American Bank of Arlington, Arlington, Texas. Comments on this application must be received not later than June 12, 1982.

C. Federal Reserve Bank of San Francisco (Harry W. Green, Vice President) 400 Sansome Street, San Francisco, California 94120:

1. *AmBank Holding Company*, Phoenix, Arizona, to become a bank holding company by acquiring 99.3 percent of the voting shares of American Bank, Phoenix, Arizona. Comments on this application must be received not later than June 12, 1982.

2. *MBC Corp.*, Modesto, California; to become a bank holding company by acquiring 100 percent of the voting shares of Modesto Banking Company, Modesto, California. Comments on this application must be received not later than June 9, 1982.

3. *Professional Bancorp*, Santa Monica, California; to become a bank holding company by acquiring 100 percent of the voting shares of First Professional Bank of Los Angeles, Santa Monica, California. Comments on this application must be received not later than June 9, 1982.

4. *TriCo Bancshares*, Chico, California; to become a bank holding company by acquiring 100 percent of the voting shares of Tri-Counties Bank, Chico, California. Comments on this application must be received not later than June 11, 1982.

C. Secretary, Board of Governors of the Federal Reserve System, Washington, D.C. 20551:

1. *NBC Bancorporation, Inc.*, Newport, Minnesota; to become bank a holding company by acquiring 100 percent of the voting shares of National Bank of Commerce in Mankato, Mankato, Minnesota. Comments on this application must be received not later than June 11, 1982.

2. *Town & Country Bancshares, Inc.*, Newport, Minnesota; to become a bank holding company by acquiring 100 percent of the voting shares of Town and Country Bank-Maplewood, Maplewood, Minnesota. Comments on this application must be received not later than June 11, 1982.

Board of Governors of the Federal Reserve System, May 12, 1982.

Dolores S. Smith,

Assistant Secretary of the Board.

[FR Doc. 82-13398 Filed 5-17-82; 8:45 am]

BILLING CODE 6210-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Consumer Participation; Open Meetings

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the following consumer exchange meetings: Atlanta District Office, Chaired by John Turner, District Director.

DATE: Thursday, May 27, 1982, 10:30 a.m.

ADDRESS: Brighton Multipurpose Center, outside Birmingham, Alabama.

FOR FURTHER INFORMATION CONTACT: Janice Moton, Consumer Affairs Officer, Food and Drug Administration, 1182 W. Peachtree St. NW., Atlanta, GA 30309, 404-881-7355.

Cincinnati District Office, Chaired by James C. Simmons, District Director.

DATE: Wednesday, June 9, 1982, 1 p.m.

ADDRESS: Rm. 504, The Federal Bldg., 200 W. Second St., Dayton, OH 45402.

FOR FURTHER INFORMATION CONTACT: Ruth E. Weisheit, Consumer Affairs Officer, Food and Drug Administration, Rm. 463, 601 Rockwell Ave., Cleveland, OH 44114, 216-522-4844.

Cincinnati District Office, Chaired by James C. Simmons, District Director.

DATE: Thursday, June 10, 1982, 1:30 p.m.

ADDRESS: Rm. 5525A, Federal Bldg., 550 Main St., Cincinnati, OH 45202.

FOR FURTHER INFORMATION CONTACT: Ruth E. Weisheit, Consumer Affairs Officer, Food and Drug Administration, Rm. 463, 601 Rockwell Ave., Cleveland, OH. 44114, 216-522-4844.

Philadelphia District Office, Chaired by Loren Johnson, District Director.

DATE: Wednesday, June 16, 1982, 1 to 3 p.m.

ADDRESS: Wm. H. Green, Federal Bldg., Rm. 7306, 6th and Arch Sts., Philadelphia, PA 19106.

FOR FURTHER INFORMATION CONTACT: Theresa A. Young, Consumer Affairs Technician, Food and Drug Administration, 2d and Chestnut Sts., Philadelphia, PA 19106, 215-597-0837.

Chicago District Office, Chaired by Mary K. Ellis, District Director.

DATE: Tuesday, June 22, 1982, 1:30-3:30 p.m.

ADDRESS: Food and Drug Administration, Rm. 1204, 433 W. Van Buren, Chicago, IL 60607.

