CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40191

CORRESPONDENCE

ANDA 40-191

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

SEP 13 1996

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to our "Refuse to File" letters dated July 1 and August 6, 1996,and to your amendments dated July 8 and August 22, 1996.

NAME OF DRUG: Meperidine Hydrochloride Tablets USP,
50 mg and 100 mg

DATE OF APPLICATION: June 4, 1996

DATE OF RECEIPT: June 5, 1996

DATE ACCEPTABLE FOR FILING: August 23, 1996

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Tim Ames
Project Manager
(301) 594-0305

Sincerely yours,

/S/ 9/13/96

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 40-191

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

AUG 6 1996

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) dated June 4, 1996, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Meperidine Hydrochloride Tablets USP, 50 mg and 100 mg.

Reference is also made to our "Refuse to File" letter dated July 1, 1996, and your amendment dated July 8, 1996.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reason:

> Regarding the test batch #062105 for the 50 mg strength, please provide additional documentation which confirms that the portion of the test batch that was packaged is representative of the entire test batch. Such documentation should include results of in-process testing, a sampling protocol, and a statement that the partial packaging procedure was performed in compliance with the Office of Generic Drugs Policy and Procedure Guide #41-95. In addition, please provide the results of an investigation regarding the rejection of approximately one-third of your test batch and information that the remaining portion of the batch meets your release specifications.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Also, please be aware that approval cannot be given for more than a ten-fold scale up of your exhibit batch. Your blank master batch record reflects a proposed production batch size of tablets for the 50 mg strength. However, your exhibit batch yield for the 50 mg strength is tablets, a scale up of which would be tablets. Please revise your blank master batch records to reflect this scale-up.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3)If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Timothy Ames
Project Manager
(301) 594-0305

Sincerely yours,

/S/

Jerry Phillips
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 40-191
cc: DUP/Jacket
Division File
HFD-82
Field Copy
HFD-600/Reading File
HFD-615/MBennett
Endorsement: HFD-615/PRickman, Acting date 8/5/96
HFD-615/CSO/Weikel date 7/29/96
HFD-647/Chem Branch date 8.5.96
X:\new\firmsnz\vintage\ltrs&rev\40191.rtf
F/T File bcw\7-29-96
ANDA Refuse to File!

ANDA 40-191

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

JAN - 6 1997

Dear Madam:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Meperidine Hydrochloride Tablets USP, 50 mg and 100 mg.

1. The Division of Bioequivalence has completed its review and has no further questions at this time.

2. The dissolution testing will need to be incorporated into your stability and quality control programs as specified in USP 23.

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

/S/

Rabindra Patnaik, Ph.D.
Acting Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 40-191

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

JUL 1 1996

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) dated June 4, 1996, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Meperidine Hydrochloride Tablets USP, 50 mg and 100 mg.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reason:

> You are required to completely package your exhibit batch in the containers proposed for marketing. Partial packaging of the test batch is not acceptable without documentation to confirm that the portion of the test batch packaged is representative of the entire batch. Such documentation should include results from in-process testing and a sampling protocol that demonstrates homogeneity of the test batch. For further reference, please refer to the letters to industry from the Director, Office of Generic Drugs, dated November 8, 1991, and August 4, 1993 and the February 8, 1995, Office of Generic Drugs Policy and Procedure Guide #41-95.
>
> We note that the inactive ingredients in the test batch formulation do not match the inactive ingredients listed in your proposed labeling. Please clarify this discrepancy. You have also failed to provide the sources and Certificates of Analysis for all of the inactive ingredients for the proposed product. Please either revise the DESCRIPTION section of the labeling or the test batch formulation accordingly.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

In addition, Form FDA 356h submitted in the archival copy of this application lacks an original signature. Please submit this form with an original signature.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3)If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Timothy Ames
Project Manager
(301) 594-0315

Sincerely yours,

/S/ 7/1/96

Jerry Phillips for
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 40-191
cc: DUP/Jacket
Division File
HFD-82
Field Copy
HFD-600/Reading File
HFD-615/MBennett
Endorsement: HFD-615/PRickman, Acting 7/1/96 date
HFD-615/CSO/Weikel date 6/27/96
HFD-647/Chem Branch date
X:new\firmsnz\vintage\ltrs&rev\40-191.f
F/T bcw/6-25-96
ANDA Refuse to File!

