CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-058

CHEMISTRY REVIEW(S)

NDA 22-058

SUPPRELIN® LA
(histrelin acetate)
Subcutaneous Implant

Valera Pharmaceuticals Inc.

Elsbeth Chikhale, Ph.D.
ONDQA – DPA I – Branch II
for
Division of Metabolism and Endocrinology Products

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Chemistry Review Data Sheet

1. NDA 22-058

2. REVIEW #: 2 (with tracked labeling changes scanned)

3. REVIEW DATE: 17-APR-2007

4. REVIEWER: Elsbeth Chikhale, Ph.D.

5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	30-JUN-2006
Amendment to original[1]	15-SEP-2006
Amendment to original[2]	27-MAR-2007
Amendment to original[3]	12-APR-2007

1) The 9/15/06 amendment provides a response to the information request in the 74 day filing letter, dated 8/17/06, including updated stability data, specifications, and pharmaceutical development.
2) The 3/27/07 amendment provides a response to the information request dated 3/12/07.
3) The 4/12/07 amendment provides a response to the information request dated 4/9/07.

7. NAME & ADDRESS OF APPLICANT:

Name: Valera Pharmaceuticals Inc.

Address: 8 Clark Drive
Cranbury, NJ 08512

Representative: William B. Gray (Senior Director, Regulatory Affairs)

Telephone: (609) 235- 3206

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Supprelin® LA
b) Non-Proprietary Name (USAN): histrelin
c) Code Name/#:

d) Chem. Type/Submission Priority:

- Chem. Type: 5
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: This NDA is submitted as a 505(b)(1) application.

10. PHARMACOL. CATEGORY: developmental disorders

11. DOSAGE FORM: implant

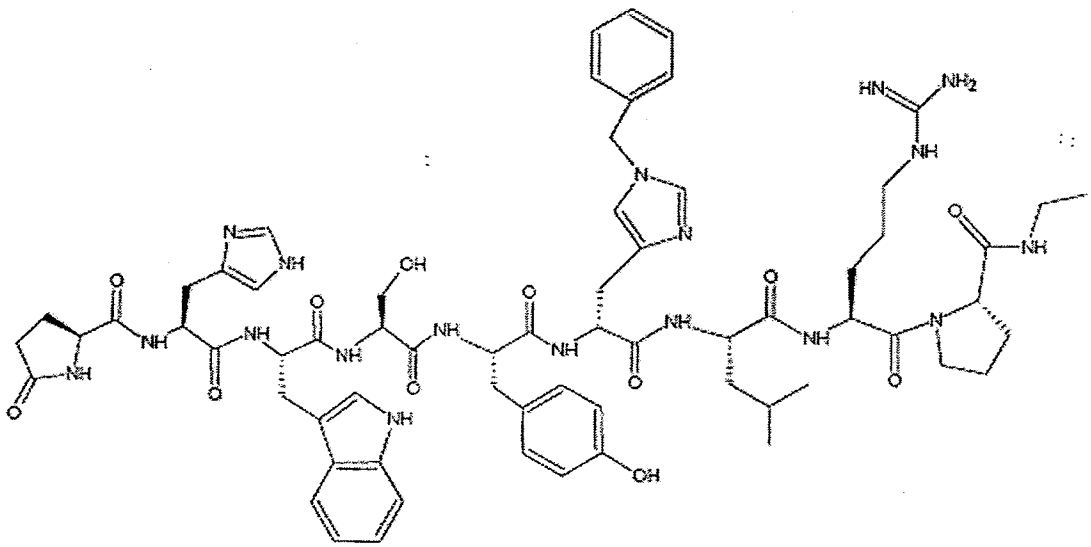
12. STRENGTH/POTENCY: 50 mg histrelin acetate/implant

13. ROUTE OF ADMINISTRATION: subcutaneous

14. Rx/OTC DISPENSED: _x_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product ___ Form Completed
__x__Not a SPOTS product