FOR FURTHER INFORMATION CONTACT: Darlene M. Bailey, Consumer Affairs Officer, Food and Drug Administration, 433 W. Van Buren, Chicago, IL 60607, 312-353-7126.

SUPPLEMENTARY INFORMATION: The purpose of these meetings is to encourage dialogue between consumers and FDA officials, to identify and set priorities for current and future health concerns, to enhance understanding and exchange information between local consumers and FDA's District Offices, and to contribute to the agency's policymaking decisions on vital issues.

Dated: May 13, 1982.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 82-13472 Filed 5-17-82; 8:45 am]

BILLING CODE 4160-01-M

[Docket Nos. 79N-0339 and 79N-0340; DESI Nos. 8615, 9152, 9188, 50168, and 10210]

Certain Ophthalmic Combination Drugs Containing a Steriod and Anti-Infective(s) for Human Use; Drug Efficacy Study Implementation; Amendment

AGENCY: Food and Drug Administration (FDA).

ACTION: Notice.

SUMMARY: This notice amends two previous **Federal Register** notices concerning ophthalmic combination drug products containing a steroid and one or more anti-infective agents. This amendment requires revised labeling which more precisely states the conditions of use for which such drugs are safe and effective. The notice also states the rationale for regarding these drugs as safe and effective.

DATES: Amendments or supplements to approved applications (NDA's, ANDA's, or antibiotic forms) due on or before July 19, 1982. Revised labeling must be put into use on or before November 15, 1982.

ADDRESSES: Communications in resonse to this notice should be identified with the appropriate DESI number, directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Supplements to full new drug applications (identify with NDA number); Division of Anti-Infective Drug Products (HFD-140), Rm. 12B-45, Bureau of Drugs.

Supplements to approved abbreviated new drug applications (identify with ANDA number): Division of Generic Drug Monographs (HFD-530), Bureau of Drugs.

Amendments to approved antibiotic forms (identify with form number); Antibiotic Drug Review Branch (HFD–535), Bureau of Drugs.

Request for opinion of the applicability of this notice to a specific product: Division of Drug Labeling Compliance (HFD–310), Bureau of Drugs.

Requests for a copy of the Health Reserach Group comments and/or FDA's response (identify with Docket Nos.): Dockets Management Branch (HFA–305), Rm. 4–65.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFD–501), Bureau of Drugs.

FOR FURTHER INFORMATION CONTACT: Douglas I. Ellsworth, Bureau of Drugs (HFD–32), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3650.

SUPPLEMENTARY INFORMATION: In two notices published in the **Federal Register** of August 29, 1980 (45 FR 57776 and 45 FR 57780), FDA announced its conclusion that certain ophthalmic combination drugs containing a steroid and one or more anti-infective agents are effective. The notices also set forth a general outline for labeling of the effective products as a condition for marketing and approval.

On December 4, 1980, the Health Research Group (HRG), 2000 P St. NW., Washington, D.C. 20036, wrote to the Commissioner of Food and Drugs concerning the agency's conclusion for this class of combinaton drug products. HRG asked that the decision be reconsidered, alleging that no adequate and well-controlled clinical trials are available to support the effectiveness of all ingredients in these combinations. Copies of HRG's letter and the FDA response have been placed in the docket of these proceedings. Copies are available from the Dockets Management Branch (address given above)

As a result of the HRG letter, the Bureau of Drugs reevaluated the August 29, 1980 notices and the record of this proceeding. Based upon this reevaluation, the Director of the Bureau has concluded (1) that the basic finding stated in those notices that these drug products are safe and effective should be reaffirmed, (2) that the rationale for concluding that these combination products are effective was not stated in the notices and should be stated clearly to avoid further confusion, and (3) that the labeling for these drug products, as described in the 1980 notices, should be revised to state more precisely the conditions of use for which these products are safe and effective.

Background

As noted in the August 29, 1980 notices, the ophthalmic steroid/anti-infective combination products covered by these notices were originally classified as possibly effective under the Drug Efficacy Study in a series of notices published in 1971 and 1972. Subsequently, the ophthalmic steroid/anti-infective combination drug products were exempted from the schedule established for completing the study (37 FR 26643). The products were exempted because of their potential effectiveness in the treatment of marginal keratitis secondary to staphylococcus blepharoconjunctivitis, vernal catarrh, and allergic conjunctivitis, and their frequent use postoperatively by ophthalmologists to reduce inflammatory reactions and prevent infection. The exemption was conditioned upon the commitment of manufacturers and distributors to conduct appropriate studies to establish which particular combinations and concentrations are effective for specific indications.