3241 Woodpark Blvd.
Charlotte, NC 28206

Vintage
Pharmaceuticals, Inc.

(704) 596-0516

June 4, 1996

RECEIVED
JUN 05 1996
GENERIC DRUGS

Office of Generic Drugs, CDER, FDA
Document Control Room, Rm 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

Dear Sir:

In accordance with Section 505(j) of the FD&C Act, as amended, and 21 CFR Part 314.94, we are submitting an original Abbreviated New Drug Application for:

Meperidine HCl Tablets, USP
50 mg and 100 mg

Vintage Pharmaceuticals, Inc. is registered as a manufacturer of controlled substances in schedules II, III, IV, and V, under DEA Registration No. RV0172976.

In-vitro bioequivalence studies are included in section VI.

The archival copy of the ANDA consists of one volumes. The review copy consists of one red-jacketed chemistry & manufacturing volumes and one separately bound, orange-jacketed bioequivalence volume. All volumes contain a complete Table of Contents. The following items are included immediately following the NDA Form 356h:

-Prescription Status Statement
-Debarment/Conviction Certification
-Field Copy Certification

We look forward to your early response. If you have any questions or comments regarding this application, please contact the undersigned, or as an alternate, Mr. John Schultz, Assistant General Manager, at Tel. (704) 596-0516.

Sincerely,
VINTAGE PHARMACEUTICALS, INC.

Rebecca A. Thurman
Manager, Regulatory Affairs

3241 Woodpark Blvd.
Charlotte, NC 28206

Vintage
Pharmaceuticals, Inc.

(704) 596-0516

NDA ORIG AMENDMENT

July 8, 1996

Office of Generic Drugs, CDER, FDA
Document Control Room, Rm 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

RE: Meperidine HCL Tablets, USP 50 mg & 100 mg
ANDA 40-191
Amendment

Dear Sir:

Please refer to our Abbreviated New Drug Application dated June 4, 1996 for Meperidine-HCl Tablets, USP 50 mg & 100 mg, ANDA# 40-191. Please refer also to your letter dated July 1, 1996.

In response to your letter, Vintage has enclosed manufacturing and packaging reconciliation and yield summaries to verify that the entire demonstration batches of Meperidine HCl Tablets, USP 50 mg & 100 mg were indeed packaged. These summaries were submitted in the original ANDA submission. The summaries can be found on pages 0211, 0232, 0252 and 0264 of the original submission and as Attachment I of this amendment. Also included in the summaries is the reference to page numbers in the submission where the data can be cross-referenced.

The inactive ingredients were noted incorrectly on the insert. Revised insert proofs are submitted as attachment II.

Attachment III contains the 356H form with original signature.

If you have any questions or comments regarding this application, please contact the undersigned, or as an alternate, Mr. John Schultz, Assistant General Manager, at Tel. (704) 596-0516.

Sincerely,
VINTAGE PHARMACEUTICALS, INC.

Rebecca A. Thurman
Manager, Regulatory Affairs

3241 Woodpark Blvd.
Charlotte, NC 28206

Vintage Pharmaceuticals, Inc.

(704) 596-0516

NDA AND AMENDMENT

9/10/96

RECEIVED

AUG 23 1996

GENERIC DRUGS

August 22, 1996

Office of Generic Drugs, CDER, FDA
Document Control Room, Rm 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

RE: Meperidine HCL Tablets, USP 50 mg & 100 mg
ANDA 40-191
Amendment

Dear Sir:

Please refer to our Abbreviated New Drug Application dated June 4, 1996 for Meperidine HCl Tablets, USP 50 mg & 100 mg, ANDA# 40-191. Please refer also to your letter dated July 1, 1996, our response dated July 8, 1996 and your letter dated August 6, 1996.

