CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40254

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA: 40-254

FIRM: Vintage Pharmaceuticals, Inc.
Attention: Rebecca A. Thurman
3241 Woodpark Blvd.
Charlotte, NC 28206

DOSAGE FORM: Tablet STRENGTH: 2 mg and 5 mg

DRUG: Trihexyphenidyl

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable 9/10/97.

BIO STUDY INFORMATION: Acceptable 10/9/97.

METHODS VALIDATION: Drug substance and drug product are compendial items. Methods verification acceptable 7/23/97.

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION? yes

The containers used in the stability study are of the same size and material as those described in the container section. The firm submitted accelerated stability data for the product packaged in all container sizes.

The firm requests an expiration date of 24 months based on the data submitted.

The stability tests and specifications are indicated in the following table:

TEST	SPECIFICATION
Appearance	White, flat-faced beveled edge round, bisected tablets debossed with "5971/V" and "5972/V" for the 5 mg tab
Hardness 2 mg tablet 5 mg tablet	 NLT kp NLT kp

Related Substances/Impurities B-(N-piperidinyl)propiophenone Related Substances	 NMT % Single unknown NMT % Total related substances NMT %
Dissolution	NLT % in 45 min
Assay	%

LABELING: Acceptable 6/11/98.

STERILIZATION VALIDATION: N/A

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?)

No information on bio-batch since a waiver was granted.

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED VIA SAME PROCESS?)

An exhibit/stability batch of tablets was manufactured.

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?

A summary of the equipment used for the demonstration batch and proposed production batch is provided in the validation summary on p. 213. The applicant states that the operating principles are the same except for differences in capacity and operating parameters.

The intended production batch size is tablets.

RECOMMENDATION: Approvable pending labeling.

SIGNATURE: /S/ DATE: 12/10/98

COMPONENTS AND COMPOSITION

2 MG TABLET

INGREDIENT	AMT PER TABLET	AMT PER BATCH
Trihexyphenidyl HCl USP	2.00 mg	kg
Microcrystalline Cellulose NF PH102	mg	kg
Sodium Starch Glycolate NF	mg	kg
Magnesium Stearate, NF	mg	g
Total weight	mg	kg

5 MG TABLET

INGREDIENT	AMT PER TABLET	AMT PER BATCH
Trihexyphenidyl HCl USP	5.00 mg	kg
Microcrystalline Cellulose NF PH102	mg	kg
Sodium Starch Glycolate NF	mg	kg
Magnesium Stearate, NF	mg	g
Total weight	mg	kg

Components used in the formulation are USP/NF grade.

The specifications for the granulation are as follows:

Blend Uniformity .0% RSD 5.0%
Bulk Density g/mL
Tap Density g/mL
Particle size

A. mesh Screen NLT %
B. Size distribution Report results

(2 mg tablet)

TESTS	SPECIFICATIONS/10 TABLETS
Weight	g

Hardness	2.4 kp -7.7 kp
Thickness	2.3 mm- 3.1 mm
Friability	%
Disintegration	NMT min

(5 mg tablet)

TESTS	SPECIFICATIONS/10 TABLETS
Weight	g
Hardness	3.3 kp -15.4 kp
Thickness	2.7 mm- 3.8 mm
Friability	%
Disintegration	NMT min

The finished product specifications are as follows:

TEST	SPECIFICATION
Appearance	White, flat-faced beveled edge round, bisected tablets debossed with "5971/V"
Avg. Tablet Weight 2 mg tablet 5 mg tablet	 mg mg
Hardness 2 mg tablet 5 mg tablet	 2.4-7.7 kp 3.3-15.4 kp
Related Substances/Impurities B-(N-piperidinyl)propiophenone Related Substances	 NMT % Single unknown NMT % Total related substances NMT %
Identification	A: IR spectrum matches std B: Chloride <191> C: RT of peak in samples matches that of std
Dissolution	NLT % in 45 min
Uniformity of Dosage units	meets USP %
Assay	%

The finished product COA for lot #049116 is on page 466. The finished product COA for lot #057106 is on page 483.

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 40-254

3. NAME AND ADDRESS OF APPLICANT
Vintage Pharmaceuticals, Inc.
Attention: Rebecca A. Thurman
3241 Woodpark Blvd.
Charlotte, NC 28206

4. LEGAL BASIS FOR SUBMISSION
The application is submitted in accordance with Section 505(j) of the FD&C Act, as amended, and 21 CFR 314, Subpart C.

The reference listed drug is ARTANE (Trihexyphenidyl Hydrochloride Tablets 2 mg and 5 mg) manufactured by Lederle.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Trihexyphenidyl Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Orig Sub.	4/28/97
Ack. Ltr.	5/27/97
Amendment	3/13/98
Amendment	10/29/98
Amendment	12/08/98
Amendment	12/10/98

10. PHARMACOLOGICAL CATEGORY
Anticholinergic, antiparkinsonian

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Tablet

14. POTENCY
2 mg and 5 mg

15. CHEMICAL NAME AND STRUCTURE
USP drug substance; USP drug product
1-piperidinepropanol, alpha-cyclohexyl-alpha-phenyl-, hydrochloride ±

16. RECORDS AND REPORTS
N/A

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS
Approvable.

19. REVIEWER:
A. Langowski

DATE COMPLETED:
11/30/98