In response to the exemption notice, several manufacturers submitted plans for studies. The agency determined that the studies as planned were inadequate to demonstrate that all active ingredients contributed to the effectiveness of the fixed-combination drug products. Because the sponsors were unable to develop appropriate protocols and because of controversy over the role of thse combination products in ophthalmology, the matter was presented to FDA's Ophthalmic Drugs Advisory Committee at a public meeting held May 8, 1973. Discussion centered on the safety of these products and the design of meaningful studies. The committee concluded that the data available to it were insufficient to make a decision on any of the issues presented and appointed a subcommittee to obtain additional information.

The subcommittee then drafted a proposal for clinical studies. This proposal was sent to affected firms for comment, and on August 6, 1973, the Advisory Committee met in open session to discuss the proposal. In spite of extensive discussion and continued subcommittee deliberations, the Committee was unable to finalize a protocol.

Therefore, the subcommittee proposed that manufacturers and distributors prepare a single document containing all available data pertaining to each indication outlined in the exemption notice. The subcommittee believed that this data search might provide sufficient evidence of effectiveness in lieu of new clinical studies. On November 2, 1973, the full Advisory Committee adopted the proposal, and representatives of the pharmaceutical industry agreed to conduct the joint data search. On September 27, 1974, the industry task force submitted its data, which consisted of published studies (domestic and foreign with translations), unpublished studies, and domestic and foreign adverse reaction surveys.

These data then underwent thorough review by agency staff with input from the Advisory Committee and the Bureau of Drugs' Combination Drugs Committee, an internal staff committee established to evaluate products with respect to the agency's combination drug policy. The Advisory Committee reviewed the data and made recommendations at public meetings held November 4, 1974, November 3, 1975, August 2, 1976, and November 7, 1977, and the Combination Drugs Committee considered the matter at its meetings of August 27, 1977 and January 18, 1978.

With respect to safety, these reviews showed that the data from adverse reaction surveys and unpublished studies reveal a low number of adverse reactions, particularly when judged against the extensive use of these products. Adverse reaction rates, as estimated by the number of adverse reaction reports divided by the distribution of these drugs, were, if anything, lower for steroid/anti-infective combination products than for single-ingredient anti-infective ophthalmological products, possibly because of a therapeutic or prophylactic effect of the steroid component on sensitivity reactions to the anti-infective component. The safety data supported the conclusions that the most serious adverse reactions resulting from the combinations are those related to the steroid component (e.g., increase in intraocular pressure, scleral perforation, and exacerbation of certain infections), that these reactions are most commonly associated with long-term use, that they are best prevented by periodic examinations during treatment, and that the only incremental risk added by the anti-infective component is occasional sensitivity reactions.

With respect to effectiveness, the Advisory Committee recommended that the agency review five potential indications for these combination products: marginal keratitis secondary to *Staphylococcus aureus*, staphylococcal blepharoconjunctivitis, phylctenular keratoconjunctivitis, vernal catarrh, and allergic conjunctivitis

secondary to infection. These indications and their supporting evidence resulted from the Advisory Committee review and industry data search conducted in 1973 and 1974. The Bureau of Drugs' staff and its Combination Drugs Committee reviewed the submitted information and concluded that there were not at least two adequate and well-controlled trials demonstrating that both the steroid component and the anti-infective component contribute to the effectiveness of the combination in these conditions. There are studies showing that the combination is more effective than the antibiotic component alone. However, of two studies designed to show whether the combination is more effective than the steroid component alone, one failed to show any such advantage and the other suggested only a marginal advantage of the combination, namely in providing more rapid resolution of symptoms. The Combination Drugs Committee thus concluded that the effectiveness of these combinations in the above conditions can be attributed to the steroid component alone.

The Combination Drugs Committee also noted, however, that these steroid-responsive conditions can be accompanied by bacterial infection or risk of infection, that bacterial overgrowth in the eye is catastrophic although fortunately rare, that animal studies using techniques to make the eye more susceptible to infection demonstrate that steroids can reduce resistance to infection and anti-infective agents can counteract this effect, and that it is medically reasonable to include both ingredients in a single preparation so that one drug does not wash out the other. For these reasons, the Committee recommended that steroid/anti-infective combination products should remain available under appropriate labeling and that the requirement for adequate and well-controlled trials to demonstrate the contribution of each ingredient should be waived.

