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Certifier	M. Bell

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 79N-0113; DESI 2847]

**Parenteral Multivitamin Products; Drugs for Human Use; Drug Efficacy Study
Implementation; Amendment**

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is amending the conditions for marketing an effective adult parenteral multivitamin drug product that published in the **Federal Register** of September 17, 1984 (49 FR 36446). The agency is notifying manufacturers of modifications in the adult formulation and certain portions of the labeling for the products.

DATES: Supplements to approved new drug applications (NDA's) and abbreviated new drug applications (ANDA's) are due on or before [*insert date 60 days after date of publication in the Federal Register*].

ADDRESSES: Communication in response to this notice should be identified with the reference number DESI 2847 and directed to the attention of the appropriate office named below.

Supplements to full NDA's (identify with NDA number): Division of Metabolic and Endocrine Drug Products (HFD-510), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Original ANDA's: Office of Generic Drugs (HFD-600), Center for Drug Evaluation and Research, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855.

Requests for opinion of the applicability of this notice to a specific product: Division of Prescription Drug Compliance and Surveillance (HFD-330), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855.

FOR FURTHER INFORMATION CONTACT: Mary E. Catchings, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2041.

SUPPLEMENTARY INFORMATION: In a notice published in the **Federal Register** of September 17, 1984 (49 FR 36446), FDA announced the conditions for marketing an effective parenteral multivitamin preparation. The effective 12-vitamin formulation set forth in the notice was based on the clinical evaluation of a guideline formulation recommended in 1975 by the American Medical Association (AMA). The notice also stated that, because parenteral multivitamin products are used and evaluated in patients with a variety of disease conditions, future adjustments to the formulation may be necessary.

On August 21, 1985, FDA's Division of Metabolic and Endocrine Drug Products and the AMA's Division of Personal and Public Health Policy sponsored a public workshop on "Multivitamin Preparations for Parenteral Use." At the workshop, additional data from clinical testing of the 1975 AMA formulation and a variety of other data were presented and discussed in light of available information on parenteral vitamin therapy. After examining the data, the AMA-FDA workshop committee recommended that the dosage of vitamins B₁, B₆, C, and folic acid be increased and that vitamin K be added to the formulation. Based on a review of the committee's recommendations, the Director of the Center for Drug Evaluation and Research has concluded that the 1975 AMA formulation for parenteral multivitamins should be modified to reflect the advice of the committee.

Accordingly, this notice amends portions of the section *Conditions for Approval and Marketing* in the September 17, 1984, notice as follows (in accordance with current labeling practice, amounts previously listed in international units (IU) have been converted to weights):

Paragraph 1(a)(i) is revised as follows:

1. *Adult formulation (intended for ages 11 and older)*

Ingredient	Amount per Unit Dose
<i>Fat Soluble Vitamins</i>	
A (retinol)	1 milligram (mg)
D (ergocalciferol or cholecalciferol)	5 micrograms (µg)
E (alpha-tocopherol)	10 mg
K (phyloquinone)	150 µg
<i>Water-Soluble Vitamins</i>	
C (ascorbic acid)	200 mg
Folic acid	600 µg
Niacin	40 mg
B ₂ (riboflavin)	3.6 mg
B ₁ (thiamine)	6.0 mg
B ₆ (pyridoxine)	6.0 mg
B ₁₂ (cyanocobalamin)	5 µg
Pantothenic acid	15.0 mg
Biotin	60 µg

2. Labeling conditions.

(a) The label must bear the statement “Rx only.”

(b) *Indication.* Paragraph 2(b)(i)(a) is revised as follows (This language may be editorially adapted to a specific product’s labeling, as appropriate.):

Adult. This formulation is indicated as a daily multivitamin maintenance dosage for adults and for children age 11 and above receiving parenteral nutrition. It is also indicated in other situations where intravenous administration is required. Such situations include surgery, extensive burns, fractures and other trauma, severe infectious diseases, and comatose states, which may provoke a stress situation with profound alterations in the body’s metabolic demands and consequent tissue depletion of nutrients. This product (administered in intravenous fluids under proper dilution) contributes intake of these vitamins that are necessary toward maintaining the body’s normal resistance and repair processes.

The physician should not await the development of clinical signs of vitamin deficiency before initiating vitamin therapy.

Patients with multiple vitamin deficiencies or with markedly increased requirements may be given multiples of the daily dosage for 2 or more days, as indicated by the clinical status. Clinical testing indicates that some patients do not maintain adequate levels of certain vitamins when this formulation in recommended amounts is the sole source of vitamins.