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



Chemical Names:
1. L-Pyroglutamyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-N-benzyl-Dhistidyl-L-leucyl-L-arginyl-L-proline N-ethylamide, acetate salt
2. Pyr-His-Trp-Ser-Tyr-D-His(Bzl)-Leu-Arg-Pro-NHEt, acetate salt

Molecular formula: $C_{66}H_{86}N_{18}O_{12}$ (free base)
$C_{66}H_{86}N_{18}O_{12} \cdot 2C_2H_4O_2$ (Histrelin Acetate)

Molecular mass: 1323.52 (base) + 120.2 (diacetate) = 1443.7 (Histrelin Acetate)

Chemical Abstracts Service (CAS) registry number: 76712-82-8

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE [1]	STATUS [2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]	II	[redacted]	Histrelin acetate	3	Adequate	August 9, 2004	Reviewed by Su Tran, Ph.D.

b(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 relevant 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)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	67,582	Histrelin subdermal implant
NDA	21-732	Vantas (histrelin subdermal implant)

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	3/22/07	
Pharm/Tox	N/A		
CDRH	Acceptable with some labeling comments	3/23/07	Gail Gantt
Clinical Pharmacology	N/A		
Methods Validation	Acceptable	3/16/07	Elsbeth Chikhale, Ph.D.
ODS/DMETS	Supprelin is acceptable, but the modifier "LA" is not recommended.	1/26/07	Loretta Holmes, PharmD.
EA	Satisfactory (consult not needed)	3/16/07	Elsbeth Chikhale, Ph.D.
Microbiology	Approval	3/27/07	John Metcalfe, Ph.D.

19. ORDER OF REVIEW: N/A

The Chemistry Review for NDA 22-058

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 22-058 is recommended for **Approval** from the standpoint of chemistry, manufacture and controls, **pending final labeling.**

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

None

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substance

1) **Drug Product**

The product is a drug-device combination product. For the purpose of this review, "drug product" refers to the implant (in the sodium chloride solution). (The insertion device tool will be reviewed by CDRH). The drug product, Suprelin® LA (histralin acetate) subcutaneous implant, is a polymeric non-biodegradable implant for subcutaneous administration. Each implant consists of 4 drug pellets containing a total of 50 mg histrelin acetate [redacted] inside a non-biodegradable, 35 mm x 3.1 mm, cylindrical hydrogel reservoir. The drug pellets also contain the inactive ingredient stearic acid NF. The hydrogel cartridge is composed of 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, trimethylolpropane trimethacrylate, benzoin methyl ether, Perkadox-16, and Triton X-100. The ratio of 2-hydroxyethyl methacrylate and 2-hydroxypropyl methacrylate in the crosslinked copolymer controls the release rate of drug from the implant. Each cartridge is [redacted] composed of 2-hydroxyethyl methacrylate, trimethylolpropane trimethacrylate, benzoin methyl ether, and Perkadox-16. The implant is stored in 2 mL of 1.8% sterile sodium chloride inside a 3.5 mL Type I clear glass vial with a teflon-coated stopper and an aluminum seal. The vial is packaged in an amber pouch in a carton. Supprelin® LA is supplied in a carton in a cooled box for the implant along with another carton for the implantation kit. The implantation kit contains: 1 # 11 disposable scalpel; 1 syringe with 18 ga. 1"needle; 1 25 Ga x 1.5" needle; 1 S/S mosquito clamp; 1 package betadine swabs; 2 alcohol prep pads; 1 fenestrated drape; 1 non-fenestrated drape; 1 sachet antiseptic ointment; 1

b(4)

b(4)

