CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40352

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA: 40-352

FIRM: Mallinckrodt Inc.
675 McDonnell Blvd.
St. Louis, MO 63134-0840

DOSAGE FORM: Tablet STRENGTH: 50 mg and 100 mg

DRUG: Meperidine Hydrochloride

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable 03/1700.

BIO STUDY INFORMATION: Bio waivers granted for both 50 mg and 100 mg strengths per reviews dated 11/25/98.

METHODS VALIDATION: N/A

STABILITY:

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:

The tests and specifications for the 50 mg tablet are as follows:

Test	Specification
Dosage Description	¼" diameter standard round convex white-to-off-white tablet with one side debossed semi-circle arc "7113" above a bisect; other side debossed "M" in a box
Dosage Weight	125 mg ± 5%
Organoleptic	No unusual odor/No visible deterioration/No tactile change
Thickness	0.146 in ± 5%
Hardness	1.9 kg to 5.9 kg
Label Content of Meperidine HCl	50 mg ± 5%
Dissolution	USP 23

The executed batch record for lot (#MHSC9836; 50 mg; tablets) begins on p. 479 Vol 1.2). The actual yield for the final blend (total wt. dried granulation) was kg; %. The yield for the lubricated granulation was %. The applicant reports a loss of % for final tablet yield. The investigation report on p. 569 states that this is due to not taking into account the tablets taken for samples, culls and sweepings kg).

The executed batch record for lot (#MHSC9854; 100 mg; begins on p. 529 Vol 3.2). The actual yield for the final blend (total wt. dried granulation) was kg; %. The yield for the lubricated granulation was %.

PROPOSED PRODUCTION BATCH:

The manufacturing process

A flow chart of the manufacturing process is provided on pp. 281-282. A comparative equipment summary for the stability batch versus the proposed production batch is included on p. 284 (50 mg) and p. 212 of vol 3.2 (100mg). The production equipment is of similar design and operating principle. The commercial batch masters for the 50 mg tablet are on pp. 373-445 of vol 1.2 and pp. 316-416 of vol 3.2 for the 100 mg tablet. The intended production batch size is 50 mg strength tablets and 100 mg strength tablets.

RECOMMENDATION: Approve.

SIGNATURE: /S/ DATE: 6/5/00

6/5/00

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1. CHEMISTRY REVIEW NO. 1

2. [redacted] # 40-352

3. NAME AND ADDRESS OF APPLICANT
Mallinckrodt Inc.
Attention: Marianne Robb
675 McDonnell Blvd.
St. Louis, MO 63134-0840

4. LEGAL BASIS FOR SUBMISSION
The reference drug is Demerol (NDA 5-010) manufactured by Abbott Laboratories Inc.

5. SUPPLEMENT(S)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Meperidine HCl

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

9. AMENDMENTS AND OTHER DATES:
Original Submission 12/23/98
Amendment (chem) 03/22/99

10. PHARMACOLOGICAL CATEGORY
Narcotic Analgesic

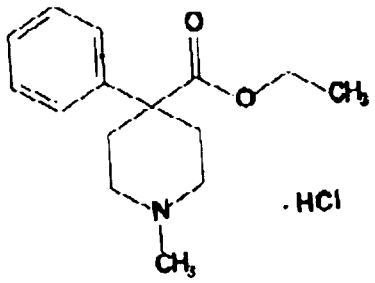
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(S)

13. DOSAGE FORM
Tablet

14. POTENCY
50 mg and 100 mg

15. CHEMICAL NAME AND STRUCTURE
4-piperidinecarboxylic acid, 1-methyl-4-phenyl, ethyl ether HCl



Meperidine Hydrochloride

$C_{15}H_{21}NO_2 \cdot HCl$ M.W. = 283.80

16. RECORDS AND REPORTS
N/A

17. COMMENTS
See item #38.

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable.

