

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-059

CHEMISTRY REVIEW(S)

ONDQA Deputy Director's CMC Memorandum on NDA 22-059

Date: December 18, 2006
From: Chi-wan Chen, Deputy Director, Office of New Drug Quality Assessment
To: NDA 22-059 File

Applicant: GlaxoSmithKline (GSK)
Drug Name: Tykerb (lapatinib) tablets, 250 mg
Indication: Advanced or metastatic breast cancer

The CMC portion of this NDA was submitted under the ONDQA Pilot Program to explore science- and risk-based approaches to assuring product quality. A comprehensive Quality Overall Summary (Module 2) and an expanded pharmaceutical development section (P.2 in Module 3) were submitted. Several quality-by-design (QbD) elements were presented with respect to product design and process understanding of the drug product.

Drug Substance

The drug substance lapatinib ditosylate is chemically synthesized from starting materials and it has no stereoisomers or geometric isomers. It is a monohydrate and is saturated aqueous solution is slightly acidic. It is a BCS II compound. A process impurity, is found to be genotoxic. is also a degradant whose level increases during drug substance (and drug product) storage.

The application presented additional information and data demonstrating its enhanced process understanding of the drug substance manufacture. This additional understanding was clearly seen in their demonstration of knowledge of the fate of, and process parameters affecting, the synthetic impurities in the drug substance. In addition, detailed studies of the process were undertaken, leading to modified process parameters and conditions and ultimately a marked reduction in the level of

The applicant has undertaken systematic impurity mapping studies of the process-related impurities, including those carried over from the starting materials, and has developed an understanding of how the various process parameters ultimately relate to the critical quality attribute (CQA) of purity for the drug substance. Although assay was included in the drug substance specification sheet, a footnote stated that it "will comply if tested," indicating assay would not be routinely performed. The applicant justified this exception on the basis of the enhanced understanding, along with their ability to quantify the related impurities using a method. While the enhanced process understanding is consistent with the principles of QbD, a drug substance must be tested for assay, either in-process or on the finished substance, before the batch can be released. It should be noted that, despite its "non-specific" nature, the analytical procedure for the drug substance assay is acceptable since that for the impurities (related substances) is specific (refer to ICH Q6A), and that there is added value in having an assay method in addition to the impurity method.

The retest period for the drug substance is The applicant agreed to always test the drug substance for within 90 days of formulation of the drug product, irrespective of the drug substance retest date, to ensure that this genotoxic impurity is within the acceptance criterion of

Drug Product

The drug product contains an equivalent of 250 mg of lapatinib and is packaged in _____ bottles (____ counts) with child-resistant closures and _____. The tablet formulation contains approximately _____ drug substance and excipients typically used in immediate release tablets including a _____ (microcrystalline cellulose), _____ (povidone), _____ (sodium starch glycolate), and _____ (magnesium stearate), with a non-functional _____ Orange film coat. The tablets are manufactured using a _____

The proposed tablet formulation was developed based on the capsule formulation used in Phase I clinical trials to mitigate the need for bioequivalence studies and simplify product development. Components were selected to _____

_____. A QbD approach was used to develop a robust manufacturing process capable of producing a high quality drug product. The applicant identified _____ as a CQA _____

The other CQAs include _____

_____. After the critical CQAs were identified and the general manufacturing process was established, process knowledge (gained from previous experience and scale-up) and Design of Experiments (DOE) were used to ascertain the critical quality parameters, referred to by the applicant as quality critical parameters (QCPP), and to develop design spaces for the various manufacturing steps. _____

At our request the applicant has provided additional process understanding information concerning the _____

Although _____ was included in the drug substance specification sheet, a footnote stated that it "will comply if tested," indicating testing for this impurity would not be performed at release. The applicant agreed to clearly state in the footnote that the level of _____ is controlled in the drug substance specification (see above). The proposed acceptance criterion for _____ in the drug product is _____ which is supported by accelerated and long-term stability data and statistical analysis.

The proposed single point dissolution specification of $Q = ______$ at 30 minutes is acceptable and is purported to discriminate between a less bioavailable batch from batches shown to be bioequivalent to a reference clinical batch.

An 18-month expiration dating period has been established for the drug product based on the stability data presented in the NDA and subsequent amendments.

Miscellaneous

All facilities proposed for the drug substance and drug product manufacturing have been found to be acceptable, according to the EER.

The proposed established name did not correspond to the labeled strength. The applicant has been advised of the FDA policy that the name and strength should match. The applicant has agreed to change the established name to "lapatinib tablet" and retain the strength as 250 mg.

The applicant proposed a CMC regulatory agreement outlining the established design space and the filing mechanisms for post-approval changes within the design space and changes to equipment and scale for the drug product. The agreement will not be approved at this time because FDA has not established a regulatory pathway to allow such an approval.

Recommendation

The application is recommended for approval from the CMC standpoint. Although the applicant has not responded to certain QbD-related comments in the 06-DEC-2006 IR letter, they are not considered approvability issues as they do not affect the overall quality assurance of the product. These comments are intended to gain further product knowledge and process understanding from the applicant under the ONDQA pilot program. They can be addressed post-approval due to the short review timeline.

**APPEARS THIS WAY
ON ORIGINAL**

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this page is the manifestation of the electronic signature.**

/s/

Chi Wan Chen
12/18/2006 06:34:10 PM
CHEMIST

NDA 22-059

Tykerb (lapatinib) Tablets

GlaxoSmithKline

**Craig M. Bertha, Ph.D.
Xiao-Hong Chen, Ph.D.
Terrance Ocheltree, Ph.D.**

Office of New Drug Quality Assessment

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Chemistry Review Data Sheet

1. NDA 22-059
2. REVIEW #1
3. REVIEW DATE: 18-DEC-2006
4. REVIEWERS: Craig M. Bertha, Ph.D.
Xiao-Hong Chen, Ph.D.
Terrance Ocheltree, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents

Document Date

N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Document Date

Original (CMC)

13-SEP-2006

Amendment (BC)

10-NOV-2006

Amendment (BC)

17-NOV-2006

Amendment (BL)

21-NOV-2006

Amendment (BC)

01-DEC-2006

Amendment (BC)

13-DEC-2006

7. NAME & ADDRESS OF APPLICANT:

Name: SmithKlineBeecham Corp. d/b/a GlaxoSmithKline (GSK)

Address: One Franklin Plaza
200 N. 16th Street, FP1005

Representative: Richard Swenson, Ph.D.

Chemistry Review Data Sheet

Telephone: 610-787-3724

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Tykerb®
b) Non-Proprietary Name (USAN): lapatinib ditosylate
Code Name/# (ONDC only): GW572016F denotes the ditosylate monohydrate of the free base, GW572016X.
c) Chem. Type/Submission Priority (ONDC only):
- Chem. Type: I
 - Submission Priority: P

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Epidermal growth factor receptor (EGFR) and erbB-2 (Her2/neu) dual tyrosine kinase inhibitor

11. DOSAGE FORM: Immediate release tablets; strength is expressed as 250 mg (as lapatinib free base) or 398 mg (as lapatinib ditosylate) (Note that drug substance is a monohydrate with equivalent weight of 405 mg).

12. STRENGTH/POTENCY: 250 mg (as lapatinib free base)

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

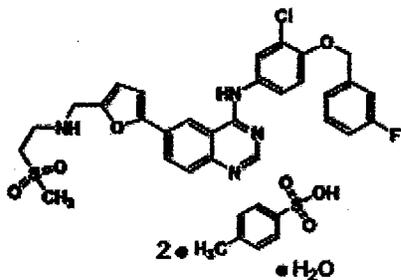
SPOTS product – Form Completed

Not a SPOTS product

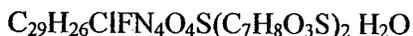
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]quinazolin-4-amine bis(4-methylbenzenesulfonate) monohydrate

Chemistry Review Data Sheet



The empirical formula is:



The molecular weight is 943.38.

17. RELATED/SUPPORTING DOCUMENTS:

A. Supporting DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS ³
—	IV	/	/	1	Adequate	03-OCT-2006	
—	III			4	N/A		Review not needed per review policy for solid oral dosage forms.
—	III			4	N/A		Review not needed per review policy for solid oral dosage forms.
—	III			4	N/A		Review not needed per review policy for solid oral dosage forms; no product contact.
—	III			4	N/A		Review not needed per review policy for solid oral dosage forms.

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

³ Include reference to location in most recent CMC review

CHEMISTRY REVIEW

Chemistry Review Data Sheet

B. Other Supporting Documents:

Doc #	OWNER	ITEM REFERENCED	STATUS	DATE REVIEW COMPLETED	COMMENTS

C. Related Documents:

DOCUMENT	APPLICATION NUMBER	OWNER	DESCRIPTION/COMMENT
IND	61,362	GSK	Original IND

18. CONSULTS/CMC-RELATED REVIEWS:

CONSULTS	SUBJECT	DATE FORWARDED	STATUS/ REVIEWER	COMMENTS
Biometrics	N/A			No statistical analysis of drug product stability data deemed necessary.
EES	Site inspections	21-SEP-2006	ACCEPTABLE	OC entered recommendation on 29-SEP-2006
Pharm/Tox	drug substance, drug product impurity qualification (organic and inorganic)	22-SEP-2006	Pending	
Biopharm	N/A			
ODS/DMETS	Labeling consult	02-OCT-2006	Final	See review in DFS
Methods Validation	Drug substance impurity method	30-NOV-2006	Pending	
EA	N/A			Applicant cites 21 CFR 25.31(b) as applicable.
Microbiology	N/A			

The Chemistry Review for NDA 22-059

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is recommended for **approval** with respect to the chemistry, manufacturing, and controls (CMC).

However, this recommendation assumes that the pharmacology/toxicology team finds the applicants drug substance and drug product impurities acceptance criteria to be acceptable from a safety perspective (pending review for 22-SEP-2006, consult request). An unacceptable recommendation from the pharmacology/toxicology team may have implications with regard to the drug substance and drug product impurities acceptance criteria and/or the retest and expiration dating periods, respectively.

Although the applicant has not responded to Comments 5-7 of the 06-DEC-2006, IR letter, the comments are not considered approvability issues as they do not affect the overall quality assurance of the product. These comments are intended to gain further product knowledge and process understanding from the applicant under the ONDQA pilot program. They can be addressed post-approval due to the short review timeline.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

The following comments and risk management statements regarding CMC should be included in the action letter:

1. As indicated in our teleconference on November 16, 2006, your proposed CMC Regulatory Agreement submitted as part of the CMC Pilot Program is under review. Your proposal outlines the regulatory mechanisms for managing changes related to process design and control spaces post-approval. While a mutually accepted CMC Agreement is not a condition for the approval of this application, it will have implications for post-approval changes. Therefore, you are reminded that, until the CMC Agreement is approved, the existing regulations and guidances should be followed, as appropriate for the post approval CMC changes.

Executive Summary Section

2. We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

II. Summary of Chemistry Assessment

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product

The Lapatinib Ditosylate Tablets are biconvex, oval, orange, film coated tablets with the identification code GS XJG debossed on one side. The tablets contain — mg of lapatinib ditosylate monohydrate (250 mg in terms of free-base lapatinib or 398 mg as lapatinib ditosylate). Lapatinib ditosylate monohydrate is a class II drug and is formulated as an immediate release dosage form. The product is packaged in — bottles (— 150 counts) with — child-resistant closures and — . The tablet formulation contains approximately — drug substance (based on coated tablet weight) and excipients typically used in immediate release tablets including — microcrystalline cellulose, — (povidone), — (sodium starch glycolate), and — magnesium stearate). No novel excipients are utilized and only the non-functional — Orange film coat is not a compendial monograph excipient. The product contains no overages. The tablets are manufactured using a —

The proposed tablet formulation was developed based on the capsule formulation used in phase I clinical trials to mitigate the need for bioequivalence studies and simplify product development. Components were selected to —

Quality by Design (QbD) approach was used to develop a robust manufacturing process capable of producing a high quality drug product. As part of a QbD approach, critical quality attributes (CQAs), critical quality parameters (CPP) [referred to as quality critical parameters (QCPP)] should be identified, understood and controlled. The applicant identified — as a CQA

CQAs include —

After the general manufacturing process was established and the critical CQAs were identified, process knowledge (gained from previous experience and scale-up) and Design of Experiments (DOE) were used to ascertain the QCPPs and develop design spaces for the various manufacturing steps.

Executive Summary Section

The proposed single point dissolution specification of Q = — at 30 minutes is acceptable and is purported to discriminate between a less bioavailable batch from batches shown to be bioequivalent to the reference clinical batch.

The applicant proposed not to test drug-related impurities including genotoxic impurity — at release. This is acceptable per ICH Q6A because the levels of all other impurities, except — do not increase during drug product manufacturing or storage. However, because the level of — does increase during drug substance storage, it will be tested in the drug substance prior (no more than 90 days prior) to manufacturing the drug product. Therefore, the level of impurities at drug product release will be controlled by the drug substance specification.

An 18-month expiration dating period has been established for the drug product based on the stability data presented in the NDA and subsequent amendments. The expiry period may be extended, if justified, when additional stability data become available.

Drug Substance

The — drug substance lapatinib ditosylate is chemically synthesized — ; from starting materials and it has no stereoisomers or geometric isomers. It is a monohydrate. The yellow solid is slightly acidic with a pH of 4.0 in a saturated aqueous solution. The drug substance is — The partition coefficient in octanol water (25°C) is 6.0. The drug substance salt has limited solubility in water (7 mcg/mL) but is more soluble in —

The drug substance is —

The retest period for the drug substance is — However, drug substance will always be tested for assurance that the genotoxic impurity — level is within the acceptance criterion, — within 90 days of formulation of drug product. The acceptance criterion of — is supported by accelerated and long-term stability data.

The application presented additional information and data demonstrating the applicant's enhanced process understanding of the drug substance manufacture. This additional understanding was clearly seen in their demonstration of knowledge of the fate of and process parameters that affected the synthetic impurities in the drug substance. In addition, detailed studies of the — were undertaken so that an alteration of parameters and conditions would lead to a marked reduction in the ultimate level of a known genotoxic impurity —

B. Description of How the Drug Product is Intended to be Used

The drug is to be used for once daily dosing as five (5) tablets in combination with capecitabine (2,000 mg/m²/day on days 1-14 in a 21 day cycle) and the proposed indication is for the treatment of patients with advanced or metastatic breast cancer whose tumors over express HER2 (ErbB2) —

Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

N/A

III. Administrative

This NDA was submitted electronically as a 505(b)(1) application. A Quality Overall Summary is included in the application. The CMC information in this NDA was accepted for review under the CMC pilot program (FR Vol. 70, No. 134, pp. 40719-40720, July 14, 2005). This program proposes innovative approaches to ensuring product quality.

The CMC section of this application was reviewed by a team. The review team members selected for the quality assessment and their individual responsibilities are listed below:

Review Team	Assessment Responsibility
Craig M. Bertha, Ph.D. Team Lead	Drug substance section including manufacturing process
Xiao-Hong Chen, Ph.D.	Drug product section excluding manufacturing process
Terrance Ocheltree, Ph.D.	Manufacturing processes including the development for the drug product

A. Reviewer's Signature

See appended electronic signature page.

B. Endorsement Block

C.Bertha/ONDQA/Reviewer/12/18/06
 X.-H.Chen/ONDQA/Reviewer
 T.Ocheltree/ONDQA/Reviewer
 C.-W.Chen/ONDQA/Deputy Director

C. CC Block

A.Bertha/ONDQA/Regulatory PM
 K.Robertson/DDOP/Regulatory PM
 S.Pope/ONDQA/PAL

156 Page(s) Withheld

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Deliberative Process

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/s/

Craig Bertha
12/18/2006 12:26:12 PM
CHEMIST
also signing for Xiao-Hong Chen, Ph.D.

Terrance Ocheltree
12/18/2006 12:30:43 PM
CHEMIST

Chi Wan Chen
12/18/2006 12:42:26 PM
CHEMIST

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Application:	NDA 22059/000	Action Goal:	
Stamp:	13-SEP-2006	District Goal:	14-MAY-2007
Regulatory Due:	13-MAR-2007	Brand Name:	TYKERB TABLETS
Applicant:	SMITHKLINE BEECHAM	Estab. Name:	
	1 FRANKLIN PLAZA	Generic Name:	LAPATINIB DITOSYLATE
	PHILADELPHIA, PA 19101		TABLETS
Priority:	1P	Dosage Form:	(TABLET)
Org Code:	150	Strength:	250 MG

Application Comment: PART OF THE CMC PILOT PROGRAM. PAT ALCOCK AND ANTHONY CHARITY ARE OC CONTACT PERSONS. THIS APPLICATION IS BEING REVIEWED BY ONDQA REVEIW TEAM: CRAIG BERTHA (LEAD), XIAO HONG CHEN, TERRY OCHELTREE. THE REVIEW TEAM WILL PROVIDE COMMENTS TO THE INVESTIGATOR BEFORE THE PAI. CLINCIAL DIVISION IS SHOOTING FOR AN ACTION BY 3 MONTHS- 13.DEC2006!!!! (on 18-SEP-2006 by A. BERTHA () 301-796-1647)

FDA Contacts:	K. ROBERTSON	301-796-1441	, Project Manager
	C. BERTHA	301-796-2410	, Review Chemist
	S. POPE	301-796-1436	, Team Leader

Overall Recommendation: ACCEPTABLE on 29-SEP-2006 by S. ADAMS (HFD-322) 301-827-9051

Establishment:	CFN 9610411	FEI 3003262904
	GLAXO OPERATIONS UK LIMITED	
	PRIORITY STREET	
	WARE, HERTFORDSHIRE, , UK	

DMF No: AADA:

FINISHED DOSAGE PACKAGER

FINISHED DOSAGE RELEASE TESTER

Profile:

TCM

OAI Status:

NONE

EMilestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	21-SEP-2006				BERTHAC
SUBMITTED TO DO	22-SEP-2006	PS			ADAMSS
DO RECOMMENDATION	29-SEP-2006			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	29-SEP-2006			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS

Establishment:

CFN

9610421

FEI

3002807078

GLAXO WELLCOME LTD

DL128DT

BARNARD CASTLE, , UK

DMF No:

AADA:

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ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Responsibilities: FINISHED DOSAGE STABILITY TESTER

Profile: CTL OAI Status: NONE

Estab. Comment: REBECCA HACKETT IN INTERNATIONAL OPERATIONS BRANCH STATES THAT FEI 3002807078 WAS MERGED INTO FEI 3003722390. (on 21-SEP-2006 by C. BERTHA () 301-796-2410)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	21-SEP-2006				BERTHAC
SUBMITTED TO DO	22-SEP-2006	PS			ADAMSS
DO RECOMMENDATION	29-SEP-2006			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	29-SEP-2006			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS

Establishment: CFN 9610414 FEI
GLAXO WELLCOME OPERATIONS UK
DA1 5AH
DARTFORD, KENT, UK

DMF No: AADA:

Responsibilities: INTERMEDIATE MANUFACTURER
INTERMEDIATE RELEASE TESTER

Profile: CSN OAI Status: NONE

Estab. Comment: GSK HAS CFN NUMBER 9617194 FOR THIS SITE, BUT THEY CLAIM THAT THERE IS ONLY ONE GSK SITE IN DARTFORD, UK AND THAT IT IS A FORMER GLAXO WELLCOME SITE. (on 21-SEP-2006 by C. BERTHA () 301-796-2410)
MANUFACTURE AND QUALITY CONTROL OF — LAPATANIB DITOSYLATE DRUG SUBSTANCE (on 18-SEP-2006 by A. BERTHA () 301-796-1647)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	21-SEP-2006				BERTHAC
SUBMITTED TO DO	22-SEP-2006	PS			ADAMSS
DO RECOMMENDATION	29-SEP-2006			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	29-SEP-2006			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS

Establishment: CFN 9610176 FEI 1000170338
 GLAXOSMITHKLINE
 CURRAGHBINNY
 CARRIGALINE, CO. CORK, , EI

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER
 DRUG SUBSTANCE RELEASE TESTER
 DRUG SUBSTANCE STABILITY TESTER

Profile: CSN OAI Status: NONE

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ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

EMilestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	21-SEP-2006				BERTHAC
SUBMITTED TO DO	22-SEP-2006	PS			ADAMSS
DO RECOMMENDATION	29-SEP-2006			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	29-SEP-2006			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS

Establishment: CFN FEI
 GLAXOSMITHKLINE RESEARCH & DEVELOPMENT LTD
 GUNNELS WOOD ROAD
 STEVENAGE, HERTFORDSHIRE, UK

DMF No: AADA:

Responsibilities: FINISHED DOSAGE STABILITY TESTER

Profile: CTL OAI Status: NONE

EMilestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	22-SEP-2006				FOLKENDTM
SUBMITTED TO DO	25-SEP-2006	GMP			ADAMSS
DO RECOMMENDATION	29-SEP-2006			ACCEPTABLE BASED ON FILE REVIEW BASED ON FUNCTIONS THAT THIS FACILITY WILL BE PERFORMING. NO GMP INSPECTION REQUIRED.	ADAMSS
OC RECOMMENDATION	29-SEP-2006			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS

Establishment: CFN

FEI

DMF No:

AADA:

Responsibilities:

Profile: CSN

OAI Status: NONE

Estab. Comment:

(on 18-SEP-2006 by A. BERTHA () 301-796-1647)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	21-SEP-2006				BERTHAC
BMITTED TO DO	22-SEP-2006	PS			ADAMSS
DO RECOMMENDATION	29-SEP-2006			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	29-SEP-2006			ACCEPTABLE	ADAMSS

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

**APPEARS THIS WAY
ON ORIGINAL**

APPEARS THIS WAY

DISTRICT RECOMMENDATION

**APPEARS THIS WAY
ON ORIGINAL**