

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
022434Orig1s000

CHEMISTRY REVIEW(S)

NDA 22,434

Argatroban Injection

Eagle Pharmaceuticals, Inc.

William Adams

Office of New Drug Quality Assessment

Division of New Drug Quality Assessment I, Branch II

for

Division of Medical Imaging and Hematology Products

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CMC Review Data Sheet

CMC Review Data Sheet

1. **NDA 22,434**
2. **REVIEW #2**
3. **REVIEW DATE:** 27 Jun 2011
4. **REVIEWER:** William M. Adams
5. **PREVIOUS DOCUMENTS:** None
6. **SUBMISSION(S) BEING REVIEWED:**

CMC Review 01	23 Nov 2009
CR Letter	29 Jan 2010
Amendment N-027 (resubmission)	12 Jan 2011
IR Letter (microbiology comments)	07 Apr 2011
IR Letter (request for labels and labeling)	07 Apr 2011
Amendment N-030 (CMC sites)	21 Apr 2011
Amendment N-029 (microbiology response)	22 Apr 2011
IR Letter (OSE labeling comments)	06 May 2011
Amendment N-031 (draft vial/carton labels)	16 May 2011
Amendment N-032 (draft package insert)	26 May 2011
IR Letter (microbiology comments)	31 May 2011
IR Letter (CMC comments)	01 Jun 2011
Amendment N-035 (CMC responses)*	23 Jun 2011

- * CMC information was submitted in parts as Emails dated 06/10/11, 06/15/11 and 06/16/11 with attachments. Due to time constraints, CMC information in this amendment is presumed to be the same as in the Emails..

7. **NAME & ADDRESS OF APPLICANT:**

Name: Eagle Pharmaceuticals, Inc.
Address: 470 Chestnut Ridge Road
Woodcliff Lake NJ 07677
Representative: Brenda Marczi, PharmD
Vice President, Regulatory Affairs
Telephone: (201) 326-5327
FAX: (201) 391-2430
Email: BMarczi@eagleus.com

8. **DRUG PRODUCT NAME/CODE/TYPE:**

CMC Review Data Sheet

- a) **Non-Proprietary Name:** Argatroban Injection
- b) **Code Name/# (ONDQA only):** None
- c) **Chem. Type/Submission Priority (ONDQA only):** 5S

- 9. **LEGAL BASIS FOR SUBMISSION:** 505(b)(2)
- 10. **PHARMACOL. CATEGORY:** Direct Thrombin Inhibitor
- 11. **DOSAGE FORM:** INJ SOL (injection, solution)
- 12. **STRENGTH/POTENCY:** 1 mg/mL as 50 mg/50 mL & (b) (4)
- 13. **ROUTE OF ADMINISTRATION:** Injection (IV infusion)
- 14. **Rx/OTC DISPENSED:** Rx OTC
- 15. **SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):**
 SPOTS product – Form Completed
 Not a SPOTS product

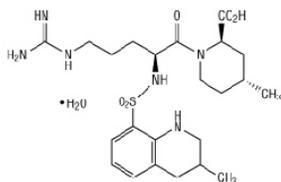
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: (2*R*,4*R*)-1-[(*S*)-5-(Amino(iminio)methylamino)-2-((*R*,*S*)-3-methyl-1,2,3,4-tetrahydroquinoline-8-sulfonamido)pentanoyl]-4-methylpiperidine-2-carboxylate monohydrate

Molecular Formula C₂₃H₃₆N₆O₅S * H₂O

Molecular Weight 526.66 gm/mole

Molecular Structure



17. RELATED/SUPPORTING DOCUMENTS:

A. Supporting DMFs:

DMF #	TYP E	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS ³
(b) (4)	II	(b) (4)	Drug Substance	1	Adequate	18 Aug 2010 (OGD)	Does not include MV studies
(b) (4)	III	(b) (4)	(b) (4)	4			

CMC Review Data Sheet

		(b) (4)				
(b) (4)	III	(b) (4)	(b) (4)	4		
	III		4			

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

B. Other Supporting Documents:

Doc #	OWNER	ITEM REFERENCED	STATUS	DATE REVIEW COMPLETED	COMMENTS
IND 102,622	Eagle	Argatroban Injection	active	---	No CMC reviews filed into Dartrts
NDA 20-883	GSK/Pfizer	Argatroban Injection	approved		RLD application