In response to your letter, Vintage has enclosed manufacturing and packaging reconciliation and yield summaries to verify that the entire demonstration batches of Meperidine HCl Tablets, USP 50 mg were indeed packaged. Included in the summaries are explanations for tablets that cannot be packaged due being set-up rejects or not meeting weight specifications. All tablets that were not rejected were packaged. (Attachment I) [refer to process validation results on page 146 and 147 for verification that the batch is indeed uniform].

Also included in our response our revised blank master batch records for the 50 mg and 100 mg to reflect a scale-up of 10x the yield actually obtained. (See Attachment II and III).

Attachment IV and V contains the revised reprocessing records to reflect a scale-up of

If you have any questions or comments regarding this application, please contact the undersigned, or as an alternate, Mr. John Schultz, Assistant General Manager, at Tel. (704) 596-0516.

Sincerely,
VINTAGE PHARMACEUTICALS, INC.

Rebecca A. Thurman
Manager, Regulatory Affairs

3241 Woodpark Blvd.
Charlotte, NC 28206

Vintage
Pharmaceuticals, Inc.

(704) 596-0516

NDA [illegible] AMENDMENT
N/FA

December 10, 1997

Office of Generic Drugs, CDER, FDA
Document Control Room, Rm 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

RE: Minor Amendment , ANDA 40-191
Meperidine Hydrochloride Tablets, USP
50 mg & 100 mg

TELEPHONE AMENDMENT

Dear Sir

Please refer to our original ANDA, submitted June 4, 1996, our amendments dated July 8, 1996 and August 22, 1996, March 20, 1997, and November 14, 1997 and your telephone call December 8, 1997. As requested by your phone call, enclosed is a commitment by Vintage for doing torque testing as an in-process check during packaging.

This completes our response to the telephone amendment. If I can be of further assistance or if you have any questions, please contact Rebecca Thurman or John Schultz at (704) 596-0516.

Sincerely,

Rebecca Thurman
Manager, Regulatory Affair

3241 Woodpark Blvd.
Charlotte, NC 28206

Vintage Pharmaceuticals, Inc.

(704) 596-0516

November 14, 1997

Office of Generic Drugs, CDER, FDA
Document Control Room, Rm 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

RE: Minor Amendment , ANDA 40-191
Meperidine Hydrochloride Tablets, USP
50 mg & 100 mg

FACSIMILE AMENDMENT

NOTE: Labeling is not included in the fax, however it is included in the hard copy that has been mailed to the document control room.

Dear Sir

Please refer to our original ANDA, submitted June 4, 1996, our amendments dated July 8, 1996 and August 22, 1996, and March 20, 1997 and your letter dated October 15, 1997. Each of the points in your letter is restated, followed by our response.

A. Chemistry Deficiencies

1. Regarding container/closures:

a. Please submit USP <671> test results for the finished product container/closure system to demonstrate that they meet USP test requirements for tight containers.

Attachment 1 - Results of USP <671> as conducted by Vintage

b. Please submit removal and application torque specifications and test results for 60 cc finished product container/closure systems.

Torques are not tested as part of our line check, however seal integrity to of the container/closure system is checked every hour by the quality assurance department.

Labeling Deficiencies:

1. CONTAINER (100s)
   Relocate the statement "WARNING: May be habit forming.", to immediately follow the established name on the principal display panel. We refer you to 21 CFR 329.10(c) for further guidance.

   Attachment II - Final print container labels

2. INSERT

   a. ADVERSE REACTIONS, Nervous System-... uncoordinated muscle movements, severe convulsions, transient hallucinations...

   b. DOSAGE AND ADMINISTRATION

   Delete the second sentence of the first paragraph.

   c. HOW SUPPLIED

   Please describe your 100 mg tablet as unscored.

Please revise your container labels and insert labeling, as instructed above, and submit final print.

Attachment II - Final print container labels
Attachment III - Final printed inserts

Please note that we reserve the right to request further changes in your labels and/or labeling based upon further changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

This completes our response to the deficiency letter issued. If I can be for further assistance or if you have any questions, please contact Rebecca Thurman or John Schultz at (704) 596-0516.