package gauze sponges; 1 package surgical closure strips; 1 vicryl sutures-coated; 1 package elastoplast; 1 vial Lidocaine HCL 1% w/epinephrine USP; [redacted] ; and 1 implant insertion device tool in sterile bag. b(4)
The drug product is sterilized by [redacted]. The hypertonic saline is necessary for storage in order to minimize drug elution from the hydrated implant during storage. The product is intended to be used for the treatment of central precocious puberty (CPP) in children. A very similar drug product made by the same manufacturer has already been approved (NDA 21-732 for Vantas (histralin subdermal implant)) for treatment of advanced prostate cancer. The only difference between Vantas and Supprelin® LA is that the new product releases drug at a higher rate than the Vantas product [redacted] b(4)
The formulation used in the phase 1/2 study and the pivotal clinical phase 3 study is identical to the proposed commercial formulation. The implant is intended to provide continuous release of histrelin acetate at a nominal rate of 65 micrograms per day over 12 months. However, the drug product specifications allow the *in vitro* elution rate to vary between [redacted] histrelin acetate per day, with a potential initial [redacted] histrelin acetate per day. The *in vitro* elution rate has been shown to be predictive of the *in vivo* release rate, although no formal *in vitro-in vivo* correlation (IVIVC) has been established. The proposed storage condition is at 2-8 °C, and the proposed expiry date is 24 months. The provided stability data support the proposed expiry date of 24 months.

2) **Drug Substance**
The drug substance histrelin acetate is a synthetic nonapeptide, an agonist of the naturally occurring ganadotropin releasing hormone (GnRH) or luteinising hormone releasing hormone (LHRH). The drug substance is derived from the natural decapeptide LHRH [redacted] b(4)
Reference is made to DMF [redacted] for information on the chemistry, manufacturing and controls of the drug substance. This DMF was found adequate on 09-AUG-2004 (Chem. Review #2 by Su Tran, Ph.D.) in support of NDA 21-732, and no updates have been submitted since that review. A Letter of Authorization to allow the Agency to review this DMF was provided.

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

The implant is inserted subcutaneously in the inner aspect of the upper arm, using the insertion tool packaged in the implantation kit together with the implant, and kept in the arm for a period of 12 months. After 12 months, the implant must be removed and another implant may be inserted to continue the therapy.

C. Basis for Approvability or Not-Approval Recommendation

The NDA is recommended for **Approval** from chemistry, manufacturing and controls (CMC) perspective, **pending final labeling**, because:

- The sponsor has satisfactorily replied to all CMC information requests dated 8/17/06, 3/12/07 and 4/9/07.
- The CMC information for the drug substance histrelin acetate is adequate.
- The CMC information for the drug product Supprelin® LA is adequate.
- The regulatory specifications for the drug substance are acceptable.
- The proposed in-process controls and regulatory drug product specifications are acceptable and assure a high quality drug product.
- NDA 22-058 is recommended for approval from a product quality microbiology perspective (see Product Quality Microbiology review dated 3/27/07).
- The CDRH review of the insertion (device) tool (AKA trocar) dated 3/23/07, has no deficiencies listed and only has two labeling comments. The insertion tool is identical to that approved for use with Valera's Vantas implant (NDA 21-732).
- The cGMP status of all manufacturing and control facilities is acceptable per EER dated 3/22/07.
- Submitted stability data support the proposed **24 month** drug product shelf life when stored in the refrigerator at 2-8 °C.

III. Administrative

A. Reviewer's Signature: in DFS

B. Endorsement Block: in DFS

C. cc Block: in DFS

21 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 2

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/s/

Elsbeth Chikhale
4/20/2007 11:09:15 AM
CHEMIST
resubmitted to DFS to show tracked labeling changes
resubmitted to DFS to show tracked labeling changes

Blair Fraser
4/20/2007 04:55:37 PM
CHEMIST

NDA 22-058

SUPPRELIN® LA
(histrelin acetate)
Subcutaneous Implant

Valera Pharmaceuticals Inc.