18. CONSULTS/CMC-RELATED REVIEWS:

CONSULTS	REVIEWER/ DATE	COMMENTS
Clinical	F.Alvandi; 06/16/11	approval
Non Clin	S.L.Lee; 06/22/11	approval
ClinPharm	L.Zhang; 06/16/11	approval
OSE/DMEPA	M.Griffis; 05/03/11	all issues resolved
Microbiology	S.Langille; 06/10/11	all issues resolved
Biopharm	A.Dorantes; 05/31/11	biowaiver granted
EES	Submitted Jan-Feb 2011	Acceptable for all sites
EA		categorical exemption justified

The CMC Review for NDA 22-434

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The proposed new drug application (NDA) is considered to be adequate for APPROVAL with respect to chemistry, manufacturing and control (CMC) information.

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

N/A

II. Summary of CMC Assessments

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

Eagle has re-submitted a 505(b)(2) application for Argatroban Injection, 1 mg/mL ready to use solution, based a referenced drug product approved under NDA 21-883 (Pfizer's Argatroban Injection, 250 mg in 2.5 mL liquid concentrate).

Drug Substance

Argatroban is a direct thrombin inhibitor synthesized from the naturally occurring L-arginine. The molecule has four chiral centers; three centers have specified orientation and the fourth is a 65(R): 35(L) ratio of isomers. The polymorphic form is the monohydrate of the freebase.

Bulk drug substance is provided by (b)(4). This site has been found to meet cGMP standards. Information regarding manufacture, in-process control, structure elucidation and impurities is provided by reference to (b)(4) type II drug master file (DMF) (b)(4). The DMF was reviewed and found acceptable. DMF information regarding the profile of process impurities (related substances, residual catalyst and residual solvents) and qualification of their proposed acceptance criteria is provided in the application.

Specifications for release of bulk drug substance by (b)(4), and for its acceptance by the drug product manufacturer use the same tests, methods and criteria. The drug product manufacturer repeats all testing for acceptable of drug substance batches. A single specification is proposed for release/acceptance and for stability testing. All impurities observed above the method limit of quantitation are reported.

CMC Assessment Section

Testing is adequate to address identity (infrared spectroscopy, ultraviolet spectroscopy, specific rotation, and R-isomer/S-isomer ratio by isocratic high pressure liquid chromatography (isocratic mobile phase HPLC); assay (isocratic mobile phase HPLC); chemical purity (related substances by gradient HPLC, residue on ignition, heavy metals, residual ^{(b) (4)} by inductively coupled plasma-mass spectrometry, residual solvents by two head space-gas chromatography methods, and water content); and microbial attributes (microbial limits and bacterial endotoxin testing). The currently proposed criteria are adequately justified and are supported by batch analysis data and stability information. Descriptions of the currently proposed analytical methods are complete and provided in sufficient detail. For the non-compendial methods, complete and acceptable validation studies performed at site of use have been provided. Reference standards for bulk drug substance, each isomer and the principle impurity are identified and characterized for the intended purpose.

The HPLC methods for R-isomer/S-isomer ratio, assay and related substances have been significantly revised twice since initial submission of this application, and the criteria for residual solvents have been significantly revised once. Test results using the various HPLC method versions show that reasonably comparable data is obtained. Comparison data for residual solvent testing was not deemed necessary.

The ^{(b) (4)} DMF provides data to support long term storage of bulk drug substance in a ^{(b) (4)}

Drug Product

Eagle's drug product is 50 mL of a 1 mg argatroban per mL, ready-to-use solution in a single-dose vial. The solution is formulated with argatroban hydrate, lactobionic acid European Pharmacopoeia (EP) ^{(b) (4)}, L-methionine USP ^{(b) (4)}, sodium chloride USP ^{(b) (4)} and sodium chloride NF (pH adjustment) in water for injection USP. The batch formulation is a multiple of the unit formulation. Excipients meet USP/NF monograph requirements. No material used in drug product manufacture is novel, or of human or animal origin.

The product development information addresses formulation compatibility with the manufacturing equipment, selection of excipients and optimal pH, stopper extractables/leachables, seal integrity, and solution stability during administration. Formulation compatibility studies with the same three intravenous solutions approved for the referenced drug – 5% dextrose injection USP, 0.9% sodium chloride injection USP and lactated ringer's injection USP – was provided in an amendment.