(c) *Contraindications:*

Known hypersensitivity to any of the vitamins or excipients in this product or a preexisting hypervitaminosis. Allergic reaction has been known to occur following intravenous administration of thiamine and vitamin K. The formulation is contraindicated prior to blood sampling for detection of megaloblastic anemia, as the folic acid and the cyanocobalamin in the vitamin solution can mask serum deficits.

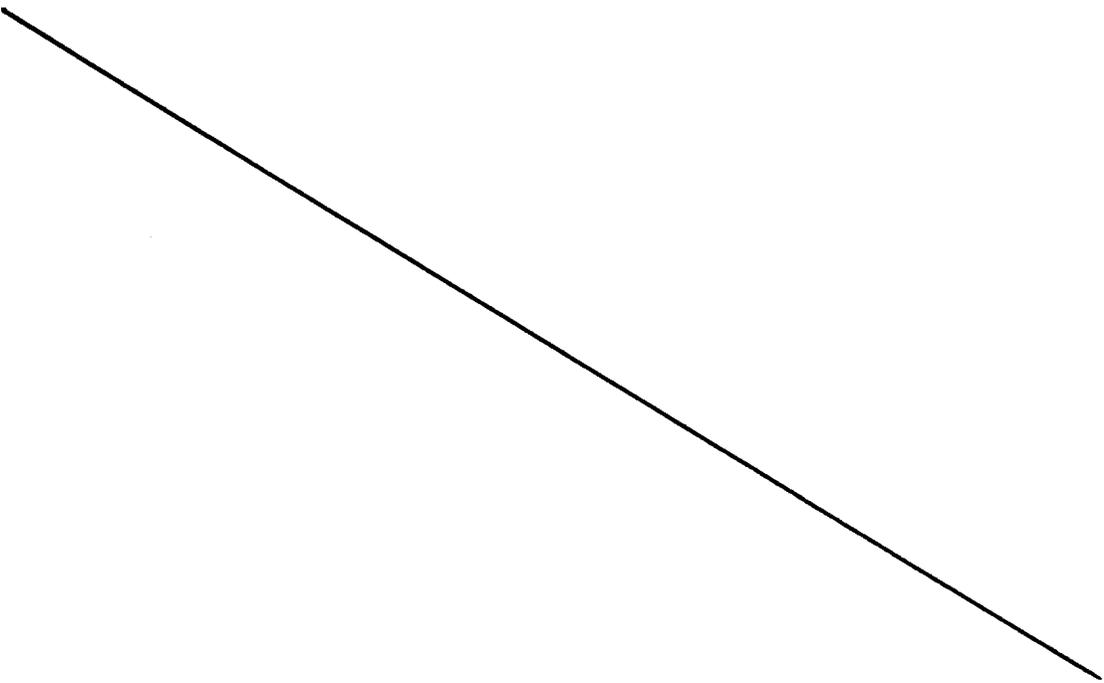
In addition, the following sections required by 21 CFR 201.57 should read as follows:

1. *Precautions*: (The following paragraph should be added and should appear in bold type.)

Caution should be exercised when administering this multivitamin formulation to patients on warfarin sodium-type anticoagulant therapy. In such patients, periodic monitoring of prothrombin time is essential in determining the appropriate dosage of anticoagulant therapy.

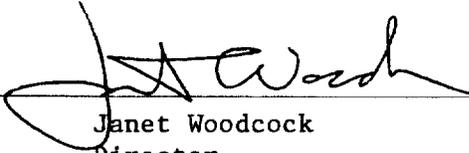
2. *Drug Reactions*: This section is revised to read “Drug Interactions” and to add aminophylline 125 mg and ampicillin 500 mg to this list.

Supplements to approved NDA’s or ANDA’s providing for appropriate revision of the labeling of drug products affected by this notice should be submitted on or before [*insert date 60 days after date of publication in the Federal Register*].



This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 201(n), 502, 505, 52 Stat. 1041, 1050-1053, as amended (21 U.S.C. 321(n), 352, 355)) and under the authority delegated to the Director of the Center for Drug Evaluation and Research (21 CFR 5.70).

Dated: 3/28/00
March 28, 2000



Janet Woodcock
Director
Center for Drug Evaluation
and Research

[FR Doc. 00-???? Filed ??-??-00; 8:45 am]

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