

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-481

CHEMISTRY REVIEW(S)

NDA #21-481

**Fuzeon™
(enfuvirtide)
for Injection**

Hoffmann-La Roche Inc.

**Rao Kambhampati, Ph.D.
Division of Antiviral Drug Products
HFD-530**

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Chemistry Review Data Sheet

1. NDA# **21-481**
2. REVIEW #: 1
3. REVIEW DATE: 03/12/2003
4. REVIEWER: Rao Kambhampati, Ph.D.
5. PREVIOUS DOCUMENTS: N/A
6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Rolling NDA Pre-Submission (RRC 001)	26/Jun/2002
Rolling NDA Pre-Submission (RRC 002)	26/Jun/2002
Rolling NDA Pre-Submission (RRZ 007)	13/Aug/2002
Rolling NDA Pre-Submission (RRZ 009)	10/Sep/2002
Original (Rolling NDA Final Submission)	13/Sep/2002
Amendment (BC)	27/Sep/2002
Amendment (BC)	07/Oct/2002
Amendment (BL)	31/Oct/2002
Amendment (BC)	19/Dec/2002
Amendment (BC)	22/Jan/2003
Amendment (BC)	27/Feb/2003
Amendment (BZ)	07/March/2003

7. NAME & ADDRESS OF APPLICANT:

Name:	Hoffmann-La Roche Inc.
Address:	340 Kingsland Street Nutley, NJ 07110
Representative:	Robin L. Conrod Group Director, Regulatory Affairs
Telephone:	973-562-3676



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Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Fuzeon™ for Injection
- b) Non-Proprietary Name (USAN): Enfuvirtide for Injection
- c) Code Name/#: Ro 29-9800-J01; RO0299800-J01; T-20; and _____
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type: 1
 - Submission Priority: P and Fast-Track

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL CATEGORY: Antiviral (blockade of gp-41 mediated membrane fusion; fusion Inhibitor)

11. DOSAGE FORM: Lyophilized solid for injection

12. STRENGTH/POTENCY: 90 mg/vial (each vial contains 108 mg of enfuvirtide for the delivery of 90 mg)

13. ROUTE OF ADMINISTRATION: Subcutaneous injection

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 Name: *N*-Acetyl-L-tyrosyl-L-threonyl-L-seryl-L-leucyl-L-isoleucyl-L-histidyl-L-seryl-L-leucyl-L-isoleucyl-L- α -glutamyl-L- α -glutamyl-L-seryl-L-glutamyl-L-asparaginyl-L-glutamyl-L-glutamyl-L- α -glutamyl-L-lysyl-L-asparaginyl-L- α -glutamyl-L-glutamyl-L- α -glutamyl-L-leucyl-L-leucyl-L- α -glutamyl-L-leucyl-L- α -aspartyl-L-lysyl-L-tryptophyl-L-alanyl-L-seryl-L-leucyl-L-tryptophyl-L-asparaginyl-L-tryptophyl-L-phenylalaninamide

CAS Reg. No.: 159519-65-0

Molecular Formula: C₂₀₄H₃₀₁N₅₁O₆₄

Molecular Weight: 4491.97

Chirality: Composed of naturally occurring L-amino acid residues

Sequence: CH₃CO-TyrThrSerLeulleHisSerLeulleGluGluSerGlnAsnGlnGlnGluLysAsnGluGln

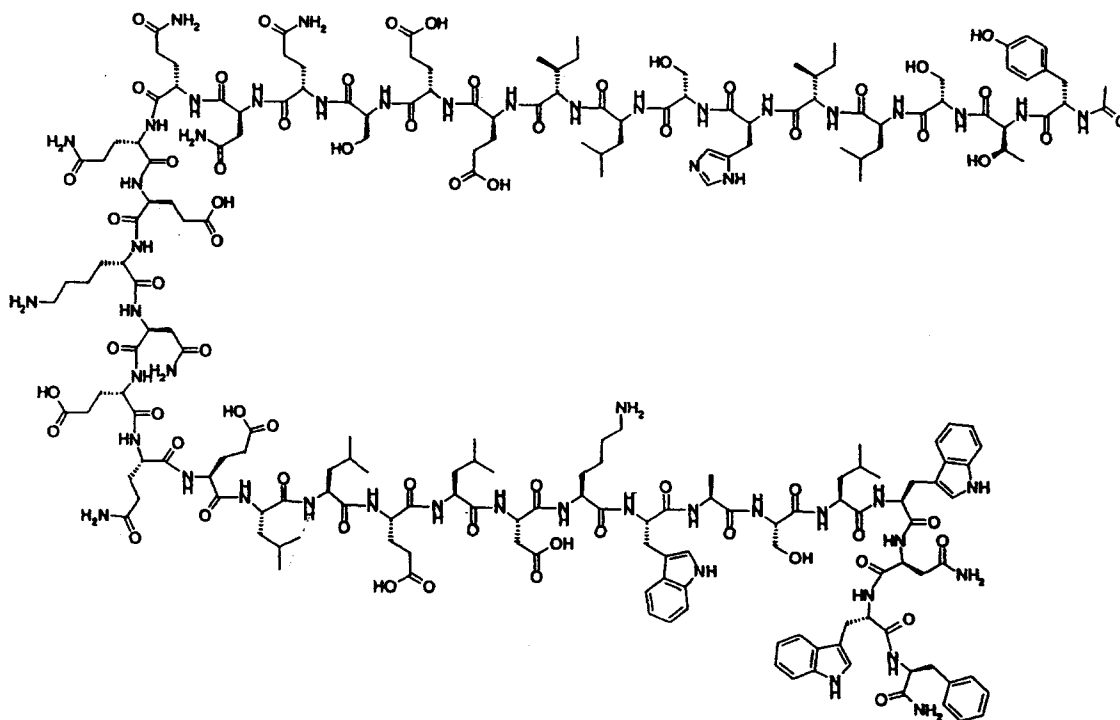
GluLeuLeuGluLeuAspLysTrpAlaSerLeuTrpAsnTrpPheNH₂

or

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CH3CO-YTSLIHSLEESQNQQEKNEQELLELDKWASLWNWF-NH₂

Structural Formula:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF or 510(K) Letter#	TYPE	HOLDER	ITEM REFERENCED	COD E ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
<div style="border: 1px solid black; width: 100%; height: 100%;"></div>					Not Applicable	Not Applicable	None
					Not Applicable	Not Applicable	None
					Not Applicable	Not Applicable	None
					Acceptable	2/27/03	Reviewed by James McVey, Ph.D. (HFD-805)
					Approved	11/08/01	Reviewed by



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			CDRH
	Approved	5/29/97	Reviewed by CDRH
	Approved	2/12/98	Reviewed by CDRH
	Approved	1/13/01	Reviewed by CDRH
	Approved	12/12/94	Reviewed by CDRH

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)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	—	[]

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EER	Acceptable	2/12/03	J.D Ambrogio (HFD-324), OC
Trademark Review	Acceptable	2/14/03	Kevin Dermanoski, R.Ph., Safety Evaluator, DMETS (HFD-420), ODS
EA	Acceptable based on categorical exclusion	3/3/03	Rao Kambhampati, Ph.D. (HFD-530)
Sterilization Process and Validation	Acceptable	03/12/03	James McVey, Ph.D., Microbiologist (HFD-805)
Methods Validation	Pending	3/7/03	Div. of Pharm. Analysis (St Louis) and Philadelphia D.O.
Organic Impurities/Degradation Products	Acceptable	1/27/03	William Taylor, Ph.D., Pharmacology Reviewer (HFD-530)

113 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.