicians' Desk Reference," 32d Ed., Medical Economics Company, Oradell, NJ, p. 943, 1979.

(*3*) "Physicians' Desk Reference," 32d Ed., Medical Economics Company, Oradell, NJ, p. 971, 1979.

(*4*) "Physicians' Desk Reference," 32d Ed., Medical Economics Company, Oradell, NJ, p. 1352, 1979.

(*5*) Kunin, C. M., and M. Finland, "Clinical Pharmacology of the Tetracycline Antibiotics," *Clinical Pharmacology and Therapeutics,* 2:51–69, 1961.

(*6*) Colaizzi, J. L., and P. R. Klink, "pH—Partition Behavior of Tetracyclines," *Journal of Pharmaceutical Sciences,* 58:1184–1189, 1969.

(*7*) Pindell, M. H., K. M. Cull, K. M. Doran, and H. L. Dickison, "Absorption and Excretion Studies on Tetracycline," *Journal of Pharmacology and Experimental Therapeutics,* 125:287–294, 1959.

(*8*) Neuvonen, P. J., "Interactions With the Absorption of Tetracyclines," *Drugs.* 11:45–54, 1976.

(*9*) Rosenblatt, J. E., "Comparison of In Vitro Activity and Clinical Pharmacology of Doxycycline With Other Tetracyclines," *Antimicrobial Agents and Chemotherapy,* pp. 134–141, 1966.

(*10*) Weinstein, L., "Antimicrobial Agents," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., Edited by Goodman, L. S. and A. Gilman, The MacMillan Co., New York, pp. 1183–1187, 1975.

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(*13*) Barr, W. H., J. Adir, and L. Garrettson, "Decrease of Tetracycline Absorption in Man by Sodium Bicarbonate," *Clinical Pharmacology and Therapeutics,* 12:779–784, 1971.

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(*15*) Albert, A., "Avidity of the Tetracyclines for the Cations of Metals," *Nature,* 177:433–434, 1956.

(*16*) Kohn, K. W., "Mediation of Divalent Metal Ions in the Binding of Tetracycline to Macromolecules," *Nature,* 191:1156–1158, 1961.

(*17*) Michel, J. C., R. J. Sayer, and W. M. M. Kirby, "Effect of Food and Antacids on Blood Levels of Aureomycin and Terramycin," *Journal of Laboratory and Clinical Medicine,* 36:632–634, 1950.

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(*19*) Harcourt, R. S. and M. Hamburger, "The Effect of Magnesium Sulfate in Lowering Tetracycline Blood Levels," *Journal of Laboratory and Clinical Medicine,* 50:464–468, 1957.

(*20*) Boger, W. P. and J. J. Gavin, "An Evaluation of Tetracycline Preparations," *New England Journal of Medicine,* 261:827–832, 1959.

(*21*) Sweeney, W. M., et al., "Absorption of Tetracycline in Human Begins as Affected by Certain Excipients," *Antibiotic Medicine and Clinical Therapy,* 4:642–656, 1957.

(*22*) Watt, B. K. and A. L. Merrill, "Composition of Foods," Agriculture Handbook No. 8, Agriculture Research Service, United States Department of Agriculture, Washington, DC, p. 39, 1964.

(*23*) Watt, B. K. and A. L. Merrill, "Composition of Foods," Agriculture Handbook No. 8, Agriculture Research Service, United States Department of Agriculture, Washington, DC, p. 153, 1964.

FDA has reviewed the data relevant to the concomitant administration of antacid drug products containing polyvalent cations and tetracycline and its derivatives, and has determined that sufficient data exist to require that all antacids containing aluminum, magnesium, and calcium bear drug interaction labeling. (In making this decision, FDA has weighed previous statements by the Advisory Review Panel for OTC Antacid Drug Products, and subsequent **Federal Register** statements regarding this possible interaction (38 FR 8718, April 5, 1973; 38 FR 31263 and 31264, November 12, 1973; and 39 FR 19868 and 19880, June 4, 1974). FDA is concerned that the interaction between the polyvalent cations (aluminum, magnesium, and calcium) present in antacid products and tetracycline or its derivatives could result in lower serum levels of tetracycline and thus inadequate therapy to the patient. The agency is also concerned that some patients may not be readily able to determine whether or not the prescription antibiotic drug that they are taking contains a form of tetracycline. Therefore, the proposed precautionary statement urges the patient to ask a physician or pharmacist whether or not the drug contains tetracycline.

The agency is considering the need for a similar precautionary statement for OTC non-antacid internal drug products containing aluminum, magnesium, and calcium, e.g., magnesium salicylate, calcium lactate, and aluminum aspirin. FDA invites comment on this issue.

FDA is unaware of data demonstrating that tetracycline and antacids containing aluminum, magnesium, and calcium may be administered sequentially at a time interval that will ensure that therapeutic levels of antibiotic would not be affected (e.g., administration of the antacid 2 hours before or 2 hours after the antibiotic). FDA invites comment and welcomes any evidence available on this issue.