Elsbeth Chikhale, Ph.D.
ONDQA – DPA I – Branch II
for
Division of Metabolism and Endocrinology Products

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III. Administrative 9

A. Reviewer's Signature 9

B. Endorsement Block 9

C. CC Block 9

Chemistry Assessment **10**

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data 10

S DRUG SUBSTANCE [Histrelin Acetate, [redacted] 10

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b(4)

Chemistry Review Data Sheet

1. NDA 22-058

2. REVIEW #: 1

3. REVIEW DATE: 16-MAR-2007

4. REVIEWER: Elsbeth Chikhale, Ph.D.

5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	30-JUN-2006
Amendment to original[1]	15-SEP-2006

1) The 9/15/06 amendment provides a response to the information request in the 74 day filing letter, dated 8/17/06, including updated stability data, specifications, and pharmaceutical development.

7. NAME & ADDRESS OF APPLICANT:

Name: Valera Pharmaceuticals Inc.

Address: 8 Clark Drive
Cranbury, NJ 08512

Representative: William B. Gray (Senior Director, Regulatory Affairs)

Telephone: (609) 235- 3206

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Supprelin® LA
b) Non-Proprietary Name (USAN): histrelin
c) Code Name/#:
d) Chem. Type/Submission Priority:
- Chem. Type: 5
- Submission Priority: S

Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION: This NDA is submitted as a 505(b)(1) application.

10. PHARMACOL. CATEGORY: developmental disorders

11. DOSAGE FORM: implant

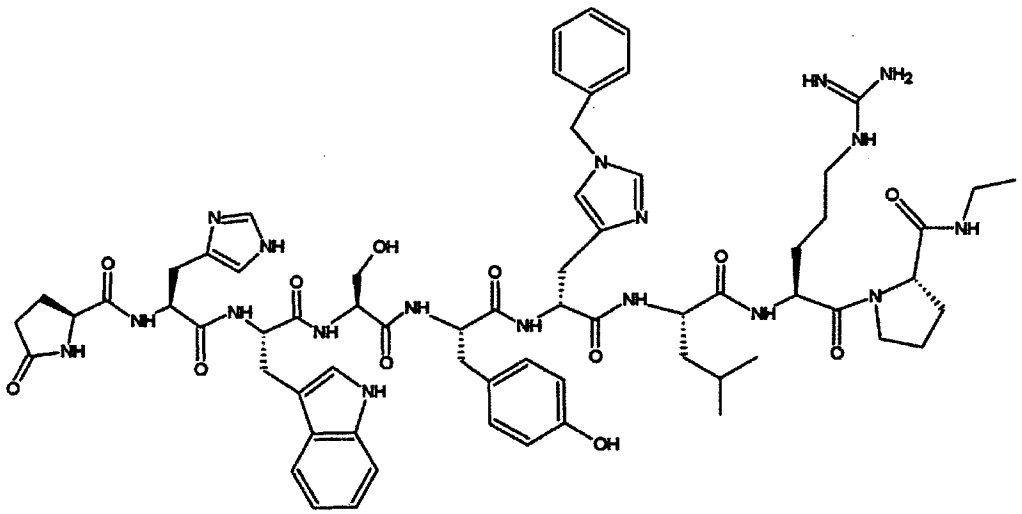
12. STRENGTH/POTENCY: 50 mg histrelin acetate/implant

13. ROUTE OF ADMINISTRATION: subcutaneous

14. Rx/OTC DISPENSED: _x_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
____SPOTS product ___ Form Completed
__x__Not a SPOTS product

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



Chemical Names:

1. L-Pyroglutamyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-N-benzyl-Dhistidyl-L-leucyl-L-arginyl-L-proline N-ethylamide, acetate salt
2. Pyr-His-Trp-Ser-Tyr-D-His(Bzl)-Leu-Arg-Pro-NHEt, acetate salt

Chemistry Review Data Sheet

Molecular formula: $C_{66}H_{86}N_{18}O_{12}$ (free base)
$C_{66}H_{86}N_{18}O_{12}\bullet 2C_2H_4O_2$ (Histrelin Acetate)

Molecular mass: 1323.52 (base) + 120.2 (diacetate) = 1443.7 (Histrelin Acetate)

Chemical Abstracts Service (CAS) registry number: 76712-82-8

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE [1]	STATUS [2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]	II	[redacted]	Histrelin acetate	3	Adequate	August 9, 2004	Reviewed by Su Tran, Ph.D.