Sincerely,

Rebecca Thurman
Manager, Regulatory Affair

3241 Woodpark Blvd.
Charlotte, NC 28206

Vintage
Pharmaceuticals, Inc.

(704) 596-0516

Labeling review drafted 8/25/97 G.Vegso

March 20, 1997

NDA 40-191 AMENDMENT

N/AC

Office of Generic Drugs, CDER, FDA
Document Control Room, Rm 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

RE: Major Amendment , ANDA 40-191
Meperidine Hydrochloride Tablets, USP
50 mg & 100 mg

Dear Sir

Please refer to our original ANDA, submitted June 4, 1996, our amendments dated July 8, 1996 and August 22, 1996 and your letter dated March 7, 1997. Each of the points in your letter is restated, followed by our response.

A. Chemistry Deficiencies

1. Regarding Composition and Components:

a. "Please indicate the type of microcrystalline cellulose as a PH 101 in your components and composition statement."

Attachment I - Revised Composition and Components Statement

b. "Please include Deionized Water and amount used in executed batch in your components and composition statement.

Attachment I - Revised Composition and Components Statement

2. **Regarding Drug Substance:**

a. **"Please revise your and manufacturer's COAs for drug substance to include individual and total related substance/degradation products limits.**

Attachment II - Revised Vintage Certificate of Analysis
Example of COA
was not testing for related substances/degradation products at the time the lot of drug substance was released. Future lots will have the testing conducted as shown on the COA.

b. **Active drug substance test results (reference standard IR, IR spectrums, test results) are provided on pages 88-93. Please provide representative chromatograms for assay, related substance and system suitability.**

Attachment III - Vintage Chromatograms
Representative chromatograms can be found on pages 368, 385, 386 and 420 of DMF (updated 6/4/96)

3. **Regarding Manufacturing and Processing:**

a. **"Please provide your target thickness and hardness specifications for the 50 mg and 100 mg tablets in your executed and production batch records. Resubmit revised batch records."**

Attachment IV - Revised executed batch record, see page 9 of 12 (50 mg) and 10 of 13 (100 mg)
Attachment V - Revised production batch record, see page 11 of 14 (50 mg) and 14 of 17 (100 mg)

b. **"According to your finished product Certificate of analysis, tablets are scored. Please revise your tablet description in you manufacturing batch records, tablet tooling, and stability reports. Resubmit revised manufacturing batch records and stability reports accordingly.**

The 50 mg tablet is scored as indicated on all documents. The tablets from the 100 mg demonstration batch were scored, however, due to guideline 40-94, the production batches of 100 mg will not be scored. This was indicated on the stability reports for production batches (batch type marked as production)[see page 453 of original submission] and on the production batch records [see page 181 and of original submission].

Attachment V - Production batch record, see page 11 of 14 (50 mg) and 14 of 17 (100 mg)
Attachment VI - Stability Reports
Attachment VII - Certificates of Analysis

c. **"Please submit correct tablet description in "How Supplied" section of your labeling."**

Attachment XVII - Revised package insert

d. **"Please submit revised master batch records identifying the compression speed and the type of the tablet machine."**

Attachment V - Production batch record, see page 11 of 14 (50 mg) and 14 of 17 (100 mg)

e. **"Your reconciliation limit after screening/milling dry granule (%) and reconciliation limit for compounding (%) are very wide. Please provide tightened limits.**

The limits as submitted in the original submission (pages 160,162, 178, 179) were submitted as %.

f. **Please provide the following limits listed below, in your batch records.**

Accountability limit for milling, process yield for milling, accountability limit for granulation, process yield for granulation, accountability limit for tabletting, process yield limit for tabletting and compression process target yield.

The accountability limits for each phase was part of the original submitted production batch records [see , , , , , and]. The yield was also calculated for each of these phases however, a limit was not given for yields. The batch records have been revised to include both accountability and yield limits.