This recommendation was discussed with the Advisory Committee at its meeting of November 7, 1977. The Advisory Committee believed that the specific indications noted previously were appropriate although it acknowledged that adequate and well-controlled trials showing that the anti-infective component contributes to the therapeutic effect in the routine management of these conditions are not available. After considerable discussion the Advisory Committee recommended a more general labeling indication for consideration by the Combination Drugs Committee: "For use in the treatment of ocular inflammation where concurrent use of anti-infectives and steroids are indicated."

This indication was considered by the Bureau staff and by the Combination Drugs Committee on January 18, 1978. The conclusion was announced in the 1980 notices that ophthalmic steroid/anti-infective combination products are considered safe and effective under a slightly modified general indication as follows: "A steroid/anti-infective combination is indicated in ocular inflammation when concurrent use of an antimicrobial is judged necessary." The notices also set forth class labeling that contained specific contraindications, warnings, and precautions. It is this decision and labeling statement that was challenged by the Health Research Group.

Decision and Rationale

The Director of the Bureau of Drugs has reviewed the record of this proceeding. On the basis of this review, the Director reaffirms that these combination products are safe and effective if properly labeled and that they meet the agency's policy with respect to combination drug products. The rationale for this conclusion was not published in the 1980 notices, nor is it adequately and completely articulated in the minutes of agency or advisory committee meetings. Furthermore, the Director finds that the labeling indication published in the 1980 notices is vague and does not adequately describe the conditions for which these products are considered safe and effective. Accordingly, the Director is announcing the rationale that supports the conclusion that these combination products are safe and effective and is also announcing a requirement for revised labeling.

The Director concludes that the available data indicate that the effectiveness of combination steroid/anti-infective products in ophthalmologic inflammatory conditions is, in most cases, due to the steroid component. If the anti-infective component contributes to the effectiveness of the combination in the treatment of these conditions, e.g., staphylococcal blepharoconjunctivitis or marginal keratitis, this alleged effect is sufficiently small or unpredictable that it has proven difficult to document in adequate and well-controlled trials. In some cases, however, steroid-responsive inflammatory conditions in the eye may be accompanied by frank bacterial infection or the risk of such infection. In such cases the safety of treatment with the steroid is increased by concomitant administration of an effective anti-infective agent to either treat or prevent accompanying bacterial infection.

The addition of an anti-infective component to an ophthalmic steroid preparation is thus done to enhance the safety of the product when bacterial infection is present or possible. Such addition of an ingredient to enhance the safety of a product is permitted under FDA's combination policy (21 CFR 300.50(a)(1)).

While clinical trials to demonstrate the contribution of each active ingredient are ordinarily required for combination drugs, clinical trials to prove the increased safety of the combination in the presence of bacterial infection are not feasible for both technical and ethical reasons. An extremely large trial would be necessary to determine the incidence of eye infections in patients undergoing treatment with steroids because such infections are relatively rare. It would also be ethically impossible to obtain a valid control group of patients with eye infections treated with steroids alone because of the risk of serious damage to the eye. For these reasons clincial trials to prove the increased safety of the combination in such circumstances are not deemed feasible or necessary.

Labeling

While the labeling indication in the 1980 notices implied this rationale, the Director concludes that modification of that indication is necessary to reflect more accurately the appropriate indication. Furthermore, because the anti-infective component is added to treat or prevent specific infections, the labeling should state those common eye pathogens that are generally sensitive to the particular anti-infective drug and those that are not. Accordingly, a requirement for revised labeling for combination steroid/anti-infective drug products is included in this notice.

Manufacturers and distributors of the following drug products, which were evaluated as effective in the 1980 notices, are required to revise their labeling in accordance with this amendment (antibiotic form numbers are stated as NDA numbers below):

DESI 8615

1. NDA 50–169; Cortisporin Ophthalmic Suspension containing neomycin sulfate, polymyxin B sulfate, and hydrocortisone; Burroughs Wellcome & Co., Inc., 3030 Cornwallis Rd., Research Triangle Park, NC 22709.