b(4)

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
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3 – Reviewed previously and no relevant 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)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	67,582	Histrelin subdermal implant
NDA	21-732	Vantas (histrelin subdermal implant)

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	pending	pending	
Pharm/Tox	N/A		
CDRH	pending	pending	
Clinical Pharmacology	N/A		
Methods Validation	Acceptable	3/16/07	Elsbeth Chikhale, Ph.D.
ODS/DMETS	Supprelin is acceptable, **but the modifier "LA" is** not recommended.	1/26/07	Loretta Holmes, PharmD.
EA	Satisfactory (consult not needed)	3/16/07	Elsbeth Chikhale, Ph.D.
Microbiology	pending	pending	

19. ORDER OF REVIEW: N/A

The Chemistry Review for NDA 22-058

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The recommendation from the standpoint of chemistry, manufacture and controls is pending:
(1) a response to the information request to be forwarded to the applicant
(2) an overall cGMP recommendation from the Office of Compliance
(3) a recommendation from the Microbiology Staff
(4) a recommendation from CDRH
(5) final labeling

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

None

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substance

1) **Drug Product**

The product is a drug-device combination product. For the purpose of this review, "drug product" refers to the implant (in the sodium chloride solution). (The device will be reviewed by CDRH). The drug product, Suprelin® LA (histralin acetate) implant, is a polymeric non-biodegradable implant for subcutaneous administration. Each implant consists of 4 drug pellets containing a total of 50 mg histrelin acetate [redacted] inside a non-biodegradable, 35 mm x 3.1 mm, cylindrical hydrogel reservoir. The drug pellets also contains the inactive ingredient stearic acid NF. The hydrogel cartridge is composed of 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, trimethylolpropane trimethacrylate, benzoin methyl ether, Perkadox-16, and Triton X-100. The ratio of 2-hydroxyethyl methacrylate and 2-hydroxypropyl methacrylate in the crosslinked copolymer controls the release rate of drug from the implant. Each cartridge [redacted] composed of 2-hydroxyethyl methacrylate, trimethylolpropane trimethacrylate, benzoin methyl ether, and Perkadox-16. The implant is stored in 2 mL of 1.8% sterile sodium chloride inside a 3.5 mL Type I clear glass vial with a teflon-coated stopper and an aluminum seal. The vial is packaged in an amber pouch in a carton. Supprelin is

b(4)

supplied in a carton containing two cartons, one for the implant and one for the implantation kit. The implantation kit contains: 1 # 11 disposable scalpel; 1 **syringe with 18 ga. 1"needle; 1 25 Ga x 1.5" needle; 1 S/S mosquito clamp; 1** package betadine swabs; 2 alcohol prep pads; 1 fenestrated drape; 1 non-fenestrated drape; 1 sachet antiseptic ointment; 1 package gauze sponges; 1 package surgical closure strips; 1 vicryl sutures- coated; 1 package elastoplast; 1 vial Lidocaine HCL 1% w/epinephrine USP; [redacted] and 1 implant insertion tool in sterile bag. b(4)

The drug product is sterilized by [redacted] The hypertonic saline is necessary for storage in order to minimize drug elution from the hydrated implant during storage. The product is intended to be used for the treatment of central precocious puberty (CPP) in children. A very similar drug product made by the same manufacturer has already been approved (NDA 21-732 for Vantas (histralin subdermal implant)) for treatment of advanced prostate cancer. The only difference between Vantas and Supprelin® LA is that the new product releases drug at a higher rate than the Vantas product [redacted] The formulation used in the phase 1/2 study and the pivotal clinical phase 3 study is identical to the proposed commercial formulation. The implant is intended to provide continuous release of histrelin acetate at a nominal rate of 65 micrograms per day over 12 months. However, the drug product specifications allow the *in vitro* elution rate to vary between [redacted] histrelin acetate per day, with a potential initial [redacted] **histrelin acetate per day. The** *in vitro* elution rate has been shown to be predictive of the *in vivo* release rate, although no formal IVIVC has been established. The proposed storage condition is at 2-8 °C, and the proposed expiry date is 24 months. The adequacy of the proposed expiry date will be determined in CMC review #2, after review of updated stability data. b(4)

