Vitamin A Oral Liquid Preparation

DEFINITION

Change to read:

Vitamin A Oral Liquid Preparation is an emulsion, suspension, or solution that contains retinyl acetate or retinyl palmitate in an amount equivalent to NLT •90.0%• (RB 1-Apr-2013) and NMT 120.0% of the labeled amount of vitamin A, as retinol ($C_{20}H_{30}O$).

IDENTIFICATION

[NOTE—Use low-actinic glassware.]

- **A.**
  Sample solution: Prepare a solution in methylene chloride containing an amount of Oral Liquid Preparation equivalent to about 6 µg of retinol in 1 mL.
  Analysis: Add 10 mL of antimony trichloride TS to 1 mL of *Sample solution*.
  Acceptance criteria: A transient blue color appears at once.
- **B. THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST ⟨201⟩**
  Standard solution: 0.5 mg/mL of retinol from USP Retinyl Acetate RS or USP Retinyl Palmitate RS in methylene chloride
  Sample solution: Dissolve or extract with methylene chloride a quantity of Oral Liquid Preparation to obtain a solution with a nominal concentration of 0.5 mg/mL of retinol.
  Application volume: 10 µL as an 8-mm band
  Developing solvent system: A mixture of cyclohexane and ether (4:1)
  Spray reagent: 0.2 g/mL of phosphomolybdic acid in alcohol. Filter, and use only the clear filtrate.
  Analysis: Apply the *Sample solution* at the starting point of the chromatogram, and proceed as directed in *Chromatography* ⟨621⟩*, Thin-Layer Chromatography*. Allow the solvent front to move 10 cm, remove the plate, and air-dry. Spray with *Spray reagent*.
  Acceptance criteria: The blue-green spot formed is indicative of the presence of retinol, and its R_F value corresponds to that of the *Standard solution*. The approximate R_F values of the predominant spots, corresponding to the different forms of retinol, are 0.1 for the alcohol form, 0.45 for the acetate, and 0.7 for the palmitate.

ASSAY

Change to read:

- **VITAMIN A**
  [NOTE—Use low-actinic glassware.]
  Mobile phase: *n*-Hexane
  Standard solution 1: 13 µg/mL of retinol from USP Retinyl Acetate RS in *n*-hexane
  Standard solution 2: 13 µg/mL of retinol from USP Retinyl Palmitate RS in *n*-hexane
  System suitability solution: Mix equal volumes of *Standard solution 1* and *Standard solution 2.*
  Sample solution
  For Oral Liquid Preparation in oil vehicles packaged in single-unit containers: Deliver the contents of NLT 30 single-unit containers, following the directions for use as stated in the labeling. Weigh directly the individual contents delivered from each single-unit container, and calculate the average. [NOTE—Do not weigh the contents delivered by difference between full containers and empty containers. Capsules intended as single-unit containers are not rinsed after expulsion of the contents.] Mix the contents to obtain a homogeneous sample. Transfer an amount of the composite to a suitable volumetric flask. Dissolve with hexane, and dilute with hexane quantitatively and stepwise, if necessary, to obtain a solution containing the equivalent of about 13 µg/mL of retinol, based on the labeled amount.
  For Oral Liquid Preparation in oil vehicles packaged in multiple-unit containers: Dissolve an accurately measured volume of Oral Liquid Preparation in a suitable volume of hexane, and dilute with hexane, quantitatively and stepwise, if necessary, to obtain a solution containing the equivalent of about 13 µg/mL of retinol, based on the labeled amount.
  For Oral Liquid Preparation in aqueous vehicles: Transfer a weighed quantity, or an accurately measured volume of Oral Liquid Preparation, into a separatory funnel, and extract quantitatively with hexane or other suitable solvent. Dilute with hexane, quantitatively and stepwise, if necessary, to obtain a solution containing the equivalent of about 13 µg/mL of retinol, based on the labeled amount.
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV 325 nm
  Column: 4.6-mm × 15-cm; packing L8
  Flow rate: 1 mL/min
  Injection volume: 40 µL
  System suitability
  Sample: *System suitability solution*
  Suitability requirements
  Resolution: NLT 10 between all-*trans*-retinyl acetate and all-*trans*-retinyl palmitate
  Relative standard deviation: NMT 3.0%
  Analysis
  Samples: *Standard solution 1* or *Standard solution 2* and *Sample solution*
  Calculate the percentage of the labeled amount of vitamin A, as retinol ($C_{20}H_{30}O$), in each individual container:

$$\text{Result} = (r_U/r_S) \times (C/W) \times (V/D) \times U \times (100/L)$$

r_U = peak response of the corresponding all-*trans*-retinyl ester from the *Sample solution*
r_S = peak response of the all-*trans*-retinyl ester from the appropriate *Standard solution*
C = concentration of retinol ($C_{20}H_{30}O$) in the appropriate *Standard solution* (mg/mL)
W = weight or volume of Oral Liquid Preparation composite taken (mg or mL)
V = volume of the *Sample solution* (mL)
D = dilution factor (dilution volume/aliquot volume)
U = for multiple-unit containers: labeled volume of each dosage unit (mL); or for single-unit containers: average mass (mg) of the contents delivered from each individual container, following the directions for use as stated in the labeling
L = labeled amount of vitamin A, as retinol ($C_{20}H_{30}O$), in each dosage unit (mg)

Acceptance criteria: •90.0%• (RB 1-Apr-2013)–120.0%

PERFORMANCE TESTS

- **DELIVERABLE VOLUME ⟨698⟩:** Meets the requirements for Oral Liquid Preparation packaged in multiple-unit containers
- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩**

  Analysis: For Oral Liquid Preparation packaged in single-unit containers, empty the single-unit containers, following the directions for use as stated in the labeling. [NOTE—Do not weigh the contents delivered by difference between full containers and empty containers. Capsules intended for use as single-unit containers are not rinsed after expulsion of the contents.]

  Acceptance criteria: The contents so delivered, and weighed directly, meet the requirements.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. It may be packaged in single-unit containers. [NOTE—Capsules may be suitable as single-unit containers provided they are packaged in critical secondary containers as described in *Good Packaging Practices* ⟨1177⟩.]
- **LABELING:** The label states that the product is Vitamin A Oral Liquid Preparation. Label the Oral Liquid Preparation to indicate the ester form in which the vitamin is present, and to indicate the amount of vitamin A delivered in each dosage unit in terms of the equivalent amount of retinol in mg/dosage unit. The amount of vitamin A delivered may be stated also in USP Units/dosage unit, on the basis that 1 USP Vitamin A Unit equals the biological activity of 0.3 µg of all-*trans*-retinol. Capsules used as single-unit containers may be exempted from the requirements of individual labeling, provided they are packaged in an appropriately labeled secondary container, including directions for use and delivery of each dosage unit of Oral Liquid Preparation. Label the Oral Liquid Preparation packaged in multiple-unit containers to indicate the volume of each dosage unit.
- **USP REFERENCE STANDARDS ⟨11⟩**

  USP Retinyl Acetate RS
  USP Retinyl Palmitate RS