CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203284Orig1s000

CHEMISTRY REVIEW(S)

MEMORANDUM

DEPATMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTARTION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: January 16, 2013

TO: NDA 203284 CMC Review # 1

FROM: Hamid R. Shafiei, Ph.D., CMC Reviewer
(ONDQA/Division II/Branch IV)

THROUGH: Moo-Jhong Rhee, Ph.D., Branch Chief
(ONDQA/Division II/Branch IV)

SUBJECT: Final CMC Recommendation

In review # 1 of NDA 203284 for Ravicti Liquid for oral use, this NDA was not recommended for approval from the CMC perspective due to the following reasons:

1) CMC related label/labeling issues were ***not*** resolved
2) An overall recommendation of "Acceptable" from the Office of Compliance regarding the facilities involved in this NDA was ***not*** yet issued

The CMC label/labeling issues have been resolved via the amendments dated December 13, 2012 and December 31, 2012 (see the **Attachment -2**).

The Office of Compliance has also made an overall recommendation of "Acceptable" for the facilities involved in this NDA on January 14, 2013 (see the **Attachment-1**).

Recommendation:

This NDA is now recommended for **approval** from the ONDQA perspective.

Appendix

Attachement-1

EES Report

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application:	NDA 203284/000	**Action Goal:**	
Stamp Date:	23-DEC-2011	**District Goal:**	24-NOV-2012
Regulatory:	23-JAN-2013		
Applicant:	HYPERION THERAP INC	**Brand Name:**	Glycerol Phenylbutyrate (HPN-100)
	601 GATEWAY BLVD STE 200	**Estab. Name:**	
	SOUTH SAN FRANCISCO, CA 94080	**Generic Name:**	Glycerol Phenylbutyrate (HPN-100)
Priority:	1	**Product Number; Dosage Form; Ingredient; Strengths**	
Org. Code:	180	001; LIQUID; GLYCEROL PHENYLBUTYRATE; 25ML 002; LIQUID; GLYCEROL PHENYLBUTYRATE; 120ML 003; LIQUID; GLYCEROL PHENYLBUTYRATE; 450ML	
Application Comment:			

FDA Contacts:	C. TRAN-ZWANETZ	Project Manager		(HFD-800)	3017963877
	H. SHAFIEI	Review Chemist			3017962326
	M. KOWBLANSKY	Team Leader			3017961390

Overall Recommendation:	ACCEPTABLE	on 14-JAN-2013	by D. SMITH	(HFD-323)	3017965321
	PENDING	on 07-FEB-2012	by EES_PROD		
	PENDING	on 07-FEB-2012	by EES_PROD		

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

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

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE OTHER TESTER

Establishment Comment:

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

Milestone Name	Milestone Date	Request Type	Planned Completion	Decision	Creator
Comment				Reason	
SUBMITTED TO OC	(b) (4)				(b) (4)
SUBMITTED TO DO		GMP Inspection			
ASSIGNED INSPECTION TO IB		GMP Inspection			
INSPECTION PERFORMED			(b) (4)		

This Pre-Approval Inspection (PAI) of a microbiological control testing laboratory was conducted in accordance with a request from DFFI/IOB and CDER/OC/DIDQ/ICB2 (International Compliance Branch 2) for a PDUFA Pre-Approval Inspection of the laboratory to evaluate their microbiological testing of the non-sterile liquid drug substance Glycerol Phenylbutyrate (GPB), under new drug application (NDA) 203284/000. The holder of the NDA is Hyperion Therapeutics, Inc., South San Francisco, CA. The manufacturer, packager and final release testing facility for the GPB drug substance is (b) (4)

Coverage for this inspection was conducted under CP 7356.002, Drug Manufacturing Inspections and CP 7346.832, Pre-Approval Inspections.

Previous inspection of this microbiological control testing laboratory was conducted (b) (4) by a team consisting of a CSO and a Microbiologist. The inspection was a PAI covering the finished dosage sterility testing of (b) (4)

The current inspection included coverage of the laboratory's Quality, Facilities & Equipment, and Laboratory systems. Profile class CTL (Control Testing Laboratory) was covered during the inspection. The inspection found that three lots of GPB were sent b

DO RECOMMENDATION	(b) (4)	ACCEPTABLE INSPECTION	(b) (4)
OC RECOMMENDATION	(b) (4)	ACCEPTABLE DISTRICT RECOMMENDATION	(b) (4)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

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

DMF No: **AADA:**

Responsibilities: DRUG SUBSTANCE MANUFACTURER
DRUG SUBSTANCE PACKAGER
DRUG SUBSTANCE RELEASE TESTER

Establishment Comment: PROVIDES FOR MANUFACTURING, QA/QC TESTING AND RELEASE, PACKAGING, STABILITY TESTING (GLYCEROL PHENYLBUTYRATE, DSM)
(b) (4)

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

Milestone Name	Milestone Date	Request Type	Planned Completion	Decision	Creator
Comment				Reason	
SUBMITTED TO OC	(b) (4)				(b) (4)
SUBMITTED TO DO		GMP Inspection			
WILL BE OVER 3 YEARS AT TIME OF PDUFA OTHER FIRMS PENDING INSPECTION REQUESTS FOR THIS NDA					
ASSIGNED INSPECTION TO IB	(b) (4)	GMP Inspection			
INSPECTION PERFORMED			(b) (4)		
INSPECTION SCHEDULED					
UNDER REVIEW					
CASE ID (b) (4) IN QUEUE FOR REVIEW; CSO NOT YET ASSIGNED					
DO RECOMMENDATION	(b) (4)			ACCEPTABLE INSPECTION	
OC RECOMMENDATION				ACCEPTABLE DISTRICT RECOMMENDATION	

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