2) **Drug Substance**

The drug substance histrelin acetate is a synthetic nonapeptide, an agonist of the naturally occurring ganadotropin releasing hormone (GnRH) or luteinising hormone releasing hormone (LHRH). The drug substance is derived from the natural decapeptide LHRH [redacted] Reference is made to DMF [redacted] for information on the chemistry, manufacturing and controls of the drug substance. This DMF was found adequate on 09-AUG-2004 (Chem. Review #2 by Su Tran, Ph.D.) in support of NDA 21-732, and no updates have been submitted since that review. A Letter of Authorization to allow the Agency to review this DMF was provided. b(4)

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

The implant is inserted subcutaneously in the inner aspect of the upper arm, using the insertion device packaged in the implantation kit together with the implant, and kept in the arm for a period of 12 months. After 12 months, the implant must be removed and another implant may be inserted to continue the therapy

C. Basis for Approvability or Not-Approval Recommendation

The recommendation from the standpoint of chemistry, manufacture and controls is pending:

(1) a response to the information request to be forwarded to the applicant.
(2) an overall cGMP recommendation from the Office of Compliance
(3) a recommendation from the Microbiology Staff
(4) a recommendation from CDRH
(5) final labeling

III. Administrative

A. Reviewer's Signature: in DFS

B. Endorsement Block: in DFS

C. cc Block: in DFS

53 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 1

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/s/

Elsbeth Chikhale
3/16/2007 04:49:03 PM
CHEMIST

Blair Fraser
3/16/2007 05:00:55 PM
CHEMIST

NDA 22-058

Supprelin® LA
(histrelin acetate)
Subcutaneous Implant

Summary of the Basis for the Recommended Action from Chemistry, Manufacturing, and Controls

Applicant: Valera Pharmaceuticals Inc.
8 Clark Drive,
Cranbury, NJ 08512

Indication: Treatment of central precocious puberty (CPP).

Presentation: Supprelin® LA (histrelin acetate) subcutaneous implant is available as an implant for subcutaneous implantation containing 50 mg histrelin acetate.

Supprelin® LA is supplied in a box enclosing 2 inner cartons, one containing the Supprelin LA implant and one containing the implantation kit for use with the implant.

The Supprelin® LA implant carton contains a cold pack for refrigerated shipment and a small box containing an amber plastic pouch. Inside the pouch is a glass vial, sealed with a Teflon-coated stopper and an aluminum seal, containing the implant immersed in 2 mL of 1.8% sterile sodium chloride.

EER Status: Acceptable 3-MAR-2007

Consults:

Clinical Pharmacology:	Pending
EA – Categorical exclusion:	Granted 16-MAR-2007
Methods Validation:	Acceptable 16-MAR-2007
CDRH:	Acceptable 23-MAR-2007
Microbiology:	Acceptable 27-MAR-2007

Original Submission: 30-JUN-2006

Post-Approval Agreements:

In the amendment of 15-SEP-2006, the applicant agreed to and provided:

- A stability protocol for the commitment batches.
- A stability protocol for the continuing batches (minimum of one batch annually).
- An updated stability testing and acceptance criteria protocol for the commitment and continuing batches.

contains the inactive ingredient stearic acid NF. The hydrogel reservoir is a cartridge composed of 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, trimethylolpropane trimethacrylate, benzoin methyl ether, Perkadox-16, and Triton X-100. Each hydrated implant is packaged in a glass vial containing 2.0 mL of 1.8% sodium chloride, sterile solution, so that it is primed for immediate release of the drug upon insertion.