Where an antacid product contains minimal amounts of aluminum, magnesium, or calcium and blood level data are sufficient to show that the normal dosage of the antacid does not cause interference with the concomitant administration of any form of tetracycline, FDA will grant an exemption from this drug interaction precaution. Anyone seeking such an exemption must submit a petition in accordance with Part 10 (21 CFR Part 10) of the agency's procedural regulations with the supporting data to the office of the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857. These petitions will be maintained in a permanent file for public review.

The agency proposes that a final regulation based on this proposal be effective 12 months after the date of its publication in the **Federal Register**. The FDA believes that a 12 month delayed effective date would provide sufficient time for manufacturers to order and begin using revised labeling. On or after the effective date, FDA would regard any drug product that is subject to this regulation and that is initially introduced or initially delivered for introduction into interstate commerce as misbranded unless the labeling of the product complies with the requirements set forth in the regulation. The regulation would also apply to a drug product that is repackaged or relabeled after the effective date, regardless of the date it was initially delivered for introduction into interstate commerce.

The Food and Drug Administration has determined that this document does not contain an agency action covered by 21 CFR 25.1(b) and consideration by the agency of the need for preparing an environmental impact statement is not required.

Therefore, under 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 the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), it is proposed that Part 331 be amended by revising § 331.30(c) to read as follows:

§ 331.30 Labeling of antacid products.

* * * * *

(c) *Drug interaction precautions.* (1) The labeling of the product contains the following drug interaction precautions under the heading "Drug Interaction Precautions":

(i) If the product is an antacid containing aluminum, calcium, or magnesium, "Do not take this product if you are presently taking a prescription antibiotic drug containing any form of tetracycline. If you are not sure whether or not you are taking a tetracycline product, contact your physician or pharmacist."

(ii) [Reserved]

(2) Any person may file a petition under Part 10 of this chapter to exempt an antacid product from the provisions of paragraph (c)(1)(i) of this section. The petition shall be supported by an adequate showing that:

(i) The product contains minimal amounts of aluminum, calcium, or magnesium; and

(ii) Blood level data are sufficient to show that the normal dosage of the antacid does not cause interference with the concomitant administration of any form of tetracycline.

Interested persons may, on or before December 18, 1979 submit to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fisher Land, Rockville, MD 20857, written comments regarding this proposal. Five copies of any comments are to be submitted, and they may be accompanied by a supporting memorandum or brief. Comments are to be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday.

In accordance with Executive Order 12044, the economic effects of this proposal have been carefully analyzed, and it has been determined that the proposed rulemaking does not involve major economic consequences as defined by that order. A copy of the regulatory analysis assessment supporting this determination is on file with the Hearing Clerk, Food and Drug Administration.

Dated: October 11, 1979.

Joseph P. Hile,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 79–31971 Filed 10–18–79; 12:00 pm]

BILLING CODE 4110–03–M

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21 CFR Part 444

[Dockets Nos. 79N–0151 and 79N–0155]

Neomycin Sulfate Preparations; Proposed Revocations of Certification; Informal Conference and Extension of Comment Period

AGENCY: Food and Drug Administration.

ACTION: Notice of Informal Conference and Extension of Comment Period.

SUMMARY: The Food and Drug Administration (FDA) announces that it will hold an informal conference in Rockville, MD, to receive information and views from interested persons on the agency's proposals to revoke provisions for certification of neomycin sulfate for prescription compounding and sterile neomycin sulfate for parenteral use. The agency is also extending the period for submission of written comments on the proposals.

DATES: A written notice of participation should be filed by November 13, 1979. The informal conference will be held on November 20, 1979; written comments by December 20, 1979.

ADDRESSES: Written notice of participation and comments to Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857. The informal conference will be held in Conference Room A, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: T. Greene Reed, Bureau of Drugs (HFD–140), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301–443–4310.

SUPPLEMENTARY INFORMATION: FDA will hold an informal conference on its proposals to amend the Code of Federal Regulations by revoking provisions for certification of neomycin sulfate for prescription compounding and neomycin sulfate for parenteral use. The proposals were published in the **Federal Register** of July 27, 1979 (44 FR 44178; 44180). The effect of the amendments would be to remove these drug products from the market.

The proposals gave interested persons an opportunity to submit written comments by September 25, 1979. They also announced that interested persons could submit a request by August 27, 1979, for an informal conference on the proposed regulations. Three requests for an informal conference and two requests for an extension of the comment period were received.

The agency has concluded that an informal conference should be held on the proposed regulations. The conference will be on November 20, 1979, at 9:30 a.m. in Conference Room A of the Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857. It will be open to the public.

Any persons who wish to present their views at the conference should file a written notice of participation with the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857 by November 13, 1979.

The notice of participation should be prominently marked "INFORMAL CONFERENCE, NEOMYCIN SULFATE" and should contain the following information:

1. Name, address, and telephone number of the person desiring to make a presentation.
2. Business affiliation, if any.
3. A summary of the presentation.
4. The approximate amount of time requested for the presentation (no more than 30 minutes unless more time can be justified).