Drug product is manufactured and controlled by Cipla, Ltd (Goa, India). Drug substance testing for acceptance is performed by Cipla and ^{(b) (4)}

Each site has been found to meet cGMP requirements.

CMC Assessment Section

A manufacturing site floor plan, and a narrative description and process flow diagram for the manufacturing process are provided. The process is in (b) (4)

(b) (4)

(b) (4)

Formulation overage and reprocessing are not proposed. Copies of the master product record for the proposed commercial scale batch and executed batch records of the three registration batches are provided. Each registration batch meets all in-process criteria and is a simulation of the proposed commercial scale manufacturing operations. Included is a list of the commercial manufacturing equipment.

The proposed batch release specification is adequate for the intended purpose. Testing includes identity (visual appearance; UV spectroscopy, R-isomer/S-isomer ratio by isocratic HPLC); assay (isocratic HPLC); related substances (gradient HPLC); physicochemical attributes (osmolality and pH); USP <1> requirements (volume in container, particulate matter, and solution clarity); and microbiological attributes (bacterial endotoxins and sterility). The analytical methods for R-isomer/S-isomer ratio, assay and related substances are the same as used for drug substance testing. Descriptions of the non-compendial analytical methods are complete and provided in sufficient detail. Analytical methods have been validated for their intended use. The proposed criteria are adequately justified and are supported by batch analysis data and stability information. Related substances are identified and their mechanisms of formation are provided.

The proposed container closure system is a clear, colorless type I glass 50cc vial; a (b) (4) rubber stopper with (b) (4) on the product contact surface and (b) (4) on the non-product contact surface; and an aluminum crimpseal with white (b) (4) flip-off cap. Provided for each component is a drawing, supplier and Cipla acceptance specifications, and example supplier certificates of analysis which establish critical dimensions and attributes. A letter of authorization to the type III DMF for each component supplier is also provided. The results of USP testing on the vial and stopper, and extractables/leachables testing on the stopper that qualify these components for safety are provided.

Stability information includes the results from NDA registration, photostability and thermal cycling stress studies; and a post approval protocol. NDA studies on three registration batches provide 20 months data for vials stored upright and inverted at ICH long term and intermediate conditions; and 6 month data on vials stored upright and inverted at ICH accelerated conditions. Testing is for assay, purity, physicochemical attributes and microbiological attributes. The results show no significant change in test values over time and storage conditions. The stress studies established that drug product is sensitive to light and should not be stored at refrigerated or freezer conditions. These studies are adequate to support the proposed initial expiry period of 24 months with storage at USP controlled room temperature, protect from light, and do not store in refrigerator or freezer.

CMC Assessment Section

The post approval stability protocol includes storage of inverted and upright vials sampled from the first three commercial batches for 36 months at ICH long term condition and 6 months at ICH accelerated condition with testing for appearance, pH, assay, chemical purity and microbiological attributes. Thereafter, a single batch will be sampled annually for stability testing. Data is to be filed in the annual reports and failures appropriately investigated.

Comparability protocols are not proposed in this application.

The CMC information on the submitted vial and carton labels, and package insert is complete, accurate and appropriately presented.

The applicant's request for categorical exclusion from the environmental assessment requirements based on 21 CGT 25.31(e) is granted.

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

Eagle's product is a single dose, ready-to-use formulation in a glass vial which is to be inverted and inserted by an medical infusion set into an intravenous infusion line ("piggyback vial") for administration as bolus and/or slow infusion by a metering pump. The solution is not to be diluted.

C. Basis for Approvability or Not-Approval Recommendation

With respect to CMC information, NDA 22-434 is considered to be adequate for APPROVAL. All CMC information in the re-submission has been reviewed and found to be complete and acceptable, and issues identified in the complete response letter dated 29 Jan 2010 and in subsequent amendments have been resolved.

III. Administrative**A. Reviewer's Signature:** (see appended electronic signature page)

William M. Adams, CMC Reviewer/Branch II/DNDQA I
Janice Brown, Ph.D., Acting Chief/Branch II/DNDQA I

B. Endorsement Block:

See appended electronic signature page)

C. CC Block: (entered electronically in Darrts)

ONDQA/PMQ/Tu-Van Lambert
ONDQA/CMC Lead/J.Brown
DRUP/RPM/G.Lyght

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/s/

WILLIAM M ADAMS
06/27/2011

JANICE T BROWN
06/27/2011
Janice Brown for Sarah Pope Miksinski, Ph.D.