Attachment V - Revised batch production records
Milling 50 mg page 8 of 14, 100 mg page 11 of 17
Granulation 50 mg page 10 of 14, 100 mg page 13 of 17
Tabletting 50 mg page 14 of 14, 100 mg page 17 of 17

4. **Regarding Container/Closures:**

a. **"Please clarify which bottles are used for packaging as container during the manufacturing and packaging process; 60 cc bottles or amber Glass Bottles.**

The correct bottle is the amber glass bottle
Attachment VIII - Revised Container/Closure summary

b. **Please provide DMF numbers for metal cap manufacturer (and supplier , for 33 mm metal cap."**

Attachment IX - DMF letters ' PS22 foam seal), (cardboard lining) and is a supplier/distributor and is not required to have a DMF

c. **"Please submit removal and application torque specifications and test results for 60 cc finished container/closure systems.**

Torque specifications are not specified due to bottles being checked on line by QA every hour for seal integrity (seal must be intact to bottle).

d. **"Please provide Vintage's and manufacturer's testing specifications and COA's for Glass containers."**

Attachment X - Vintage specifications and test results. The QA inspection report for the bottle also serves as the Vintage COA.
Attachment XI - Manufacturer's specifications and results (COA)

e. **Please submit USP <661> and <671> test results for glass containers and the finished product container/closure system (tight, light resistant) demonstration that they meet USP test requirements."**

Attachment XII - USP testing results
Moisture permeability results can be found in the DMF (DMF

f. **Please explain using colorant in amber glass bottles and provide DMF authorization letter to reference .**

is incorrect for colorant and has been removed from the summary statement.

Attachment VIII - Revised Summary of Container/Closure system

5. **Regarding laboratory controls:**

a. **"The hardness variation limits are (2.8 kp - 7.0 kp) and (3.1 kp-13.3 kp) for 50 mg and 100 mg tablets, respectively, These limits are very broad. Please include tightened specifications based on actual data."**

Based on actual data, the hardness limits for the 100 mg have been tightened to 5.0 kp - 13.3 kp) Due to the 50 mg tablet having a hardness range of only 4.2 kp, the range will not change.

Attachment XIII - laboratory procedure
Attachment XIV - Finished product and In-process specifications

b. **"Please provide moisture content limits for dry granulation and tablets. Please include these limits in your batch records, finished product and stability testing protocol."**

Attachment V - Revised batch production records, see page 10 of 14 (50 mg) and page 13 of 17 (100 mg)
Attachment XIV - Finished Product specifications
Attachment VI - Stability Protocols

c. **According to finished product descriptions, 50 mg and 100 mg tablets are scored. Your executed batch record and stability records indicate that tablets are unscored. Please be consistent and resubmit revised your executed and production batch records and stability reports accordingly.**

The 50 mg tablet is scored as indicated on all documents. The tablets for the 100 mg demonstration batch were scored, however, due to guideline 40-94, the production batches of 100 mg will not be scored. This was indicated on the stability reports for production batches and on the production batch records.

Attachment IV - Executed demonstration batch records, see page 9 of 12 (50 mg) and 10 of 13 (100 mg)
Attachment V - Production batch records, see page 11 of 14 (50 mg) and 14 of 17 (100 mg)
Attachment VI - Stability protocols

d. **Please specify your individual degradants/impurities limits based on your test results.**

Attachment XIV - Finished product specifications

e. **Please provide packaging and labeling reconciliation limits for finished products.**

Reconciliation limits are specified on page 256 and 268 of the original submission as %
Attachment XV - Packaging record, see page 4 of 8

6. **Regarding Stability:**

a. **Please include moisture content specifications and test results in your stability report forms and resubmit.**

Attachment VI - Stability protocol

b. **Please revise tablet description section in your stability reports and resubmit**

Attachment VI - Stability protocol

c. **Please include the limit for friability in your stability protocol and reports.**

Attachment VI - Stability protocol

d. i. **Please revise your post approval commitment as follows: Results of the testing will be submitted as part of the routine annual reports, or as specified by the Agency.**

ii. **Please revise your statement as indicated: Withdraw from market any lots which will fall out of specifications for the drug product.**