19. REVIEWER:
A. Mangowski

DATE COMPLETED:
07/01/99

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Chem #1

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 40-352

3. NAME AND ADDRESS OF APPLICANT
Mallinckrodt Inc.
Attention: Marianne Robb
675 McDonnell Blvd.
St. Louis, MO 63134-0840

4. LEGAL BASIS FOR SUBMISSION
The reference drug is Demerol (NDA 5-010) manufactured by Sanofi Winthrop Pharmaceuticals.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Meperidine HCl

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

9. AMENDMENTS AND OTHER DATES:

Original Submission	12/23/98
Amendment (chem)	03/22/99
NA LTR (chem)	08/02/99
Amendment (chem)	09/30/99

10. PHARMACOLOGICAL CATEGORY
Narcotic Analgesic

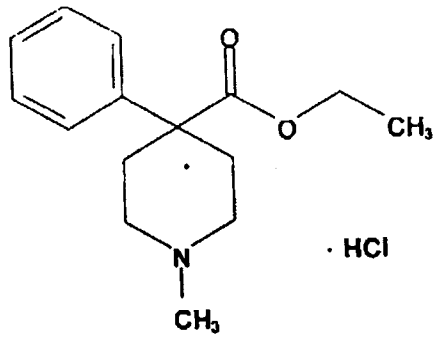
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Tablet

14. POTENCY
50 mg and 100 mg

15. CHEMICAL NAME AND STRUCTURE
4-piperidinecarboxylic acid, 1-methyl-4-phenyl, ethyl ether HCl



Meperidine Hydrochloride

$C_{15}H_{21}NO_2 \bullet HCl$ M.W. = 283.80

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Chem fax def; label AP 9/30/99; MV N/A; BIO AP 11/25/98;

18. CONCLUSIONS AND RECOMMENDATIONS
Fax deficiency chem.

19. REVIEWER:
A. Langowski

DATE COMPLETED:
02/25/00

Redacted 23

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Chem #2

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 40-352

3. NAME AND ADDRESS OF APPLICANT
Mallinckrodt Inc.
Attention: Marianne Robb
675 McDonnell Blvd.
P.O. BOX 5840
St. Louis, MO 63134-0840

4. LEGAL BASIS FOR SUBMISSION
The reference drug is Demerol® (NDA 5-010) manufactured by Sanofi Winthrop Pharmaceuticals.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Meperidine HCl

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

9. AMENDMENTS AND OTHER DATES:

Original Submission	12/23/98
Amendment (chem)	03/22/99
NA LTR (chem)	08/02/99
Amendment (chem)	09/30/99
NA LTR (fax)	03/24/00
Amendment (chem)	03/30/00

10. PHARMACOLOGICAL CATEGORY
Narcotic Analgesic

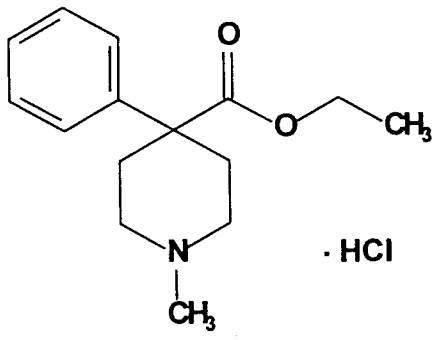
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Tablet

14. POTENCY
50 mg and 100 mg

15. CHEMICAL NAME AND STRUCTURE
4-piperidinecarboxylic acid, 1-methyl-4-phenyl, ethyl ether HCl



Meperidine Hydrochloride

$C_{15}H_{21}NO_2$• HCl M.W. = 283.80

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Chem fax def; label AP 9/30/99; MV N/A; BIO AP 11/25/98;

18. CONCLUSIONS AND RECOMMENDATIONS
Approval

19. REVIEWER: DATE COMPLETED:
A. Langowski 04/25/00;05/02/00

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Chem #3

AUG 2 1999

38. Chemistry Comments to be Provided to the Applicant

ANDA: 40-352 APPLICANT: Mallinckrodt Inc.

DRUG PRODUCT: Meperidine Hydrochloride Tablets USP, 50 mg and 100mg

The deficiencies presented below represent MAJOR deficiencies.

Deficiencies:

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Sincerely yours,

/S/

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research