NDA 22-434

Argatroban Injection

Eagle Pharmaceuticals, Inc.

Mark Sassaman, Ph.D.
Review Chemist

**Office of New Drug Quality Assessment
Division of Premarketing Assessment and Manufacturing
Science (Branch V)
for
Division of Medical Imaging and Hematology Products
(HFD-160)**

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Chemistry Review Data Sheet

1. NDA 22-434
2. REVIEW #1
3. REVIEW DATE: 20 NOV 2009
4. REVIEWER: Mark Sassaman, Ph.D.

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original Application	26 SEP 2008

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Amendment	29 OCT 2008
Amendment	02 JUN 2009
Amendment	03 JUN 2009

7. NAME & ADDRESS OF APPLICANT:

Name: Eagle Pharmaceuticals, Inc.
Address: 470 Chestnut Ridge Road
Woodcliff Lake NJ 07677
Representative: Brenda Marzi, PharmD
Vice President, Regulatory Affairs
Telephone: (201)326-5327
FAX: (201)391-2430
E-mail: BMarzi@eagleus.com

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Argatroban Injection RTU
b) Non-Proprietary Name: Argatroban Injection
c) Code Name/#: None
d) Chem. Type/Submission Priority:
 • Chem. Type: **5**
 • Submission Priority: **S**

9. LEGAL BASIS FOR SUBMISSION:

FDC Act	505(b)(2)
RLD	Argatroban Injection
Dosage Form	Injection, solution, concentrate (INJ SOL CONC) Each single-use vial contains 2.5 mL of Argatroban solution at a concentration of 100 mg/mL (250 mg/vial);
Strength	vials are diluted with 0.9% Sodium Chloride Injection, 5% Dextrose Injection, or Lactated Ringer's Injection to a final concentration of 1 mg/mL prior to administration.
RLD NDA	20-883
NDA Holder	Pfizer Inc.

10. PHARMACOL. CATEGORY: Direct Thrombin Inhibitor

11. DOSAGE FORM: INJ SOL (Injection, solution)

12. STRENGTH/POTENCY: 1 mg/mL (50 mg/50 mL (b) (4))

13. ROUTE OF ADMINISTRATION: Injection (intravenous infusion)

14. Rx/OTC DISPENSED: Rx OTC

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

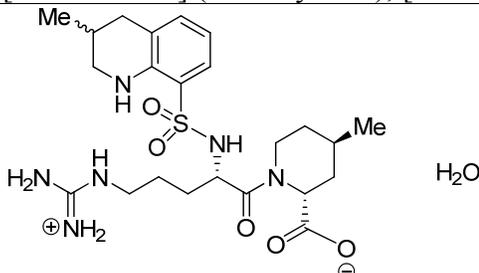
SPOTS product – Form Completed
 Not a SPOTS product

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

Chemical Name(s)

2-Piperidinecarboxylic acid, 1-[5-[(aminoiminomethyl) amino]-1-oxo-2-[[[(1,2,3,4-tetrahydro-3-methyl-8-quinoliny) sulfonyl]amino]pentyl]-4-methyl-, monohydrate

Chemistry Review Data Sheet

1-[5-[(Aminoimino methyl)amino]-1-oxo-2-[[1,2,3,4-tetrahydro-3-methyl-8-quinolinyl)sulfonyl]amino]pentyl]-4-methyl piperidine-2-carboxylic acid monohydrate	
(2 <i>R</i> ,4 <i>R</i>)-4-Methyl-1-[<i>N</i> ² -[(1,2,3,4-tetrahydro-3-methyl-8-quinolinyl)sulfonyl]-L-arginyl]pipercolic acid monohydrate; (2 <i>R</i> ,4 <i>R</i>)-1-[(2 <i>S</i>)-5-[(aminoiminomethyl)amino]-1-oxo-2-[[1,2,3,4-tetrahydro-3-methyl-8-quinolinyl)sulfonyl]amino]pentyl]-4-methyl-2-piperdinecarboxylic acid monohydrate	
(2 <i>R</i> ,4 <i>R</i>)-4-Methyl-1- <i>N</i> ² -[[(<i>R</i> , <i>S</i>)-1,2,3,4-tetrahydro-3-methyl-8-quinolinyl)sulfonyl]-L-arginyl]pipercolic acid monohydrate.	
(2 <i>R</i> ,4 <i>R</i>)-1-[(<i>S</i>)-5-(Amino(iminio)methylamino)-2-((<i>R</i> , <i>S</i>)-3-methyl-1,2,3,4-tetrahydroquinoline-8-sulfonamido)pentanoyl]-4-methylpiperidine-2-carboxylate monohydrate	
Empirical Formula	C ₂₃ H ₃₆ N ₆ O ₅ S.H ₂ O
Molecular Weight	526.65
CAS Registry Number	[141396-28-3] (monohydrate); [74863-84-6] (anhydrous)
Structural Formula	