Attachment XVI - Stability Commitment

e. **Please monitor and report room temperature and humidity conditions in your stability reports.**

Attachment VI - Stability protocol

f. **Please indicate test methods and limits in your stability protocol for this specific product.**

Attachment VI - Stability protocol

g. **The related substances, degradation products limit, test methods and results should be included in your product stability protocol and reports.**

Attachment VI - Stability protocol

VINTAGE PHARMACEUTICALS, INC.
Meperidine Hydrochloride Tablets, USP
50 mg & 100 mg ANDA #40-191
Major Amendment

Labeling Deficiencies:

1. CONTAINER (100s)
   Satisfactory

Attachment XVII - Final print container labels

2. **INSERT**

   a. **Include the controlled substance symbol with prominence in the upper right hand corner of the package insert. We refer you to 21 CFR 1302.05 for guidance.**

   b. **DESCRIPTION**

      i. **Please include the structural formula, chemical formula, and molecular weight for meperidine hydrochloride in this section.**

      ii. **Combine the second and third paragraphs and revise as follows:**

      Each tablet, for oral administration, contains 50 mg or 100 mg meperidine hydrochloride. IN additions, each tablet contains the following inactive ingredients...

   c. **CLINICAL PHARMACOLOGY**

      Add the following text as the last two sentences of this section:

      Meperidine, in 60 mg to 80 mg parenteral doses, is approximately equivalent in analgesic effect to 10 mg of morphine. The onset of action is slightly more rapid than with morphine, and the duration of action is slightly shorter.

      Meperidine is significantly less effective by the oral than by the parenteral route, but the exact ration of oral to parenteral effectiveness is unknown.

VINTAGE PHARMACEUTICALS, INC.
Meperidine Hydrochloride Tablets, USP
50 mg & 100 mg ANDA #40-191
Major Amendment

d. INDICATIONS AND USAGE

Meperidine hydrochloride tablets USP are indicated for...

e. WARNINGS

Delete the penultimate paragraph,
, as the tablets do not have this indication.

f. ADVERSE REACTIONS

i. Nervous System
Delete the adverse reaction, , as it does not appear in the approved labeling of the listed drug.

ii. Cardiovascular

....(see WARNINGS)...

iii. Add the following as the last subsection:

Other. Antidiuretic effect.

g. DOSAGE AND ADMINISTRATION

i. Relocate this section so that it follows the OVERDOSAGE section and precedes the HOW SUPPLIED section.

ii. Regarding the first line, ; this subsection heading may be deleted since oral meperidine is only indicated for pain.

h. OVERDOSAGE (Symptoms)

Make the following revision in the last sentence, "...overdosage, particularly by the intravenous route, apnea, circulatory...".

i. HOW SUPPLIED

i. We encourage the inclusion of the established name of your product in this section.

ii. Please include appropriate information in this section to facilitate identification of your tablets such as shape, color, scoring, and the National Drug Code. We refer you to 21 CFR 201.57 (k) (3) for guidance.

In addition, please include information regarding the tablet imprints for your product which in conjunction with the product's size, shape, and color, permits the unique identification of the drug product and the manufacturer or distributor of the product. We refer you to 21 CFR 206.10 (a) for guidance.

iii. We encourage the inclusion of storage and dispensing recommendations in this section which are consistent with those found on your container labels.

iv. Please also include the "CAUTION: Federal law..." statement in this section as it appears on your container labels.

Please prepare and submit final printed labels and labeling.

Attachment XVIII - Final printed inserts

Please note that we reserve the right to request further changes in your labels and/or labeling based upon further changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94 (a) (8) (iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Attachment XIX - Side-by-side comparison

VINTAGE PHARMACEUTICALS, INC.
Meperidine Hydrochloride Tablets, USP
50 mg & 100 mg ANDA #40-191
Major Amendment

This completes our response to the deficiency letter issued. If I can be for further assistance or if you have any questions, please contact Rebecca Thurman or John Schultz at (704) 596-0516.

Sincerely,

Rebecca Thurman
Manager, Regulatory Affair