2. NDA 50–202; Chloromycetin Hydrocortisone Ophthalmic Suspension containing chloramphenicol and

hydrocortisone acetate; Parke-Davis, Division of Warner-Lambert Co., Morris Plains, NJ 07950.

3. NDA 50–272; Achromycin Ophthalmic Ointment with Hydrocortisone containing tetracycline hydrochloride and hydrocortisone; Lederle Laboratories Division, American Cyanamid Co., Pearl River, NY 10965.

4. NDA 50–362; Metimyd with Neomycin Ophthalmic Ointment containing neomycin sulfate, prednisolone acetate, and sodium suflacetamide; Schering Corp., Galloping Hill Rd., Kenilworth, NJ 07033.

5. NDA 60–310; Neomycin Sulfate with Hydrocortisone Acetate Ophthalmic Ointment; Biocraft Laboratories, Inc., 92 Route 42, East Patterson, NJ 07407.

6. NDA 60–452; Isopto P-H-N Ophthalmic Suspension containing neomycin sulfate, polymyxin B sulfate, and hydrocortisone acetate; Alcon Laboratories, Inc., 2601 South Freeway, Fort Worth, TX 76134.

7. NDA 60–464; Neo-Deltef Eye Drops containing neomycin sulfate and prednisolone; The Upjohn Co., 7171 Portage Rd. Kalamazoo, MI 49001.

8. NDA 60–788; Di-Hydrin Ophthalmic Solution containing neomycin sulfate, polymyxin B sulfate, and hydrocortisone; Broemmel Pharmaceuticals, 1235 Sutter St., San Francisco, CA 94109.

9. NDA 60–790; Neo-Polycin HC Ophthalmic Ointment containing bacitracin, neomycin sulfate, polymyxin B sulfate, and hydrocortisone acetate; Pitman-Moore Co., Division of the Dow Chemical Co., 55 West Sheffield, Englewood, NJ 07631.

10. NDA 60–925; Florinef-S Ophthalmic Ointment and Suspension containing neomycin sulfate, gramicidin, and fludrocortisone acetate; E. R. Squibb & Sons, Inc., P.O. Box 4000, Princeton, NJ 08540.

11. NDA 61–045; Neosone Ophthalmic Ointment containing neomycin sulfate and cortisone acetate; The Upjohn Co.

12. NDA 61–075; Hydrocortisone-Neomycin Ophthalmic Ointment containing neomycin sulfate and hydrocortisone acetate; Day-Baldwin, Inc., 1460 Chestnut Ave., Hillside, NJ 07205.

13. NDA 61–107; Neomycin Sulfate with Hydrocortisone Acetate Ophthalmic Ointment; Kasco Laboratories, Inc., Cantiaque Rd., P.O. Box 73, Hicksville, NY 11802.

DESI 9152

1. NDA 61–016; Terra-Cortril Ophthalmic Suspension containing oxytetracycline hydrochloride and hydrocortisone acetate; Pfizer Laboratories, Division of Charles Pfizer & Co., Inc., 235 East 42d St., New York, NY 10017.

DESI 9188

1. NDA 50–322; Neo-Decadron Ophthalmic Solution containing dexamethasone sodium phosphate and neomycin sulfate; Merck Sharp & Dohme, Division Merck & Co., Inc., West Point, PA 19486.

2. NDA 50–324; Neo-Decadron Ophthalmic Ointment containing dexamethasone sodium phosphate and neomycin sulfate; Merck Sharp & Dohme.

3. NDA 50–378; Neo-Hydeltrasol Ophthalmic Ointment containing prednisolone sodium phosphate and neomycin sulfate; Merck Sharp & Dohme.

4. NDA 50–379; Neo-Hydeltrasol Ophthalmic Solution containing prednisolone sodium phosphate and neomycin; Merck Sharp & Dohme.

5. NDA 60–188; Cor-Oticin Ophthalmic Suspension containing hydrocortisone acetate and neomycin sulfate; Maurry Biological Co., Inc., 6109 South Western Ave., Los Angeles, CA 90047.

6. NDA 60–442; Neo-Aristocort Ophthalmic Ointment containing triamcinolone acetonide and neomycin sulfate; Lederle Laboratories.