Chemical names which account for all four chiral centers are shaded in blue.

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Argatroban Drug Substance	1	Inadequate	10 SEP 2008	CMC Reviewer: Barbara Scott, Ph.D.
(b) (4)	III	(b) (4)	(b) (4)	7	Inadequate	02 NOV 2009	These vials and manufacturer are not used in the proposed commercial presentation (amended 24 SEP 2009). Mark Sassaman, Ph.D.
(b) (4)	III	(b) (4)	(b) (4)	7	Inadequate	02 NOV 2009	This stopper is not used in the proposed commercial presentation (amended 24 SEP 2009). Mark Sassaman, Ph.D.
(b) (4)	III	(b) (4)	7				
(b) (4)	III	(b) (4)	7				

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)

Chemistry Review Data Sheet

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	ACCEPTABLE*	21 OCT 2009	Office of Compliance
Pharm/Tox	N/A		
Biopharm			Joseph Grillo, Ph.D.
Bioequivalence			
LNC	N/A		
Methods Validation	N/A		
DMEPA	Information not available		
EA	Categorical Exclusion Claim under 21 CFR 25.31(a) - ACCEPTABLE	30 JUN 2009	Mark Sassaman, Ph.D.
Microbiology	Information not available		

**Inspections have to be rescheduled. Cipla's facility was accepted based on file review only. FDA has not received process (sterility) validation documents for the facility in which the drug product is to be made (b) (4). At the time of filing, this facility was not operational; registration batches of drug product were manufactured using different equipment than will be used in the commercial process and in a different facility (b) (4) dedicated for oncology drugs). The new manufacturing process and site have not been evaluated by CMC.*

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

Yes No If no, explain reason(s) below:

The Chemistry Review for NDA 22-434

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

In its current form, NDA 22-434 cannot be approved. There are numerous deficiencies, including the drug product never having been made in the facility intended for commercial production, no available stability data, and a recently announced change in presentation, such that the originally submitted application is, by definition, for a different drug product. These are due, in part, to the applicant having altered substantial portions of the application after it was filed. Only a small portion of the total deficiencies, however, is amenable to correction by editing or appending; it would be to the applicant's advantage to resubmit the entire CMC portion of the application after major revisions rather than add to non-reviewable material.

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

N/A

II. Summary of Chemistry Assessments

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

Argatroban is a direct thrombin inhibitor synthesized from the naturally occurring amino acid, L-arginine. There are four chiral centers, one of which is not defined (*i.e.*, both stereoisomers are present). Type I (21-*R*) and Type II (21-*S*) isomers are present in a 2:1 molar ratio. The ratio is controlled by specifications.

Eagle's drug product contains lactobionic acid and L-methionine (b)(4) and sodium chloride as a (b)(4); it is intended to be a ready-to-use formulation for intravenous administration. Argatroban concentration is 1 mg/mL.

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

Eagle's ready-to-use formulation is intended for intravenous administration. The company believes this type of formulation offers advantages over the innovator's drug product, which requires dilution prior to administration.

C. Basis for Approvability or Not-Approval Recommendation

The application has numerous deficiencies. There are very few areas that can be adequately reviewed. Under normal circumstances, CMC reviewers would itemize deficiencies and expect the applicant to provide complete responses. In this case, that policy would be counterproductive. If a list of deficiencies were assembled, the

Executive Summary Section

applicant would be obligated to respond only to items on that list. Due to the large volume of missing and/or unsatisfactory information, the most prudent recommendation is to begin afresh. On several occasions, FDA communicated interim assessments of problems with the application, informed Eagle that the application could neither be approved nor reviewed, and recommended withdrawal and resubmission under a new NDA number. The Office of Regulatory Policy assured the company that no new PDUFA fees would be assessed. Still, Eagle decided in favor of not withdrawing, possibly in hope of being able to respond to deficiencies after only a brief delay.