A very similar drug product, made by the same manufacturer, has already been approved (NDA 21-732 for Vantas (histrelin subdermal implant)) for treatment of advanced prostate cancer. The only difference between Vantas and Supprelin® LA is that the new product releases drug at a higher rate than the Vantas product [redacted]. The ratio of 2-hydroxyethyl methacrylate and 2-hydroxypropyl methacrylate in the crosslinked copolymer controls the release rate of drug from the implant. The Supprelin® LA implant is intended to provide continuous release of histrelin acetate at a nominal rate of 65 micrograms per day over 12 months. b(4)

Specifications for the drug product include: appearance, identification by FTIR and HPLC, assay, impurities, content uniformity, sterility, elution rate, and microbial limits. All tests methods have been appropriately validated for their intended purpose.

Submitted stability data support the proposed expiration dating of 24 months at 2-8 °C (refrigerated) for the drug product protected from light.

Conclusion: Drug product is satisfactory.

Additional Items:

All associated Drug Master Files (DMFs) are adequate or the pertinent information has been adequately provided in the application.

Overall Conclusion:

From a CMC perspective, the application is recommended for **Approval**, pending agreement on product labeling.

Blair Fraser, Ph.D.
Division Director
DPA I/ONDQA

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/s/

Blair Fraser
4/18/2007 03:04:39 PM
CHEMIST

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Application:	NDA 22058/000	Action Goal:	
Stamp:	03-JUL-2006	District Goal:	04-MAR-2007
Regulatory Due:	03-MAY-2007	Brand Name:	SUPPRELIN LA 50MG
Applicant:	VALERA PHARMACEUTICALS	Estab. Name:	
	NO CITY, , XX	Generic Name:	HISTRELIN ACETATE SUBCUTANEOUS IMPL
NT			
Priority:	510	Dosage Form:	(DRUG DELIVERY SY
TEM)			
Org Code:		Strength:	50 MG

Application Comment: ORPHAN DRUG DESIGNATION GRANTED ON 18-NOV-2006.
NON-DEGRADABLE IMPLANT (RESERVOIR. (on 19-JUL-2006 by S.
TRAN ()
301-796-1764)

FDA Contacts:	J. JOHNSON	301-796-2194	, Project
anager			
	E. CHIKHALE	301-796-1659	, Review C
emist			
	S. TRAN	301-796-1764	, Team Lea
er			

Overall Recommendation: ACCEPTABLE on 22-MAR-2007by S. FERGUSON(HFD-322)30
-827-9009

Establishment: [redacted] FEI [redacted]

[redacted] b(4)

DMF No: AADA:

Responsibilities: [redacted] [redacted]

Profile: CTX OAI Status: NONE

Estab. Comment: [redacted] b(4)
by S.

TRAN () 301-796-1764)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	C
eator					
SUBMITTED TO OC TRANS	19-JUL-2006				
SUBMITTED TO DO BROGIOJ	19-JUL-2006	GMP			DA
DO RECOMMENDATION RPENTA	24-AUG-2006			ACCEPTABLE	
				INSPECTION	
EI 8/16/06 OF TEAM	[redacted]	[redacted]		IS NAI AND COVERED 76 755/004 AND 76 722/0	
BIO EI OF 6/2/06 COVERED MFGR PORTION OF FACILITY AND A FDA483 WAS ISSUED. b(4)					
OC RECOMMENDATION BROGIOJ	27-AUG-2006			ACCEPTABLE	DA
				DISTRICT RECOMMENDATION	

Establishment: [redacted] FEI [redacted]

[redacted] b(4)

DMF No: [redacted] AADA:

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Responsibilities: [redacted] b(4)

Profile: CSN OAI Status: NONE

EMilestone Name eator	Date	Type	Insp. Date	Decision & Reason	C
SUBMITTED TO OC TRANS	19-JUL-2006				
OC RECOMMENDATION ADAMSS	20-JUL-2006			ACCEPTABLE BASED ON PROFILE	

Establishment: [redacted] FEI [redacted] b(4)

DMF No: AADA:

Responsibilities: [redacted]

Profile: CTL OAI Status: NONE

Estab. Comment: [redacted]