7. NDA 60–610; Neo-Cortef Ophthalmic Ointment containing hydrocortisone acetate and neomycin sulfate; The Upjohn Co.

8. NDA 60–612; Neo-Cortef Eye Drops containing hydrocortisone acetate and neomycin sulfate; The Upjohn Co.

9. NDA 60–645; Neo-Medrol Ophthalmic Ointment containing methylprednisolone and neomycin sulfate; The Upjohn Co.

10. NDA 61–037; Neo-Delta-Cortef Ophthalmic Ointment containing hydrocortisone acetate and neomycin sulfate; The Upjohn Co.

11. NDA 61–039; Neo-Delta-Cortef Ophthalmic Ointment containing prednisolone acetate and neomycin sulfate; The Upjohn Co.

DESI 10210

1. NDA 10–210; Metimyd Ophthalmic Susension, each milliliter containing 5 mg prednisolone acetate and 100 mg sodium sulfacetamide; Schering Corp.

The following drug products were listed in one notice (45 FR 57776) as lacking substantial evidence of effectiveness because they contained less than 10,000 units of polymyxin B. The notice provided that if the manufacturers reformulated these products to contain no less than 10,000 units of polymyxin B, the products would be regarded as effective when labeled as described in thie notice. These products have since been reformulated and the reformulated products are regarded as effective. Manuafacturers and distributors of these reformulated products are also required to revise their labeling in accordance with this amendment.

DESI 8615

1. NDA 50–081; Predmycin-P Liquifilm Ophthalmic Suspension containing neomycin sulfate, polymyxin B sulfate, and prednisolone acetate; Allergan Pharmaceuticals, 1000 South Grand Ave., Santa Ana, CA 92705.

2. NDA 50–201; Ophthocort Ophthalmic Ointment containing chloramphenicol, polymyxin B sulfate, and hydrocortisone acetate; Parke-Davis.

3. NDA 60–731; Bacitracin-Polymyxin-Neomycin with Hydrocortisone Ophthalmic Ointment containing zinc bacitracin, neomycin sulfate, polymyxin B sulfate, and hydrocortisone acetate; Kasco Laboratories, Inc.

DESI 50168

1. NDA 50–416; Cortisporin Ointment containing polymyxin B sulfate, zinc bacitracin, neomycin sulfate, and hydrocortisone; Burroughs Wellcome & Co.

Manufacturers or distributors of the following drug products, which were not listed in either of the 1980 notices, are also required to revise their labeling in accordance with this amendment:

1. NDA 50–023; Maxitrol Suspension containing neomycin sulfate, ploymyxin B sulfate, and dexamethasone, Alcon Laboratories, Inc.

2. NDA 50–065; Maxitrol Ointment containing neomycin sulfate, ploymyxin B sulfate, and dexamethasone; Alcon Laboratories, Inc.

3. NDA 61–188; Chloroptic-P Ointment containing chloramphenicol and prednisolone; Allergan Pharmaceuticals.

4. ANDA 87–547; Isoptocetapred containing prednisolone acetate and sodium sulfacetamide; Alcon Laboratories, Inc.

All Steroid/anti-infective combination drug products recommended for ophthalmic use that are the subject of an approved new drug application or are eligible for certification or release, whether or not listed above, are subject to this notice. All manufacturers and distributors are required to revise the labeling of such products in accordance with this amendment.

CONDITIONS FOR MARKETING AND APPROVAL

The conditions for marketing and approval stated in the August 29, 1980 notices are amended to read as follows:

I. Steroid/Anti-Infective Combination Drug Products for Ophthalmic Use Containing One or More Antibiotic Components

(Subject to Section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357)) (see 45 FR 57776) (DESI Nos. 8615, 9152, 9188, and 50168).

Batches of such drugs with labeling not in accordance with the "Labeling Requirement" listed below will no longer be acceptable for certification or release after November 15, 1982.

II. The Combination of 5 mg Prednisolone Acetate and 100 mg Sodium Sulfacetamide for Ophthalmic Use

(Subject to Section 505 of the Act (21 U.S.C. 355)) (see 45 FR 57780) (DESI 10210).

Such drugs are regarded as new drugs (21 U.S.C. 321(p)). Supplemental new drug applications are required to revise the labeling in and to update previously approved applications providing for such drugs. An approved new drug application is a requirement for marketing such drug products.

