CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-332

Microbiology Review(s)

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #3 OF NDA 21-332
21 June 2001

A. 1. NDA 21-332 N 000 BI

APPLICANT: Amylin Pharmaceuticals, Inc.
9373 Towne Center Drive
San Diego, CA 92121

2. PRODUCT NAMES: Symlin™ (pramlintide acetate) Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is intended for subcutaneous injection. The product is packaged [ ] 0.6 mg/mL in 5 mL vials.

4. METHODS OF STERILIZATION:
The drug product is [ ]

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug product is used as an adjunct to insulin for glycemic and metabolic control in patients with Type 1 or Type 2 diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 7 December 2000

2. DATE OF AMENDMENT: 18 May 2001 (Subject of this Review)

3. RELATED DOCUMENTS: IND 39,897, DMF [ ] DMF [ ] DMF [ ] DMF [ ], DMF [ ] DMF [ ] DMF [ ] DMF [ ]

4. ASSIGNED FOR REVIEW: 18 June 2001

C. REMARKS: [ ]

[ ]

The vial presentation of the product is to be manufactured at:

[ ]

[ ]

D. CONCLUSIONS: The application is recommended for approval on the basis of sterility assurance.

/S/

Paul Stinavage, Ph.D.

cc: Original NDA 21-332
HFD-805/Stinavage/Consult File
HFD-510/Div File/J. Rhee

Drafted by: P. Stinavage, 21 June 2001
R/D initialed by P. Cooney

1 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

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/s/

Paul Stinavage
7/12/01 06:38:04 AM
MICROBIOLOGIST
Response to deficiency.

Peter Cooney
7/12/01 10:29:14 AM
MICROBIOLOGIST

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	**REQUEST FOR CONSULTATION**			
TO (Division/Office): Paul Stinavage, Ph.D., HFD-805			FROM: Julie Rhee, HFD-510	
DATE May 21, 2001	IND NO.	NDA NO. 21-332	TYPE OF DOCUMENT Response (BI)	DATE OF DOCUMENT May 18, 2001
NAME OF DRUG Symlin™ (pramlintide acetate) injection	PRIORITY CONSIDERATION		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE June 22, 2001
NAME OF FIRM: Amylin Pharmaceuticals, Inc.				

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	*STATISTICAL APPLICATION BRANCH*
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Paul,

This is the sponsor's response to your additional information request. I am attaching a copy of your request which was faxed to the sponsor on 5/17/01 is attached for your information. Is the response satisfactory? Thank you.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Julie Rhee
5/21/01 03:08:58 PM
CSO

David Orloff
5/21/01 07:20:20 PM
MEDICAL OFFICER

Comments faxed to the sponsor on 5/17/01

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #2 OF NDA 21-332
8 May 2001

A. 1. NDA 21-332 BI

APPLICANT: Amylin Pharmaceuticals, Inc.
9373 Towne Center Drive
San Diego, CA 92121

2. PRODUCT NAMES: Symlin™ (pramlintide acetate) Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is intended for subcutaneous injection. The product is packaged [
1 0.6 mg/mL in 5 mL vials.

4. METHODS OF STERILIZATION:
The drug product is [ ]

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug product is used as an adjunct to insulin for glycemic and metabolic control in patients with Type 1 or Type 2 diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 7 December 2000

2. DATE OF AMENDMENT: 10 April 2001 (Subject of this Review)

3. RELATED DOCUMENTS: IND 39,897, DMF [ ] DMF [ ] DMF [ ] DMF [ ] DMF [ ] DMF [ ] DMF [ ] DMF [ ] DMF [ ]

4. ASSIGNED FOR REVIEW: 7 May 2001

C. REMARKS: [ ]

[ ]

The vial presentation of the product is to be manufactured at:

[ ]

[ ]

D. CONCLUSIONS: The application is approvable pending resolution of microbiology concerns. Specific comments are provided in "E. Review Notes" and "List of Microbiology Deficiencies".

/S/

Paul Stinavage, Ph.D.

cc: Original NDA 21-332
HFD-805/Stinavage/Consult File
HFD-510/Div File/J. Rhee

Drafted by: P. Stinavage, 8 May 2001
R/D initialed by P. Cooney

4 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

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/s/

Paul Stinavage
5/11/01 08:30:18 AM
MICROBIOLOGIST
Response to deficiencies. Still needs data generated during [illegible] studies.

Peter Cooney
5/14/01 11:43:04 AM
MICROBIOLOGIST

Comments faxed 5/08/01

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #1 OF NDA 21-332
21 March 2001

A. 1. NDA 21-332

APPLICANT: Amylin Pharmaceuticals, Inc.
9373 Towne Center Drive
San Diego, CA 92121

2. PRODUCT NAMES: Symlin™ (pramlintide acetate) Injection

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The drug product is used as an adjunct to insulin for glycemic and metabolic control in patients with Type 1 or Type 2 diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 7 December 2000

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: IND 39,897, DMF[ ] DMF[ ] DMF[ ] DMF[ ] DMF[ ] DMF[ ] DMF[ ] DMF[ ] DMF[ ]

4. ASSIGNED FOR REVIEW: 17 January 2001

C. REMARKS: [ ]

[ ]

The vial presentation of the product is to be manufactured at:

[ ]

[ ]

D. CONCLUSIONS: The application is approvable pending resolution of microbiology concerns. Specific comments are provided in "E. Review Notes" and "List of Microbiology Deficiencies".

/S/

Paul Stinavage, Ph.D.

cc: Original NDA 21-332
HFD-805/Stinavage/Consult File
HFD-510/Div File/J. Rhee

Drafted by: P. Stinavage, 21 March 2001
R/D initialed by P. Cooney

/s/

Paul Stinavage
3/26/01 02:38:58 PM
MICROBIOLOGIST
New NDA. E

J

Peter Cooney
3/27/01 01:25:39 PM
MICROBIOLOGIST

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*: Peter Cooney, Ph.D., HFD-805			FROM: Julie Rhee, HFD-510, 7-6424	
ATE ecember 19, 2000	IND NO.	NDA NO. 21-332	TYPE OF DOCUMENT New NDA	DATE OF DOCUMENT December 7, 2000
NAME OF DRUG Symlin™ (pramlintide acetate)	PRIORITY CONSIDERATION		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE July 20, 2001

NAME OF FIRM: Amylin Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
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- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

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- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISION RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Please review a sterility aspect of this NDA. Filing meeting is scheduled on Jan 17 between 3:00-4:00 in room 14B45. I am forwarding volumes 1.1, 1.4, 1.5, 1.6, 1.9, 1.10, and 1.11 for your review. Thank you.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

/s/

Julie Rhee
12/19/00 01:30:34 PM