Milestone Name eator	Date	Type	Insp. Date	Decision & Reason	C
SUBMITTED TO OC ANS	19-JUL-2006				
SUBMITTED TO DO BROGIOJ	19-JUL-2006	GMP			DA
ASSIGNED INSPECTION T JARRELL	10-OCT-2006	PS			

INSPECTION PERFORMED 23-FEB-2007 23-FEB-2007
JARRELL

[redacted]

:ECOMMENDATION 20-MAR-2007 ACCEPTABLE
J. ELL

INSPECTION

INSPECTION CONDUCTED 2/21-23/07.

OC RECOMMENDATION 22-MAR-2007 ACCEPTABLE F
RGUSONS

DISTRICT RECOMMENDATION

Establishment: FEI [redacted]

[redacted]

D No: AADA: b(4)

Re.ponsibilities: [redacted]

Profile: NEC OAI Status: NONE

Estab. Comment: [redacted]
-796-

1764)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	C
eator					

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

SUBMITTED TO OC TRANS	19-JUL-2006				
SUBMITTED TO DO BROGIOJ	19-JUL-2006	GMP			DA
ASSIGNED INSPECTION T MARTIN1	03-AUG-2006	PS			
INSPECTION PERFORMED MARTIN1	24-JAN-2007		24-JAN-2007.		
DO RECOMMENDATION MARTIN1	26-JAN-2007			ACCEPTABLE INSPECTION	
OC RECOMMENDATION BROGIOJ	29-JAN-2007			ACCEPTABLE DISTRICT RECOMMENDATION	DA

Establishment: CFN [redacted] FEI [redacted]

[redacted] b(4)

DMF No: AADA:

Responsibilities: [redacted]

Profile: SSP OAI Status: NONE

Milestone Name	Date	Type	Insp. Date	Decision & Reason	C
SUBMITTED TO OC TRANS	19-JUL-2006				
SUBMITTED TO DO BROGIOJ	19-JUL-2006	10D			DA

DO RECOMMENDATION 20-JUL-2006 ACCEPTABLE
SPATARO

BASED ON FILE REVIEW

INSPECTED 5/18/06, ALL PROFILES ACCEPTABLE, INSPECTION VAI

RECOMMENDATION 21-JUL-2006 ACCEPTABLE F
R. ONS

DISTRICT RECOMMENDATION

Establishment: [redacted] FEI [redacted]

[redacted]

b(4)

DMF No: [redacted] AADA:

Responsibilities: [redacted]

Profile: CTL OAI Status: NONE

Estab. Comment:
S. TRAN

() 301-796-1764)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	C
SUBMITTED TO OC TRANS	19-JUL-2006				
SUBMITTED TO DO ADAMSS	20-JUL-2006	GMP			
DO RECOMMENDATION ADAMSS	26-JUL-2006			ACCEPTABLE	

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

BASED ON FILE REVIEW

OC RECOMMENDATION 26-JUL-2006 ACCEPTABLE
ADAMSS

DISTRICT RECOMMENDATION

Establishment: [redacted] FEI [redacted]

b(4)

DMF No: AADA:

Responsibilities: [redacted]

Profile: NEC OAI Status: NONE

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	19-JUL-2006				TRANS
SUBMITTED TO DO	19-JUL-2006	10D			DA BROGIOJ
ASSIGNED INSPECTION T	14-AUG-2006	PS			NROLLI
INSPECTION PERFORMED	29-AUG-2006				J [illegible]ENA

AUTOMATIC WITHHOLD STATUS ISSUED BY FACTS, DUE TO FIRM BEING OUT OF BUSINESS OR M RGED

DO RECOMMENDATION 12-SEP-2006 ACCEPTABLE

KOZLOWS

INSPECTION

INSPECTION CONDUCTED 8/24/06, CLASSIFIED NAI.

ECOMMENDATION 12-SEP-2006 ACCEPTABLE DA
B OJ

DISTRICT RECOMMENDATION