In addition to the product specifically named above, this notice applies to any drug product that is not the subject of an approved new drug application and is identical to the product named above. It may also be applicable, under 21 CFR 310.6, to a similar or related drug product that is not the subject of an approved new drug application. It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product that the person manufactures or distributes. Such person may request an opinion of the applicability of this notice to a specific drug product by writing to the Division of Drug Labeling Compliance (address given above).

A. *Effectiveness classification.* The Food and Drug Administration has reviewed all available evidence and concludes that the drug product is effective for the indication described in the "Labeling Requirement" listed below.

B. *Conditions for approval and marketing.* The Food and Drug Administration is prepared to approve abbreviated new drug applications and abbreviated supplements to previously approved new drug applications under conditions described herein.

1. *Form of drug.* The drug product contains 5 mg prednisolone acetate and 100 mg sodium sulfacetamide, and is in a form suitable for ophthalmic administration.

2. *Labeling conditions.* a. The label bears the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drug is labeled to comply with all requirements of the act and regulations, and the labeling bears adequate information for safe and effective use of the drug. The labeling conforms to the "Labeling Requirement" listed below.

3. *Marketing status.* a. Marketing of such drug products that are now the subject of an approved or effective new drug application may be continued provided that, on or before July 19, 1982, the holder of the application has submitted (i) a supplement for revised labeling as needed to be in accord with the labeling conditions described in this notice, and complete container labeling if current container labeling has not been submitted, and (ii) a supplement to provide updating information with respect to items 6 (components), 7 (composition), and 8 (methods, facilities, and controls) of new drug application form FD-356H (21 CFR 314.1(c)) to the extent required in abbreviated application (21 CFR 314.1(f)), if such information has not previously been submitted. Revised labeling in accord with the labeling conditions described in this notice must be put into use on or before November 15, 1982. The revised labeling may be put into use before approval of the supplemental new drug applications, as provided for in 21 CFR 314.8(d) and (e).

b. Approval of an abbreviated new drug application (21 CFR 314.1(f)) must be obtained before marketing such products. An abbreviated application will be acceptable only for the formulation containing 5 mg prednisolone acetate and 100 mg sodium sulfacetamide. Any new combination requires a full new drug application and appropriate studies. Marketing before approval of a new drug application will subject such products, and those persons who caused the products to be marketed, to regulatory action.

III. Labeling Requirement

A. The indication is as follows:

For steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial infection or a risk of bacterial ocular infection exists.

Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical radiation, thermal burns, or penetration of foreign bodies.

The use of a combination drug with an anti-infective component is indicated where the risk of infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

The particular anti-infective drug(s) in this product is [are] active against the following common bacterial eye pathogens: [*insert appropriate organisms from the list in the Appendix to this notice*].

The product does not provide adequate coverage against: [*insert appropriate organisms from the list in the Appendix to this notice*].

B. If the combination contains neomycin sulfate, the WARNINGS section of the labeling must contain an appropriate statement concerning the potential of neomycin sulfate to cause cutaneous sensitization.

(Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 507, 52 Stat. 1050-1053, 59 Stat. 463 as amended (21 U.S.C. 352, 355, 357) and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.70)))

Dated: May 5, 1982.

J. Richard Crout,

Director, Bureau of Drugs.

Appendix

Organisms To Be Included in Labeling, as Appropriate.

(If a manufacturer wishes to claim that its particular anti-infective component is active against an organism(s) not covered in the following list, the manufacturer must submit current susceptibility data supporting the inclusion of the additional organism(s) and receive FDA approval before including the organism(s) in the labeling).

I. Neomycin sulfate

Active against:
- *Staphylococcus aureus*
- *Escherichia coli*
- *Haemophilus influenzae*
- *Klebsiella/Enterobacter* species
- *Neisseria* species

Does not provide adequate coverage against:
- *Pseudomonas aeruginosa*
- *Serratia marcescens*
- Streptococci, including *Streptococcus pneumoniae*

II. Neomycin sulfate, polymyxin B sulfate.

Active against:
- *Staphylococcus aureus*
- *Escherichia coli*
- *Haemophilus influenzae*
- *Klebsiella/Enterobacter* species
- *Neisseria* species
- *Pseudomonas aeruginosa*

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