

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-333

ADMINISTRATIVE DOCUMENTS

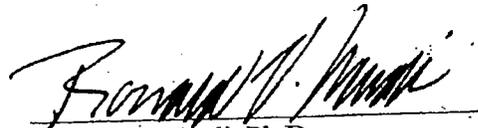
Ferring Pharmaceuticals Inc.
Minirin™ Nasal Spray

Confidential

NDA #21-333
10/27/00

14.0 A PATENT CERTIFICATION WITH RESPECT TO ANY PATENT WHICH CLAIMS THE DRUG

In the opinion and to the best knowledge of Ferring Pharmaceuticals Inc., there are no patents, except patents listed in the orange book for NDA #17-922 or owned by Ferring Pharmaceuticals to which we have right of reference, that claim the drug or drugs on which investigations that are relied upon in this application were conducted, or that claim the use of such drug or drugs.



Ronald V. Nardi, Ph.D.
Vice-President
Scientific and Regulatory Affairs

EXCLUSIVITY SUMMARY for NDA # 21-333 SUPPL # _____
Trade Name Desmopressin Acetate Nasal Spray 0.1 mg/mL
Generic Name _____
Applicant Name Ferring Pharmaceuticals Inc.
HFD- 510
Approval Date _____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

a) Is it an original NDA? YES / / NO / /

b) Is it an effectiveness supplement? YES / / NO / /

If yes, what type (SE1, SE2, etc.)? _____

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

YES / / NO / /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /___/ NO /_x_/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_x_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /_x_/ NO /___/

NDA # 17-922_Drug Name DDAVP Nasal Spray (desmopressin acetate) Nasal Solution_____

Note that NDA 21-333 is a refrigerated form of the Adventis product (NDA 17-922

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____

NDA # _____

NDA # _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____

NDA # _____

NDA # _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the

investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

- (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:

- (b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

- (1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES / ___ / NO / ___ /

If yes, explain: _____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

(c) If the answers to (b) (1) and (b) (2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

- (b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

- (c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
!
IND # _____ YES /___/ ! NO /___/ Explain: _____
!
!
!
!
!

Investigation #2 !
!
IND # _____ YES /___/ ! NO /___/ Explain: _____
!
!
!
!
!

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !
!
YES /___/ Explain _____ ! NO /___/ Explain _____
!
!
!
!
!

Investigation #2 !
!
YES /___/ Explain _____ ! NO /___/ Explain _____
!
!

_____ !
_____ !
_____ !
_____ !

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

Signature of Preparer
Title: _____

Date

Signature of Office or Division Director

Date

cc:
Archival NDA
HFD- /Division File

HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

FDA Links Searches Check Lists Tracking Links Calendars Reports Help

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)

View as Word Document

NDA Number: 021333 Trade Name: DESMOPRESSIN ACETATE NASAL SPRAY
 Supplement Number: 000 Generic Name: DESMOPRESSIN ACETATE
 Supplement Type: N Dosage Form:
 Regulatory Action: OP COMIS Indication: PRIMARY NOCTURNAL ENURESIS/CENTRAL CRANIAL DIABETES INSPIDUS.
 Action Date: 11/3/00

Indication # 1 management of primary nocturnal enuresis, management of central cranial diabetes and for the management of temporary polyuria and polydypsia

Label Adequacy: Adequate for SOME pediatric age groups

Formulation Needed: Other

Comments (if any): A new refrigerated formulation of desmopressin acetate. For Specific recommendations, see below.

Ranges for This Indication

<u>Lower Range</u>	<u>Upper Range</u>	<u>Status</u>	<u>Date</u>
0 years	6 years	Waived	9/3/01

Comments: Pediatric study requirements for primary enuresis in children under 6 should be waived for the treatment of primary enuresis since it is difficult to diagnose in children below the age of 6.

0 months	3 months	Deferred
----------	----------	----------

Comments: Pediatric study requirements for central diabetes insipidus patients younger than three months should be deferred. The number of patients younger than 3 months make it difficult to conduct an adequate and well controlled study. The sponsor will be requested to evaluate whether data from published literature are available and sufficient for this population.

This page was last edited on 8/16/01

Stephan M. Gust

Signature

8/16/01

Date

16.0 DEBARMENT CERTIFICATION

Ferring Pharmaceuticals Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.