The application is not reviewable; had Eagle been forthcoming with correct establishment information, the application would not have been filed.

CMC reviewers remain open to the possibility of discussing deficiencies and a path forward with the applicant during a face-to-face meeting or telephone conference but do not plan on issuing an itemized list.

III. Administrative

A. Reviewer's Signature

Mark Sassaman, Ph.D. 23 NOV 2009
Review Chemist

Eldon Leutzinger, Ph.D. 23 NOV 2009
Pharmaceutical Assessment Lead

Sarah Pope Miksinski, Ph.D. 23 NOV 2009
Branch Chief

Richard T. Lostritto, Ph.D. 23 NOV 2009
Division Director

B. Endorsement Block:

Chemist: Mark Sassaman, Ph.D./ 20 NOV 2009
Pharmaceutical Assessment Lead: Eldon Leutzinger, Ph.D./ 23 NOV 2009
Branch Chief: Sarah Pope Miksinsky, Ph.D./ 23 NOV 2009



CHEMISTRY REVIEW



Executive Summary Section

Division Director: Richard T. Lostritto, Ph.D./23 NOV 2009

ONDQA Project Manager: Deborah Mesmer/ 23 NOV 2009

DMIHP Project Manager: Ebla Ali Ibrahim/ 23 NOV 2009

C. CC Block:

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22434	ORIG-1	EAGLE PHARMACEUTICA LS INC	ARGATROBAN INJECTION

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/s/

MARK B SASSAMAN
11/23/2009

RICHARD T LOSTRITTO
11/23/2009

**ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT**

Application:	NDA 22434/000	Sponsor:	EAGLE PHARMS
App. Code:	161		470 CHESTNUT RIDGE RD
Priority:	5		WOODCLIFF LAKE, NJ 07677
Approval Date:	29-SEP-2008	Brand Name:	ARGATROBAN INJECTION
JFA Date:	12-JUL-2011	Estab. Name:	
Approval Goal:		Generic Name:	ARGATROBAN INJECTION
Approval Goal:	11-JAN-2011	Product Number; Dosage Form; Ingredient; Strengths	001; INJECTABLE; ARGATROBAN; 1MG
<hr/>			
Key Contacts:	T. LAMBERT	Project Manager	301-796-4246
	X. CHEN	Review Chemist	301-796-1337
	J. BROWN	Team Leader	301-796-1652

Overall Recommendation: ACCEPTABLE on 27-JUN-2011 by D. SMITH ()
ACCEPTABLE on 21-OCT-2009 by JOHNSONE

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

File No: (b) (4) **AADA:**

Responsibilities: (b) (4)
(b) (4)

File: (b) (4) **OAI Status:** NONE

Next Milestone: OC RECOMMENDATION

Milestone Date: 25-JAN-2011

Decision: ACCEPTABLE

Final Decision: DISTRICT RECOMMENDATION

FDA OVERVIEW
**ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT**

Establishment: **CFN:** **FEI:** 3004081307
CIPLA LIMITED
L138-147 L150 S103-105 S107-112 M61-63
VERNA, SALCETTE, GOA, , INDIA

F No: **AADA:**

Responsibilities: DRUG SUBSTANCE RELEASE TESTER
DRUG SUBSTANCE STABILITY TESTER
FINISHED DOSAGE LABELER
FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER

File: STERILE-FILLED SMALL VOLUME PARENTERAL DRUGS **OAI Status:** NONE

Next Milestone: OC RECOMMENDATION

Next Milestone Date: 02-FEB-2011

Disposition: ACCEPTABLE

Disposition: DISTRICT RECOMMENDATION

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

F No: **AADA:**

Responsibilities: (b) (4)

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

Next Milestone: OC RECOMMENDATION

Next Milestone Date: 27-JUN-2011

Disposition: ACCEPTABLE

Disposition: DISTRICT RECOMMENDATION

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

F No: **AADA:**

Responsibilities: (b) (4)

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

Next Milestone: OC RECOMMENDATION

Next Milestone Date: 24-JAN-2011

Disposition: ACCEPTABLE

Disposition: BASED ON PROFILE

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

/s/

NIKOO N MANOCHEHRI-KALANTARI
07/06/2011