CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-265

CHEMISTRY REVIEW(S)

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-265 **DATE REVIEWED: 02-05-01**

REVIEW #: 1 **REVIEWER:** David B. Lewis, Ph.D.

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	04-20-00	04-21-00	06-07-00
AMENDMENT	06-05-00	06-13-00	
AMENDMENT	08-25-00	08-30-00	
AMENDMENT	10-06-00	10-10-00	
AMENDMENT	11-02-00	11-06-00	
AMENDMENT	11-27-00	11-29-00	
AMENDMENT	01-09-01	01-11-01	
AMENDMENT	01-10-01	01-12-01	
AMENDMENT	01-25-01	01-25-01	

NAME & ADDRESS OF APPLICANT: SABEX Pharmaceutical Products (Produits Pharmaceutiques)
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Authorized U.S. Agent:
Ken Muhvich, Ph.D.
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DRUG PRODUCT NAME

Proprietary:	Multi-12®/K$_1$ Pediatric (original proposed name) INFUVITE PEDIATRIC (alternate name — see review notes)
Established:	Multiple Vitamins for infusion
Code Name/#:	
Chem.Type/Ther.Class:	5S

PHARMACOL. CATEGORY/INDICATION: Daily multi-vitamin maintenance supplement for adults and children (aged 11 and older) receiving parenteral nutrition. [3042500]

DOSAGE FORM:	Injection (Vial 1, 4-mL and Vial 2, 1-mL)
STRENGTHS:	See Chemist's Review Notes
ROUTE OF ADMINISTRATION:	Intravenous
Rx/OTC:	X **Rx** __ **OTC**

SUPPORTING DOCUMENTS: Letters of Authorization, allowing reference to the following DMF's:

RELATED DOCUMENTS (if applicable): Official minutes (meeting between [redacted] and the FDA, dated 8-20-98), and the following Drug Master Files:

Type/Number	Subject	Holder	Status	Review Date
[redacted]				

CONSULTS: Microbiology and Office of Post-Marketing Risk Assessment (OPDRA)

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Ascorbic Acid (Vitamin C), Retinyl palmitate (Vitamin A), Cholecalciferol (Vitamin D_3), Thiamine (Vitamin B_1), Riboflavin phosphate (Vitamin B_2) Niacinamide, Pyridoxine hydrochloride (Vitamin B_6), Dexpanthenol (Vitamin B_5), *dl*-α-tocopheryl acetate (Vitamin E), Folic acid, Biotin, Phytonodione (Vitamin K_1), and Cyanocobalamin (Vitamin B_{12}). The structures, empirical formulae, and molecular weights are provided in this review in the Chemist's Review Notes.

REMARKS: NDA 21-265 provides chemistry, manufacturing and controls information for Multi-12®/K_1 Pediatric (multiple vitamins for infusion), which is described as a sterile product consisting of two single-dose vials. Vial 1 has a 4-mL fill volume and Vial 2 has a 1-mL fill volume; the drug product, in its entirety (both vials) makes available a combination of 13 essential oil- and water-soluble vitamins in an aqueous solution. The components and composition corresponds to those, which were dictated by the Federal Register Notice issued on January 26th, 2000 (65 CFR 4253). CMC information, regarding Vitamin K_1 (phytonadione) is supplied directly to NDA 21-265 as a confidential document by the supplier [redacted] dated 6-26-00. CMC information, regarding niacinamide is supplied by [redacted] directly to NDA 21-265 (Appendix 1.0), and also in the amendment dated 8-25-00. CMC information on the remaining eleven vitamin substances is documented *via* reference to Sabex NDA 21-163 (Multi-12®), which is the adult formulation. The amendment dated 6-05-00 provides a "notification of US Agent Letter", which was omitted from the original application, along with corrections to the drug product specifications and stability protocol. The amendment dated 10-06-00 provides microbiological information. The amendment dated 11-02-00 provides updated stability data, along with alternate analytical methods for individual vitamin assays. The amendment dated 11-27-00 provides aluminum-related information (data, labeling, analytical methodology, and MV, as required by 65 FR 4103 and 21 CFR 201.323). The amendment dated 1-09-01 clarifies the maximum proposed batch size for the drug product solution(s). The amendment dated 1-10-01 provides revisions to the immediate container label for Vial # 2. The amendment dated 1-25-01 contains a revised stability protocol, which includes aluminum testing. The TeleCon dated 1-25-01 contains information, regarding the specified limits for aluminum during stability testing. The TeleCon dated 2-02-01 provided an alternate tradename "Infuvite Pediatric" for the drug product. Issues of sterility assurance are addressed in the Microbiology Review; the application is recommended for approval, Micro. Review dated 10-18-00, C. Vincent, reviewer. An EER was submitted on 6-08-00, An EES (acceptable, dated 11-24-00) is attached. The labeling (immediate container, carton labeling, and package insert, along with the proposed tradename [Multi-12®/K_1 Pediatric]) was submitted to OPDRA for review; a review of the OPDRA consult is attached (see "Labeling" section of review notes, and memorandi dated 2-02-01 and 2-05-01. *A MV package was submitted to the field testing laboratories (Philadelphia and San Juan), regarding the assay for Vitamin K_1; results are pending.*

CONCLUSIONS & RECOMMENDATIONS: Adequate information, regarding chemistry, manufacturing and controls has been provided. The application is recommended for approval concerning chemistry.

cc:
Org. NDA 21-265 Review
HFD-510
HFD-510/D Lewis/
HFD-510/S. McCort
HFD-102/
R/D Init by: /S/ 2/9/01

David B. Lewis, Ph.D.
Review Chemist

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38 **page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.**