[DOH ADMINISTRATIVE ORDER NO. 96, September 19, 1990]

GUIDELINES ON THE REGISTRATION OF FIXED-DOSE COMBINATION DRUG PRODUCTS

Pursuant to the provisions of R.A. 3720, also known as the Food, Drugs and Cosmetics Act, as amended by E.O. 175, the following guidelines are hereby issued relative to the registration of Fixed-Dose Combination Drug Products.

SECTION 1. Definition of Fixed Dose Combination Drug Products — Fixed Dose Combination Drug Products (FDC's) are pharmaceutical preparations containing two or more pharmacologically-active ingredients in a single formulation or dosage form.

SECTION 2. Scope of These Guidelines — All products classified as FDC's are covered by these guidelines. There are three categories of products included:

2.1 Currently registered products already recognized and identified by Bureau of Food and Drugs (BFAD) as FDC's.

2.2 Currently registered products which may later be classified as FDC's by BFAD.

2.3 Products with pending or for future initial registration under the category of FDC's.

All these categories of FDC's are covered but the specific applicability will be defined below.

SECTION 3. Safety, Efficacy, and Quality Criteria — The drug regulatory criteria of safety, efficacy, and quality shall be applied by the BFAD to the specific class of FDC's using the following rules:

3.1 The FDC drug product must comply with the appropriate requirements of **A.O. 67 s. 1989** on the registration of drug products.

3.2 The drug establishment seeking to register the FDC drug product should comply with the appropriate requirements of **A.O. 56 s. 1989** on the registration of drug establishments.

3.3 In addition to the above, the FDC drug product in its final dosage form must be proven to adhere to all the following criteria:

a. The active and inactive ingredients should be pharmaceutically (i.e. chemically, physically) and pharmacologically compatible in combination.

b. The FDC taken as a whole should have clinical and therapeutic advantage over the individual active ingredients taken separately. In this respect, acceptable clinical and therapeutic advantage involves more than additive effect, convenience, or better compliance. It should include such

advantages as complementary or synergistic pharmacological action or therapeutic effect, or reduction in adverse drug reaction.

c. It must not contain any ingredient whose proper administration or clinical use require special adjustments different from or in conflict with its other ingredients.

d. It must not contain active ingredients with abuse potential (those identified in *List A* of **A.O. 63, s. 1989)**, with a narrow margin of safety, and/or requires special precautions in its use, and/or with bioequivalence problems (those identified in List B of A.O. 63, s. 1989), and which are banned or not yet registered in the Philippines.

3.4 FDC's that are listed in International Compendia, such as the United States Pharmacopeia, British Pharmacopeia, World Health Organization Compendia and other similar listings, and deemed essential by the Department of Health may be exempted from the criteria described in 3.3 above.

SECTION 4. Applicability to FDC's with Pending or for Future Initial Registration —

4.1 The new and initial registration of all FDC's shall be governed by the above criteria upon effectivity of this Order. At whatever stage of such registration, provided the registration certificate has not yet been issued, compliance with the above criteria (Section 3) shall be required prior to issuance of registration.

4.2 All registration applications of FDC's shall henceforth be required to present the following:

a. A detailed statement stipulating the therapeutic/clinical rationale for FDC.

b. Information on the pharmaceutical, pharmacological and therapeutic properties, and any adverse reaction(s).

c. Clinical documentation to support efficacy and safety.

d. Bioequivalence studies, where applicable, to be done on Filipino patients demonstrating no unfavorable effect on the bioavailability of any of its active ingredients.

SECTION 5. Applicability to Currently Registered FDC's — All currently registered FDC's shall be required to comply with criteria stipulated in Section 3. In order to effect the orderly and systematic application of these regulations, the following procedures shall be undertaken:

5.1 Identification of all FDC drug products currently registered and their classification into the following use groups and order of priority for BFAD Review:

Priority I

1. Anti- infectives
2. Anti-asthmatics
3. Cough/cold remedies

Priority II