CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 40-298

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA: 40-298

FIRM: Mylan Pharmaceuticals Inc.

DOSAGE FORM: Capsules STRENGTH: 100 mg

DRUG: Phenytoin Sodium

CGMP STATEMENT/EIR UPDATE STATUS

The firm presents their CGMP certification, stating that the drug product will be manufactured, processed, tested (release and stability), packaged and labeled at Mylan's plant, located at 781 Chestnut Ridge Road, Morgantown, WV 265052730 (p. 1776).

EIR pending as October 23, 1998; Acceptable dated 11/17/98

BIO STUDY INFORMATION:

As recommended by the Division of Bioequivalence the firm will incorporate the dissolution procedure into Mylan's stability and quality control program as of September 28, 1998. The firm states that the finished drug product specifications and dissolution procedure have been revised to incorporate the changes requested.

The revised documents are appended in Attachments A and B, respectively (pp.4 - 6, Att. A) and (pp. 8 - 10, att. B).

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S)

The analytical methods which were validated are: dissolution, assay and related compounds and are presented as follows:

a. Dissolution: The dissolution procedure was validated with respect to the following parameters: linearity, specifity and precision and ruggedness.

Dissolution, USP XIII. (pp. 2132 - 2134)
Linearity (pp. 2136 - 2140)
Specifity (pp. 2142 - 2144)
Precision and ruggedness (pp. 2146 - 2154).

b. Assay: The assay procedure was validated with respect to the following parameters: linearity, specifity and precision and ruggedness.

Assay (pp. 2156 & 2157)
Linearity (pp. 2159 - 2166)
Accuracy and specifity (pp. 2168 - 2173)
Precision (pp. 2175 - 2179)
Ruggedness (2181 - 2185)

c. Related compounds: The related compounds assay procedure was validated with respect to the following parameters: linearity, accuracy, limit of quantitation and specifity, and precision and rugdness.

Related compounds (pp. 2188 - 2190) Linearity (pp. 2192 - 2201)
Accuracy, specifity and limit quantitation (pp. 2203 - 2226).

d. Intentional degradation (pp. 2228 - 2232).

Analytical procedures, ref. USP XXIII (pp. 2234 - 2238).
Representative chromatograms (pp. 2240 - 2248).

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

Yes, as per the following container/closure configurations:

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Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

1./

1. CHEMISTRY REVIEW NO 1

2. ANDA 40-298

3. NAME AND ADDRESS OF APPLICANT

Mylan Pharmaceuticals
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P. O. Box 4310
Morgantown, WV 26504-4310

4. LEGAL BASIS FOR SUBMISSION

The legal basis for the application (p. 6) and patent certification/exclusivity statement certifying that according to the patent and the exclusivity information published by the FDA, there are no patents that claim the listed drug and the reference drug product is not covered by any exclusivity (p. 8).

5. SUPPLEMENT(s)

Amendment dated March 10, in response to the Agency's telephone call on March 9, 1998, to provide for a reduced finished product production batch size of capsules of the exhibit batch).

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Extended Phenytoin Sodium Capsules USP, 100 mg

8. SUPPLEMENT(s) PROVIDE(s) FOR:

See point No 5 of this review.

9. AMENDMENTS AND OTHER DATES:

Original:	February 27, 1998
Telephone amendment:	March 10, 1998
FDA letter of acknowledgment:	March 17, 1998
Date acceptable for filing:	March 2, 1997

10. PHARMACOLOGICAL CATEGORY

Antiepileptic

11. Rx or OTC

Rx.

12. RELATED IND/NDA/DMF(s)

DMF

DMF

DMF

DMF
DMF

DMF
DMF
DMF
DMF

DMF

DMF

DMF

DMF

13. DOSAGE FORM

Capsule

14. POTENCY

100 mg

15. CHEMICAL NAME AND STRUCTURE

2.4-imidazolidinedione, 5,5-diphenyl-monosodium salt ($C_{15}H_{11}N_2NaO_2$). M.W. 274.26

CAS No. 630-93-3.

16. RECORDS AND REPORTS

N/A

17. COMMENTS

N/A

18. CONCLUSIONS AND RECOMMENDATIONS

Please see No. 38.

19. REVIEWER: /S/ 11/2/98 DATE COMPLETED:

A. Croitoru August 4, 1998

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pages of trade

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commercial

information

Chem. Review #1

1. CHEMISTRY REVIEW NO 2

2. ANDA 40-298

3. NAME AND ADDRESS OF APPLICANT

Mylan Pharmaceuticals
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P. O. Box 4310
Morgantown, WV 26504-4310

PURPOSE OF AMENDMENT/SUPPLEMENT

Response to our deficiency letter dated September 22, 1998.

DATE(S) OF SUBMISSION(S)

Original:	February 27, 1998
Telephone amendment:	March 10, 1998
FDA letter of acknowledgment:	March 17, 1998
Date acceptable for filing:	March 2, 1997
Deficiency letter:	September 22, 1998
Amendment:	September 28, 1998

PHARMACOLOGICAL CATEGORY	TRADE NAME
Antiepileptic	N/A

NONPROPRIETARY NAME

Extended Phenytoin Sodium Capsules USP, 100 mg

DOSAGE FORM	POTENCY	RX OR OTC
Capsules	100 mg	Rx

SAMPLES	RELATED IND/NDA/DMF	STERILIZATION
N/A	See chem/review #1	N/A

LABELING

Acceptable. See review dated 10/7/98.

BIOEQUIVALENCY STATUS

As recommended by the Division of Bioequivalence, the firm will incorporate the dissolution procedure into Mylan's stability and quality control program as of September 28,

1998. The firm states that the finished drug product specifications and dissolution procedure have been revised to incorporate the changes requested.

The revised documents are appended in Attachments A and B, respectively (pp.4 - 6, Att. A) and (pp. 8 - 10, att. B).

ESTABLISHMENT INSPECTION

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Commercial/Confidential

Information and are not

releasable.

Chemistry Review #2

Application: **ANDA 40298/000**
Stamp: **02-MAR-1998** Regulatory Due:
Applicant: **MYLAN PHARMS**
781 CHESTNUT RIDGE RD
MORGANTOWN, WV 265052730

Priority:
Org Code: **600**
Action Goal:
District Goal: **02-MAY-1999**
Brand Name:
Established Name: **PHENYTOIN SODIUM, EXTENDED**
Generic Name:
Dosage Form: **CAP (CAPSULE)**
Strength: **100MG**

FDA Contacts: **K. SHERROD** **(HFD-617)** **301-827-5849** **, Project Manager**
B. ARNWINE **(HFD-645)** **301-827-5849** **, Team Leader**

Overall Recommendation:

Establishment: **1110315**
MYLAN PHARMACEUTICALS INC
781 CHESTNUT RIDGE RD
MORGANTOWN, WV 265054310

DMF No:
AADA No:

Profile: **CTR** OAI Status: **NONE**
Last Milestone: **SUBMITTED TO OC**
Milestone Date: **17-MAR-1998**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

Establishment:

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **SUBMITTED TO OC**
Milestone Date: **17-MAR-1998**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**