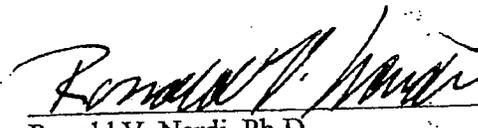


Ronald V. Nardi, Ph.D.
Vice-President
Scientific and Regulatory Affairs

19.0 FINANCIAL INFORMATION

The application cross-references the approved NDA #17-922 for all drug product information (see item 3 for copy of letter of reference) and no additional clinical studies are submitted in support of this application.

Ferring Pharmaceuticals Inc. hereby certifies that it did not enter into any financial arrangements with clinical investigators or perform any clinical studies in support of this application



Ronald V. Nardi, Ph.D.
Vice-President
Scientific and Regulatory Affairs

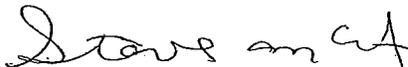
MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: August 21, 2001
TO: File for NDA 21-333
FROM: Steve McCort
SUBJECT: **Financial Disclosure for NDA**
NDA 21-333, Desmopressin Acetate Nasal Spray, 100 mcg/mL

In Dr. Mary Park's medical review, dated July 17, 2001, page 2, the following comment/recommendation was made regarding the necessity for financial disclosure information for this application:

No financial disclosure information is required since no clinical studies were conducted under this NDA.



Steve McCort, Project Manager, DMEDP

**DIVISION OF METABOLIC AND ENDOCRINE DRUG PRODUCTS
CONSUMER SAFETY OFFICER LABEL REVIEW 3**

Application Number: 21-333

Name of Drug: Desmopressin Acetate Nasal Spray

Sponsor: Ferring Pharmaceuticals

Material Reviewed:

Submission Dates: July 14, 2002
July 18, 2002

Receipt Dates: July 16, 2002
July 22, 2002

Background and Summary

The sponsor has submitted revised labeling response to the Agency's Approvable letter dated August 29, 2001. The application with draft labeling (package insert, patient package insert, carton and vial labels) was found approvable pending the deletion of the phrase "nasal spray" from the second sentence of the **Pharmacokinetics** subsection of the **CLINICAL PHARMACOLOGY** section of the package insert.

Review

The submitted labeling dated July 14, 2002 (ID # 48XXFEX, no rev date) was compared with the draft labeling dated August 13, 2001 (package insert, patient package insert, vial and carton labeling). The following difference was noted:

The identical labeling dated July 18, 2002, was submitted as an electronic file and is identical to the July 14, 2002, paper submission.

The phrase "nasal spray" has been deleted from the second sentence of the **Pharmacokinetics** subsection of the **CLINICAL PHARMACOLOGY** section of the package insert.

There is a spelling error in the PPI. IN the last sentence of the section "What is Desmopressin Acetate?", the word "note" should be changed to "nose".

Conclusions

The sponsor has revised the labeling for the package insert in response to the Agency's approvable letter requesting such change. The labeling submitted in the July 14, 2002 and July 18, 2002, electronic version (revised package insert as well as the August 13, 2001 (patient package insert, vial and carton labeling) submission is approvable. The spelling error will be corrected in the electronic version of the labeling that will be attached to the approval letter. The firm will be notified by phone rather than as a minor revision in the approval letter. An approval letter for NDA 21-333 should be drafted.

¶

Package Insert: Identifier (48XXFEX) Date: None
Patient Package Insert: Identifier (48XXFEX)
Vial label: Identifier (47XXFE2X)
Carton Label: Identifier (46XXFEX)

Stephen McCort
Regulatory Project Manager, HFD-510

Supervisory Comment/Concurrence:

Enid Galliers
Chief, Project Management Staff

Drafted: smm/August 14, 2002
Revised: /smm/September 9, 2002
Intialed: E Galliers 9.05.02/9.11.02
Finalized:smm/September 12, 2002
Filename: n21333lab3.doc

CSO LABELING REVIEW

15 Page(s) Withheld

 § 552(b)(4) Trade Secret / Confidential

 4 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

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this page is the manifestation of the electronic signature.**

/s/

Stephen McCort
9/12/02 09:49:57 AM
CSO

Enid Galliers
9/12/02 08:07:28 PM
CSO

Desmopressin Acetate Nasal Spray is a refrigerated formulation that
duplicates a room-temp product marketed by Aventis Behring.
The drug is used for primary nocturnal enuresis
and the management of central cranial diabetes insipidus.

