DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

AUG 25 1997

Robert B. Clark
Senior Associate Director
Regulatory Affairs
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

RE: **NDA # 50-670; 50-710**
Zithromax (azithromycin) Capsules/Suspension
MACMIS # 5379

Dear Mr. Clark:

Reference is made to Pfizer's brochure #XC127V96 for Zithromax capsules & Suspension. The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed this promotional piece and finds it to be in violation of the Federal Food, Drug, and Cosmetic Act and the applicable regulations. Specifically, DDMAC objects to the following claim:

- **Reliable criteria for interpreting susceptibility of *S pneumoniae* to Augmentin are not currently available. Strains that are resistant to penicillins are assumed to be resistant to Augmentin."**

  The graphic presentation titled "Susceptibility Rates," on page 9 of the brochure, and the accompanying footnote are misleading because they fail to reveal material facts concerning the efficacy of Augmentin in light of the susceptibility rates presentation. The presentation gives the susceptibility rates for Zithromax against *Hemophilus influenzae, Moraxella catarrhalis, Streptococcus pneumonia and Streptococcus pyrogens.* It also presents the susceptibility rates for Augmentin against *H influenzae, M catarrhalis* and *S pyrogens*, but omits the susceptibility rates for *S pneumonia*. The graphic presentation states that the susceptibility rates for Augmentin against *S pneumoniae* are "not available." This statement is not true, and is selectively based on an editorial letter from a 1995 journal. By failing to include information that addresses the efficacy of Augmentin against *S pneumoniae*, Pfizer is implying a greater efficacy for Zithromax against *S pneumonia.*

  The statement, "Strains that are resistant to penicillins are assumed to be

resistant to Augmentin," is also misleading because it implies a greater efficacy for Zithromax against *S pneumonia* than Augmentin. Pfizer has failed to include information that addresses the efficacy of Agumentin against this organism. Thus, Pfizer is selectively presenting data for its product and implying that Zithromax has greater activity against conditions caused by *S pneumoniae* than Augmentin.

Augmentin is an antibacterial combination product consisting of amoxicillin and a *B*-lactamase inhibitor, clavulanate potassium. The formulation of amoxicillin and clavulanic acid in Augmentin protects amoxcillin from degradation by *B*-lactamase enzymes and effectively extends the antibiotic spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin and other *B*-lactam antibiotics. Thus, infections caused by ampicillin susceptible organisms are also amenable to Augmentin in treatment due to its amoxicillin content. According to the approved product labeling (PI) for Augmentin, amoxicillin has greater *in vitro* activity against *S pneumoniae* than does ampicillin or penicillin. The majority of *S pneumoniae* strains with intermediate susceptibility to ampicillin or penicillin are fully susceptible to amoxicillin and Augmentin. Additionally, the National Committee for Clinical Laboratory Standards (NCCLS) published interpretive standards for Augmentin in its 1995 and 1997 publications. This organization publishes performance standards for antimicrobial susceptibility testing and its interpretive criteria are regarded as reliable when their data is supported by substantial clinical evidence. The interpretive standards for Augmentin are as follows.

Susceptible	Intermediate	Resistant
$\leq$ 0.5/0.25	1/0.5	$\geq$ 2/1

In order to address the above objections, DDMAC recommends that Pfizer take the following actions:

1. Immediately discontinue the use of the brochure and any other like promotional materials for Zithromax that contain the same or similar claims.

2. Provide a written response to DDMAC of your intent to comply with the above request and a list of promotional materials, containing this misleading presentation and footnote, that will be discontinued.

Pfizer's response should be received no later than September 8, 1997. If Pfizer

Robert B. Clark
Pfizer Inc.
NDA # 50-760; 50-710

has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

DDMAC reminds Pfizer that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 5379; 5204 in addition to the NDA number.

Sincerely,

Jo Ann Spearmon, Pharm.D., M.P.A.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications