

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022283Orig1s000

CHEMISTRY REVIEW(S)

NDA 22-283

Document Date: December 14, 2012 & January 25, 2013

Zegerid OTC powder for oral suspension

Omeprazole 20 mg and Sodium Bicarbonate 1680 mg

MSD Consumer Care INC.

SWAPAN K. DE, Ph.D.

CMC-Lead

Office of New Drug Quality Assessment

Division of Pre-Marketing Evaluation

Division III, Branch VII

**CMC-REVIEW of NDA 22-283 for
Division of Non-Prescription Clinical Evaluation**

CHEMISTRY REVIEW

Chemistry Assessment Section

Background:

Zegerid OTC® powder for oral suspension (NDA 22-283) is a 505(b)(2) application, resubmitted December 14, 2012 in response to Agency's December 28, 2011 Complete Response (CR) letter and as amended January 25, 2013. The NDA is in its fourth review cycle and previous CR action dates are January 9, 2009 [first cycle], July 12, 2010 [second cycle] and December 28, 2011 [third cycle]. Subsequent to FDA's July 12, 2010 CR letter to the firm, the sponsor changed ownership from Schering-Plough Healthcare Products to MSD Consumer Care, Inc.

Regarding CMC, the application was recommended for "Approval" pending satisfactory completion of cGMP inspections (see review dated 12/20/2011 by Swapan K De). Thus, complete response letter dated December 28, 2011 indicated the following deficiency.

"During a recent inspection of the two manufacturing facilities [REDACTED] (b)(4) [REDACTED] for this submission, our field investigators conveyed deficiencies to the representative of the facilities. Satisfactory resolution of these deficiencies is required before this application may be approved."

The applicant updated manufacturing facilities in its resubmission (NDA 22-283) dated December 14, 2012 and an establishment evaluation request (EER) was placed (dated 30 January, 2013) to the Office of Compliance through the Establishment Evaluation System (EES) to assure the manufacturing facilities remain in acceptable status regarding cGMP compliance. In response to the EER, the Office of Compliance issued an overall "acceptable" recommendation on 04-June-2013 (see attached EER report).

Conclusion: There are no outstanding issues from a chemistry, manufacturing, and controls point of view and this NDA is recommended for "Approval".

CHEMISTRY REVIEW

Chemistry Assessment Section

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Application: NDA 22283/000 **Action Goal:**
Stamp Date: 20-MAR-2008 **District Goal:** 18-APR-2013
Regulatory: 17-JUN-2013
Applicant: MSD CONSUMER **Brand Name:** Zegerid OTC (omeprazole 20 mg & sodium b
556 MORRIS AVE **Estab. Name:**
SUMMIT, NJ 07901 **Generic Name:** OMEPRAZOLE 20MG/SODIUM BICARBONATE
1680M
Priority: 8 **Product Number; Dosage Form; Ingredient; Strengths**
Org. Code: 560 001; POWDER, FOR ORAL SUSPENSION; OMEPRAZOLE; (b) (4)
001; POWDER, FOR ORAL SUSPENSION; SODIUM
BICARBONATE; 1680MG
Application Comment: N 22283 IS A NEW DOSAGE FORM WITH SAME DRUG SUBSTANCES AS N 22281 (on 24-APR-2008 by C. HOUGH ()
3017960323)

TESTING OF RAW MATERIALS (on 03-APR-2013 by T. SHARP () 3017963208)

FDA Contacts:	S. DE	Prod Qual Reviewer	3017961664
	L. RIVERA	Product Quality PM	3017964013
J. BUCHANAN S. DE		Regulatory Project Mgr (HFD-560)	3017961007
		Team Leader	3017961664

Overall Recommendation:	ACCEPTABLE	on (b) (4)	by J. WILLIAMS	()	3017964196
	PENDING	on 02-APR-2013	by EES_PROD		
	PENDING	on 02-APR-2013	by EES_PROD		
	PENDING	on 02-APR-2013	by EES_PROD		
	PENDING	on 02-APR-2013	by EES_PROD		
	PENDING	on 31-JAN-2013	by EES_PROD		
	PENDING	on 30-JAN-2013	by EES_PROD		
	PENDING	on 30-JAN-2013	by EES_PROD		
	PENDING	on 30-JAN-2013	by EES_PROD		
	PENDING	on 30-JAN-2013	by EES_PROD		
	PENDING	on 16-JAN-2013	by EES_PROD		
	WITHHOLD	on 19-DEC-2011	by EES_PROD		
	WITHHOLD	on 08-NOV-2011	by EES_PROD		
	WITHHOLD	on 06-JUL-2011	by EES_PROD		
	ACCEPTABLE	on (b) (4)	by EES_PROD		

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)
 (b) (4)
 (b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment Comment: RAW MATERIALS TESTER SUBCONTRACTOR (on 24-APR-2008 by C. HOUGH () 3017960323)

Profile: CONTROL TESTING LABORATORY OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	03-JUN-2008				HOUGH C
OC RECOMMENDATION	05-JUN-2008			ACCEPTABLE BASED ON PROFILE	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	Product Specific			TOULOUSEM
DO RECOMMENDATION	31-OCT-2011			WITHHOLD QA FUNCTIONS	MROSE
OC RECOMMENDATION	31-OCT-2011			WITHHOLD DISTRICT RECOMMENDATION	INYARDA
SUBMITTED TO DO	30-JAN-2013	10-Day Letter			STOCKM
SITE WAS PREVIOUSLY WITHHELD DUE TO QA FUNCTIONS. PLEASE RE-EVALUATE					
DO RECOMMENDATION	10-FEB-2013			ACCEPTABLE BASED ON FILE REVIEW	PHILPYE
OC RECOMMENDATION	11-FEB-2013			ACCEPTABLE DISTRICT RECOMMENDATION	SHARPT

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)
(b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE RELEASE TESTER

Establishment Comment: RAW MATERIAL TESTING (on 22-MAR-2013 by L. RIVERA () 3017964013)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>					<u>Reason</u>
SUBMITTED TO OC	03-JUN-2008				HOUGHCH
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
DO RECOMMENDATION	17-JUN-2008			ACCEPTABLE	ADAMSS
				BASED ON FILE REVIEW	
OC RECOMMENDATION	19-JUN-2008			ACCEPTABLE	ADAMSS
				DISTRICT RECOMMENDATION	
SUBMITTED TO OC	27-SEP-2011				LIUY
OC RECOMMENDATION	07-DEC-2011			ACCEPTABLE	SMITHDE
RECOMMENDATION ENTERED W/O SPECIFICATION OF TESTING ROLES BASED ON KNOWN SITE FUNCTIONS				BASED ON PROFILE	
SUBMITTED TO DO	30-JAN-2013	10-Day Letter			STOCKM
UNDER REVIEW	10-FEB-2013				PHILPYE
DO RECOMMENDATION	20-MAR-2013			ACCEPTABLE	PHILPYE
				BASED ON FILE REVIEW	
OC RECOMMENDATION CTL	20-MAR-2013			ACCEPTABLE	PRABHAKARAR
				DISTRICT RECOMMENDATION	
SUBMITTED TO OC	02-APR-2013				RIVERAL
SUBMITTED TO DO CTL INITIAL.	02-APR-2013	10-Day Letter			SHARPT
UNDER REVIEW	02-APR-2013				PHILPYE
DO RECOMMENDATION	23-APR-2013			ACCEPTABLE	PHILPYE
				ADEQUATE FIRM RESPONSE	
OC RECOMMENDATION	24-APR-2013			ACCEPTABLE	SAFAAJAZIR
				DISTRICT RECOMMENDATION	

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)

(b) (4)

(b) (4)

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Establishment Comment: MANUFACTURER OF SODIUM BICARBONATE (on 24-APR-2008 by C. HOUGH () 3017960323)

Profile: NON-STERILE API BY CHEMICAL SYNTHESIS OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	24-APR-2008				HOUGH C
SUBMITTED TO DO	(b) (4)	GMP Inspection			FERGUSONS
SUBMITTED TO OC	03-JUN-2008				HOUGH C
SUBMITTED TO DO	(b) (4)	GMP Inspection			FERGUSONS
DO RECOMMENDATION	03-DEC-2008			ACCEPTABLE BASED ON FILE REVIEW	ESMITH1
OC RECOMMENDATION	03-DEC-2008			ACCEPTABLE DISTRICT RECOMMENDATION	FERGUSONS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	GMP Inspection			TOULOUSEM
ASSIGNED INSPECTION TO IB	(b) (4)	Product Specific			NALINIL
INSPECTION SCHEDULED	(b) (4)		28-OCT-2011		NALINIL
INSPECTION PERFORMED 667794 See Endorsement Text.	(b) (4)		21-OCT-2011		MATTHEW.DIONNE
INSPECTION PERFORMED	(b) (4)		21-OCT-2011		NALINIL
DO RECOMMENDATION	03-NOV-2011			WITHHOLD QA FUNCTIONS	NALINIL
OC RECOMMENDATION CDER OC CONCURS WITH DISTRICT'S WH REC BASED ON UNKNOWN PRODUCT COANTAMINANTS AND POTENTIAL WRNG LTR.	19-DEC-2011			WITHHOLD DISTRICT RECOMMENDATION	CRUZC
SUBMITTED TO OC	16-JAN-2013				RIVERAL
OC RECOMMENDATION	16-JAN-2013			ACCEPTABLE BASED ON PROFILE	SHARPT

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: 3002861690

(b) (4)

977 CENTURY DRIVE
BURLINGTON, ONTARIO, CANADA

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment Comment: RAW MATERIAL MICROBIAL ANALYSIS, RAW MATERIAL TESTING (on 24-APR-2008 by C. HOUGH () 3017960323)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	02-MAY-2008				HOUGH C
OC RECOMMENDATION	02-MAY-2008			ACCEPTABLE BASED ON PROFILE	ADAMSS
SUBMITTED TO OC	03-JUN-2008				HOUGH C
OC RECOMMENDATION	05-JUN-2008			ACCEPTABLE BASED ON PROFILE	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	Product Specific			TOULOUSEM
DO RECOMMENDATION	03-OCT-2011			ACCEPTABLE BASED ON FILE REVIEW	MROSE
OC RECOMMENDATION	04-OCT-2011			ACCEPTABLE DISTRICT RECOMMENDATION	SMITHDE
OC RECOMMENDATION	30-JAN-2013			ACCEPTABLE BASED ON PROFILE	STOCKM
SUBMITTED TO OC	02-APR-2013				RIVERAL
OC RECOMMENDATION	02-APR-2013			ACCEPTABLE BASED ON PROFILE	SHARPT

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4)
(b) (4)

FEI: (b) (4)

DMF No:

AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE OTHER TESTER

FINISHED DOSAGE PACKAGER FINISHED DOSAGE RELEASE

TESTER FINISHED DOSAGE STABILITY TESTER

Establishment Comment: RAW MATERIAL RELEASE, IN-PROCESS AND FINAL DRUG PRODUCT TESTING, RELEASE, MANUFACTURE, PACKAGING AND STABILITY TESTING. (on 24-APR-2008 by C. HOUGH () 3017960323)

Profile: POWDERS (INCLUDES ORAL AND TOPICAL) **OAI Status:** NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	24-APR-2008				HOUGHGC
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
DO RECOMMENDATION	29-MAY-2008			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	29-MAY-2008			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS
SUBMITTED TO OC	03-JUN-2008				HOUGHGC
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
ASSIGNED INSPECTION TO IB	(b) (4)	GMP Inspection			ADAMSS
INSPECTION PERFORMED	(b) (4)				FACTS_EES
AUTOMATIC WITHHOLD STATUS ISSUED BY FACTS, DUE TO FIRM BEING OUT OF BUSINESS OR MERGED					
DO RECOMMENDATION	04-FEB-2009			ACCEPTABLE INSPECTION	ADAMSS
BASED ON REVIEW OF 483 OBSERVATIONS AND INVESTIGATOR'S RECOMMENDATION. AWAITING EIR AND FIRM'S RESPONSE.					
OC RECOMMENDATION	04-FEB-2009			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	Product Specific			TOULOUSEM
DO RECOMMENDATION	06-OCT-2011			ACCEPTABLE BASED ON FILE REVIEW	MROSE
OC RECOMMENDATION	11-OCT-2011			ACCEPTABLE DISTRICT RECOMMENDATION	SMITHDE

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

SUBMITTED TO DO	(b) (4)	Product Specific		STOCKM
DO RECOMMENDATION BASED ON CHG, TCM/TTR COVERAGE	(b) (4)		ACCEPTABLE BASED ON FILE REVIEW	PHILPYE
OC RECOMMENDATION	(b) (4)		ACCEPTABLE DISTRICT RECOMMENDATION	SHARPT
SUBMITTED TO OC	02-APR-2013			RIVERAL
SUBMITTED TO DO	02-APR-2013	10-Day Letter		SHARPT
PREVIOUS PS/GMP WAIVED FOR POW BASED ON CHG, TCM/TTR COVERAGE. PDUFA JUN 17 2013. EER RESUBMITTED APRIL 2 2013				
DO RECOMMENDATION BASED ON TCM/CHG COVERAGE	02-APR-2013		ACCEPTABLE BASED ON FILE REVIEW	PHILPYE
OC RECOMMENDATION	04-APR-2013		ACCEPTABLE DISTRICT RECOMMENDATION	SHARPT
PAI WAIVED: BASED ON CHG, TCM/TTR COVERAGE				

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4)
(b) (4)

FEI: (b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment Comment: RAW MATERIAL TESTING (on 22-MAR-2013 by L. RIVERA () 3017964013)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	03-JUN-2008				HOUGHG
OC RECOMMENDATION	03-JUN-2008			ACCEPTABLE BASED ON PROFILE	KIEL
SUBMITTED TO OC	27-SEP-2011				LIUY
OC RECOMMENDATION	07-DEC-2011			ACCEPTABLE	SMITHDE
RECOMMENDATION ENTERED W/O SPECIFICATION OF TESTING ROLES BASED ON KNOWN SITE FUNCTIONS				BASED ON PROFILE	
SUBMITTED TO OC	02-APR-2013				RIVERAL
SUBMITTED TO DO	02-APR-2013	10-Day Letter			SHARPT
EER RESUBMITTED. CTL INITIAL PDUFA JUN 17 2013					
DO RECOMMENDATION	19-APR-2013			ACCEPTABLE	SBERRYMA
THE PREVIOUS INSPECTION OF (b) (4) WAS NAI. BASED ON FILE REVIEW, (b) (4) RECOMMENDS APPROVABLE FOR THIS APPLICATION.				BASED ON FILE REVIEW	
OC RECOMMENDATION	(b) (4)			ACCEPTABLE	PRABHAKARAR
RAW MATERIAL TESTER - THE PREVIOUS INSPECTION OF (b) (4) 1 WAS NAI. BASED ON FILE REVIEW, (b) (4) RECOMMENDS APPROVABLE FOR THIS APPLICATION.				DISTRICT RECOMMENDATION	

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4)
(b) (4)

FEI: (b) (4)

DMF No:

AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment Comment: REQUESTED CLARIFICATION ON 1/16 OF TESTING RESPONSIBILITIES. NO RESPONSE RECEIVED AS OF 1/28. (on 28-JAN-2013 by D. SMITH (HFD-620) 2402769592)
TESTING OF RAW MATERIALS (on 30-JAN-2013 by STOCKM)

Profile: CONTROL TESTING LABORATORY

OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	03-JUN-2008				HOUGHG
OC RECOMMENDATION	03-JUN-2008			ACCEPTABLE BASED ON PROFILE	KIEL
SUBMITTED TO OC	27-SEP-2011				LIUY
REQUEST CANCELLED	18-NOV-2011			LIUY FACILITY WITHDRAWN	
SUBMITTED TO OC	16-JAN-2013			RIVALAL	
OC RECOMMENDATION	30-JAN-2013			ACCEPTABLE BASED ON PROFILE	STOCKM
SUBMITTED TO OC	02-APR-2013				RIVALAL
OC RECOMMENDATION	03-APR-2013			ACCEPTABLE BASED ON PROFILE	SHARPT

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)

(b) (4)

DMF No: (b) (4) **AADA:** N 021636

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Establishment Comment: DRUG SUBSTANCE MANUFACTURER: OMEPRAZOLE (on 24-APR-2008 by C. HOUGH () 3017960323)

Profile: NON-STERILE API BY CHEMICAL SYNTHESIS **OAI Status:** NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	24-APR-2008				HOUGH C
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
ASSIGNED INSPECTION TO IB	(b) (4)	GMP Inspection			ADAMSS
INSPECTION SCHEDULED	(b) (4)		19-SEP-2008		IRIVERA
INSPECTION PERFORMED	(b) (4)		19-SEP-2008		IRIVERA
DO RECOMMENDATION ADEQUATE FIRM RESPONSE INSPECTION	22-DEC-2008			ACCEPTABLE	ADAMSS
OC RECOMMENDATION	22-DEC-2008			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	GMP Inspection			TOULOUSEM
DO RECOMMENDATION ACCEPTABLE THROUGH PDUFA	06-OCT-2011			ACCEPTABLE BASED ON FILE REVIEW	PHILPYE
OC RECOMMENDATION	11-OCT-2011			ACCEPTABLE DISTRICT RECOMMENDATION	SMITHDE
SUBMITTED TO DO	(b) (4)	GMP Inspection			STOCKM
UNDER REVIEW	09-FEB-2013				PHILPYE
DO RECOMMENDATION	14-MAR-2013			ACCEPTABLE BASED ON FILE REVIEW	PHILPYE
OC RECOMMENDATION	15-MAR-2013			ACCEPTABLE DISTRICT RECOMMENDATION	STOCKM

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SWAPAN K DE
06/10/2013

DANAE D CHRISTODOULOU
06/10/2013

NDA 22-283

**Zegerid OTC™ Powder for Oral Suspension
(omeprazole/sodium bicarbonate 20 mg/1680 mg)**

MSD Consumer Care INC.

**Swapan K De, Ph.D.
CMC-Lead
Office of New Drug Quality Assessment
Division of New Drug Quality Assessment III
Branch VII**

**CMC REVIEW OF NDA 22-283
For the Division of Nonprescription Clinical Evaluation
(HFD-560)**

Chemistry Assessment Section

Introduction:

The drug product is identical in all Chemistry manufacturing and Controls aspects (composition, manufacture, development, specifications, container closure systems, stability etc.) as the approved NDA 21-636 for Rx Zegerid™ Powder for Oral Suspension (20 mg omeprazole). This application does not include 40 mg omeprazole drug product that is also approved in NDA 21-636.

The drug product is provided in single use, child resistant packets containing 20 mg omeprazole USP, 1680 mg of sodium bicarbonate USP, (b) (4) Xylitol (b) (4) NF, (b) (4) of Sucrose NF, (b) (4) Sucralose NF, (b) (4) Xanthan gum (b) (4) NF, (b) (4) flavor (b) (4) and (b) (4) (b) (4) flavor (u) (u). Chemistry review dated 3 December, 2008 contains details of the Chemistry, Manufacturing and Controls information for the drug substances and drug product and has no outstanding CMC issues.

Background:

This is the third review cycle for this NDA. The original NDA was submitted in 2008. The applicant received a complete response letter on 16 January, 2009. Following submission for another cycle, the application remain deficient and a second CR letter was issued on 12 July, 2010. The current submission (dated 30 June, 2011) contains response for clinical pharmacology deficiencies outlined in the second Complete Response letter. Since the inspection for the manufacturing facilities were more than two years old during the submission of this application, an establishment evaluation request (EER) was placed (dated 27 September, 2011) to the Office of Compliance through the Establishment Evaluation System (EES) to assure the manufacturing facilities remain in acceptable status regarding cGMP compliance.

In response to the EER, the Office of Compliance issued a “withhold” recommendation for this application on 19 December, 2011 due to unsatisfactory inspection findings in two of the manufacturing facilities included in this application. The drug substance manufacturer facility at Green River (b) (4) and finished dosage tester at (b) (4) was found to be not in compliant with cGMP (see attached EER summary report).

Thus, although there are no outstanding issues from a CMC perspective, the application is recommended for “Approval” pending satisfactory completion of cGMP inspections. The complete response letter should include following deficiency in the “Complete Response” letter.

“During a recent inspection of two manufacturing facilities (b) (4) for this submission, our field investigator conveyed deficiencies to the representative of the facilities. Satisfactory resolution of these deficiencies is required before this application may be approved.”



CHEMISTRY REVIEW



Chemistry Assessment Section

ESTABLISHMENT EVALUATION REPORT:

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Application:	NDA 22283/000	Action Goal:	
Stamp Date:	20-MAR-2008	District Goal:	31-OCT-2011
Regulatory:	30-DEC-2011		
Applicant:	MSD CONSUMER 556 MORRIS AVE SUMMIT, NJ 07901	Brand Name:	Zegerid OTC (omeprazole 20 mg & sodium b
		Estab. Name:	
		Generic Name:	OMEPRAZOLE 20MG/SODIUM BICARBONATE 1680M
Priority:	8	Product Number; Dosage Form; Ingredient; Strengths	
Org. Code:	580		001; POWDER, FOR ORAL SUSPENSION; OMEPRAZOLE; 21MG 001; POWDER, FOR ORAL SUSPENSION; SODIUM BICARBONATE; 1680MG
Application Comment:	N 22283 IS A NEW DOSAGE FORM WITH SAME DRUG SUBSTANCES AS N 22281 (on 24-APR-2008 by C. HOUGH ()) 301-796-0323)		
FDA Contacts:	Y. LIU	Project Manager	
	C. HOUGH	Review Chemist	301-796-0323
	S. DE	Team Leader	301-796-1664

Overall Recommendation:	WITHHOLD	on 19-DEC-2011	by C. CRUZ	(HFD-323)	301-796-3254
	WITHHOLD	on 08-NOV-2011	by EES_PROD		
	WITHHOLD	on 06-JUL-2011	by EES_PROD		
	ACCEPTABLE	on 04-FEB-2009	by EES_PROD		

Chemistry Assessment Section

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment Comment: RAW MATERIALS TESTER SUBCONTRACTOR (on 24-APR-2008 by C. HOUGH () 301-796-0323)

Profile: CONTROL TESTING LABORATORY OAI Status: OAI ALERT

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	03-JUN-2008				HOUGHG
OC RECOMMENDATION	05-JUN-2008			ACCEPTABLE BASED ON PROFILE	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	Product Specific			TOULOUSEM
DO RECOMMENDATION	31-OCT-2011			WITHHOLD INADEQUATE QA FUNCTIONS	MROSE
OC RECOMMENDATION	31-OCT-2011			WITHHOLD DISTRICT RECOMMENDATION	INYARDA



CHEMISTRY REVIEW



Chemistry Assessment Section

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)
(b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE RELEASE TESTER

Establishment
Comment:

Profile: CONTROL TESTING LABORATORY

OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	03-JUN-2008				HOUGHG
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
DO RECOMMENDATION	17-JUN-2008			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	19-JUN-2008			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
OC RECOMMENDATION	07-DEC-2011			ACCEPTABLE RECOMMENDATION ENTERED W/O SPECIFICATION OF TESTING ROLES BASED ON KNOWN SITE FUNCTIONS	SMITHDE
				BASED ON PROFILE	



CHEMISTRY REVIEW



Chemistry Assessment Section

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)
 (b) (4)
 (b) (4)
 DMF No: AADA:
 Responsibilities: DRUG SUBSTANCE MANUFACTURER
 Establishment Comment: MANUFACTURER OF SODIUM BICARBONATE (on 24-APR-2008 by C. HOUGH () 301-796-0323)
 Profile: NON-STERILE API BY CHEMICAL SYNTHESIS OAI Status: POTENTIAL OAI

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	24-APR-2008				HOUGHG
SUBMITTED TO DO	(b) (4)	GMP Inspection			FERGUSONS
SUBMITTED TO OC	03-JUN-2008				HOUGHG
SUBMITTED TO DO	(b) (4) 8	GMP Inspection			FERGUSONS
DO RECOMMENDATION	03-DEC-2008			ACCEPTABLE BASED ON FILE REVIEW	ESMITH1
OC RECOMMENDATION	03-DEC-2008			ACCEPTABLE DISTRICT RECOMMENDATION	FERGUSONS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4) 1	GMP Inspection			TOULOUSEM
ASSIGNED INSPECTION TO IB	(b) (4)	Product Specific			NALINIL
INSPECTION SCHEDULED	(b) (4)				NALINIL
INSPECTION PERFORMED			(b) (4)		NALINIL
INSPECTION PERFORMED 667794 See Endorsement Text.	(b) (4)				MATTHEW.DIONNE
DO RECOMMENDATION	03-NOV-2011			WITHHOLD INADEQUATE QA FUNCTIONS	NALINIL
OC RECOMMENDATION CDER OC CONCURS WITH DISTRICT'S WH REC BASED ON UNKNOWN PRODUCT COANTAMINANTS AND POTENTIAL WRNG LTR.	19-DEC-2011			WITHHOLD DISTRICT RECOMMENDATION	CRUZC



CHEMISTRY REVIEW



Chemistry Assessment Section

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment
Comment:

Profile: CONTROL TESTING LABORATORY

OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	03-JUN-2008				HOUGHG
OC RECOMMENDATION	05-JUN-2008			ACCEPTABLE BASED ON PROFILE	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
OC RECOMMENDATION	07-DEC-2011			ACCEPTABLE RECOMMENDATION ENTERED W/O SPECIFICATION OF TESTING ROLES BASED ON KNOWN SITE FUNCTIONS	SMITHDE



CHEMISTRY REVIEW



Chemistry Assessment Section

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)
 (b) (4)
 (b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment Comment: RAW MATERIAL MICROBIAL ANALYSIS, RAW MATERIAL TESTING (on 24-APR-2008 by C. HOUGH ()) 301-796-0323)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	02-MAY-2008				HOUGHG
OC RECOMMENDATION	02-MAY-2008			ACCEPTABLE BASED ON PROFILE	ADAMSS
SUBMITTED TO OC	03-JUN-2008				HOUGHG
OC RECOMMENDATION	05-JUN-2008			ACCEPTABLE BASED ON PROFILE	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	Product Specific			TOULOUSEM
DO RECOMMENDATION	03-OCT-2011			ACCEPTABLE BASED ON FILE REVIEW	MROSE
OC RECOMMENDATION	04-OCT-2011			ACCEPTABLE DISTRICT RECOMMENDATION	SMITHDE



CHEMISTRY REVIEW



Chemistry Assessment Section

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)

(b) (4)

DMF No: AADA:

- Responsibilities:
- FINISHED DOSAGE MANUFACTURER
 - FINISHED DOSAGE OTHER TESTER
 - FINISHED DOSAGE PACKAGER
 - FINISHED DOSAGE RELEASE TESTER
 - FINISHED DOSAGE STABILITY TESTER

Establishment Comment: RAW MATERIAL RELEASE, IN-PROCESS AND FINAL DRUG PRODUCT TESTING, RELEASE, MANUFACTURE, PACKAGING AND STABILITY TESTING. (on 24-APR-2008 by C. HOUGH () 301-796-0323)

Profile: POWDERS (INCLUDES ORAL AND TOPICAL) OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	24-APR-2008				HOUGH C
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
DO RECOMMENDATION	29-MAY-2008			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS
OC RECOMMENDATION	29-MAY-2008			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS
SUBMITTED TO OC	03-JUN-2008				HOUGH C
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
ASSIGNED INSPECTION TO IB	(b) (4)	GMP Inspection			ADAMSS
INSPECTION PERFORMED	(b) (4)				FACTS_EES
AUTOMATIC WITHHOLD STATUS ISSUED BY FACTS, DUE TO FIRM BEING OUT OF BUSINESS OR MERGED					
DO RECOMMENDATION	04-FEB-2009			ACCEPTABLE INSPECTION	ADAMSS
BASED ON REVIEW OF 483 OBSERVATIONS AND INVESTIGATOR'S RECOMMENDATION. AWAITING EIR AND FIRM'S RESPONSE.					
OC RECOMMENDATION	04-FEB-2009			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	Product Specific			TOULOUSEM
DO RECOMMENDATION	06-OCT-2011			ACCEPTABLE BASED ON FILE REVIEW	MROSE
OC RECOMMENDATION	11-OCT-2011			ACCEPTABLE DISTRICT RECOMMENDATION	SMITHDE



CHEMISTRY REVIEW



Chemistry Assessment Section

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST DETAIL REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment
Comment:

Profile: CONTROL TESTING LABORATORY

OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	03-JUN-2008				HOUGHHC
OC RECOMMENDATION	03-JUN-2008			ACCEPTABLE BASED ON PROFILE	KIEL
SUBMITTED TO OC	27-SEP-2011				LIUY
OC RECOMMENDATION	07-DEC-2011			ACCEPTABLE RECOMMENDATION ENTERED W/O SPECIFICATION OF TESTING ROLES BASED ON KNOWN SITE FUNCTIONS	SMITHDE

Chemistry Assessment Section

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)
 (b) (4)
 DMF No: (b) (4) AADA: (b) (4)
 Responsibilities: DRUG SUBSTANCE MANUFACTURER
 Establishment Comment: DRUG SUBSTANCE MANUFACTURER: OMEPRAZOLE (on 24-APR-2008 by C. HOUGH () 301-796-0323)
 Profile: NON-STERILE API BY CHEMICAL SYNTHESIS OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	24-APR-2008				HOUGHHC
SUBMITTED TO DO	(b) (4)	GMP Inspection			ADAMSS
ASSIGNED INSPECTION TO IB	(b) (4)	GMP Inspection			ADAMSS
INSPECTION SCHEDULED	(b) (4)		19-SEP-2008		IRIVERA
INSPECTION PERFORMED	(b) (4)		19-SEP-2008		IRIVERA
DO RECOMMENDATION	22-DEC-2008			ACCEPTABLE ADEQUATE FIRM RESPONSE INSPECTION	ADAMSS
OC RECOMMENDATION	22-DEC-2008			ACCEPTABLE DISTRICT RECOMMENDATION	ADAMSS
SUBMITTED TO OC	27-SEP-2011				LIUY
SUBMITTED TO DO	(b) (4)	GMP Inspection			TOULOUSEM
DO RECOMMENDATION ACCEPTABLE THROUGH PDUFA	06-OCT-2011			ACCEPTABLE BASED ON FILE REVIEW	PHILPYE
OC RECOMMENDATION	11-OCT-2011			ACCEPTABLE DISTRICT RECOMMENDATION	SMITHDE

Recommendations: From chemistry, manufacturing and controls point of view, this NDA is recommended for "Approval" pending satisfactory completion of cGMP inspections. The complete response letter should include following deficiency in the "Complete Response" letter.

"During a recent inspection of two manufacturing facilities (b) (4) for this submission, our field investigator conveyed deficiencies to the representative of the facilities. Satisfactory resolution of these deficiencies is required before this application may be approved."

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/s/

SWAPAN K DE
12/20/2011

ALI H AL HAKIM
12/20/2011

Initial Quality Assessment
Branch III
Pre-Marketing Assessment Division II

OND Division: Division of Nonprescription Clinical Evaluation
NDA: 22-283
Applicant: Schering-Plough HealthCare Products, Inc.
Stamp Date: Mar. 20, 2008
PDUFA Date: Jan. 20, 2009
Trademark: Zegerid OTC™
Established Name: Omeprazole 20 mg/Sodium Bicarbonate 1680 mg
Dosage Form: Powder for Oral Suspension
Route of Administration: Oral
Indication: Frequent heartburn

PAL: Shulin Ding

	YES	NO
ONDQA Fileability:	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Comments for 74-Day Letter	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Summary and Critical Issues

A. Summary

This NDA is submitted by Schering-Plough HealthCare under section 505(b)(2) of the Federal Food Drug and cosmetic Act in support of the nonprescription marketing of Zegerid OTC™ powder for oral suspension (omeprazole 20 mg/sodium bicarbonate 1680 mg) for the treatment of frequent heartburn. This is a partial switch of NDA 21-636 Zegerid powder for oral suspension, which was approved in 2004 for two strengths (20 mg and 40 mg). The OTC product is identical to the approved Rx product in drug substance suppliers, formulation, drug product manufacturer, drug product manufacturing process, specification, and container/closure system.

The applicant references to NDA 21-636 Zegerid powder for oral suspension for most of CMC information. The two NDAs are virtually the same. Minor differences are in the sections on raw material testing sites, and excipient controls (addition of compendial methods to the controls of some excipients).

Zegerid OTC™ powder for oral suspension is provided in child resistant, single dose, multilayer foil packets. The packets are assembled in different quantities for various finished product market presentations.

The stability data supporting the proposed (b) (4) month expiry period at the storage of (b) (4) are referenced to NDA 21-636. A categorical exclusion from the requirement to prepare an Environmental Assessment is claimed for this NDA.

B. Critical issues for review

There are no critical review issues identified for this NDA. This is because all important CMC aspects of this NDA have been reviewed and approved under NDA 21-636.

C. Comments for 74-Day Letter

None.

D. Comments/Recommendation

This NDA is **fileable** from chemistry, manufacturing and controls (CMC) perspective. There are no major review issues.

GMP inspections have been requested. The omeprazole drug substance manufacturing site is in (b) (4). The drug product manufacturing site is in (b) (4). The sodium bicarbonate drug substance manufacturing site is in the U.S.

Shulin Ding
Pharmaceutical Assessment Lead, Branch III

Moo-Jhong Rhee
Chief, Branch III

Filing Checklists

A. Administrative Checklists

YES	NO		Comments
x		On its face, is the section organized adequately?	
x		Is the section indexed and paginated adequately?	
x		On its face, is the section legible?	
x		Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	
x		Has an environmental assessment report or categorical exclusion been provided?	

B. Technical Checklists

1. Drug Substance: Omeprazole USP referenced to DMF (b) (4)

	x	Does the section contain synthetic scheme with in-process parameters?	
	x	Does the section contain structural elucidation data?	
x		Does the section contain specifications?	
	x	Does the section contain information on impurities?	
x		Does the section contain validation data for analytical methods?	
	x	Does the section contain container and closure information?	
	x	Does the section contain stability data?	

Drug Substance: Sodium Bicarbonate USP

x		Does the section contain synthetic scheme with in-process parameters?	
	x	Does the section contain structural elucidation data?	Not applicable
x		Does the section contain specifications?	
	x	Does the section contain information on impurities?	Compendial material
	x	Does the section contain validation data for analytical methods?	Compendial method
x		Does the section contain container and closure information?	The applicant states that it is stored in the original sealed container.
	x	Does the section contain stability data?	The applicant states that the stability data can be obtained from the supplier.

2. Drug Product

x		Does the section contain manufacturing process with in-process controls?	
x		Does the section contain quality controls of excipients?	
x		Does the section contain information on composition?	
x		Does the section contain specifications?	
x		Does the section contain information on degradation products?	Also referenced to NDA 21-636.

x		Does the section contain validation data for analytical methods?	
x		Does the section contain information on container and closure systems?	
x		Does the section contain stability data with a proposed expiration date?	Referenced to NDA 21-636.
x		Does the section contain information on labels of container and cartons?	
x		Does the section contain tradename and established name?	

C. Review Issues

x		Has all information requested during the IND phases, and at the pre-NDA meetings been included?	
	x	Is a team review recommended?	
x		Are DMFs adequately referenced?	

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Shulin Ding
4/29/2008 03:28:51 PM
CHEMIST

Moo-Jhong Rhee
4/29/2008 04:16:44 PM
CHEMIST
Chief, Branch III