ORIGINAL

FERRING

PHARMACEUTICALS

July 18, 2002

N 000 BL

ORIG AMENDMENT

David G. Orloff, M.D.
Director, Division of Metabolism and Endocrine Drug Products, HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RECEIVED

JUL 22 2002

HFD-510 / CDER

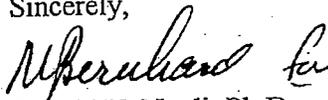
Re: NDA № 21-333, Desmopressin Acetate Nasal Spray
Final Draft Labeling: Electronic Files

Dear Dr. Orloff:

On July 14, 2002 we submitted printed draft labeling, including the correction requested in your approvable letter of August 29, 2001. In this amendment we submit the electronic files for this labeling in both Word and PDF format.

We appreciate your prompt review of this material and we look forward to approval in the near future. If you have any questions please do not hesitate to call me at (914) 333-8328 or Dr. Michael Bernhard at (914) 333-8958.

Sincerely,



Ronald V. Nardi, Ph.D.
Executive Vice President and Chief Scientific Officer

ORIGINAL **FERRING**
 PHARMACEUTICALS

July 14, 2002

Noted
See Memo
dated on 6/20/02
elli 7/18/02

RECEIVED

JUL 16 2002

HFD-510/CDER

David G. Orloff, M.D., Director
 Center for Drug Evaluation and Research
 Division of Metabolism and Endocrine Drug Products (HFD-510)
 Document Control Room, 14B-19
 Food and Drug Administration
 5600 Fishers Lane
 Rockville, MD 20857

NOV AZ

ORIG AMENDMENT

Re: NDA #21-333 Desmopressin Acetate Nasal Spray
 Final Draft Labeling

Dear Dr. Orloff:

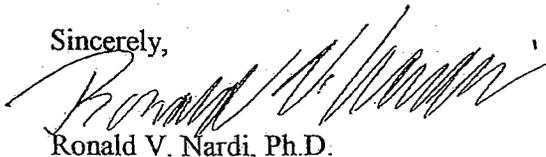
Per your letter of August 29, 2001, this application was found approvable pending satisfactory facility inspections and deletion of the phrase "nasal spray" from the second sentence of the **Pharmacokinetics** subsection of the **CLINICAL PHARMACOLOGY** section of the package insert.

On June 20, 2002 we were notified that our manufacturing facility is satisfactory and the Compliance Branch recommends approval of pending new drug applications listing this facility (please see enclosed letter from LuAnn M. Pallas, Compliance Officer).

In this amendment we submit the above noted labeling change. We certify that a copy of this supplement has been sent to the New York FDA field office.

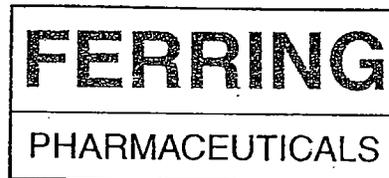
We appreciate your prompt approval of this NDA. If you have any questions please do not hesitate to call me at (914) 333-8932 or Dr. Michael Bernhard at (914) 333-8958.

Sincerely,



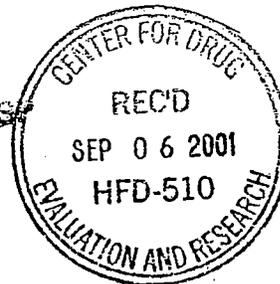
Ronald V. Nardi, Ph.D.
 Executive Vice President and Chief Scientific Officer

ORIGINAL



September 5, 2001

N-00-C
NEW CORRESP



David G. Orloff, M.D., Director
Center for Drug Evaluation and Research
Division of Metabolism and Endocrine Drug products (HFD-510)
Document Control Room, 14B-19
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: NDA #21-333 Desmopressin Acetate Nasal Spray

Dear Dr. Orloff:

This letter is to notify you of our intent to amend the above referenced NDA in response to the "approvable" letter received August 29, 2001.

The manufacturing facilities issues will be addressed through the inspections and compliance functions at the FDA and the required labeling amendment will be submitted once the manufacturing facilities issues have been resolved.

If you need any other information, please feel free to contact me at 914-333-8929 or by fax 914-631-5120.

Sincerely,

Martin Hedenfalk
Regulatory Affairs

08-14-01 FIELD OFFICE CERTIFICATION

1.0 INDEX

2.0 LABELING

Amendment 1

8/10/01

**Division of Metabolic and Endocrine Drug Products
CONSUMER SAFETY OFFICER
LABELING REVIEW 2**

Application Number: 21-333

Name of Drug: Desmopressin Acetate Nasal Spray, 0.1 mg/mL

Sponsor: Ferring Pharmaceuticals Incorporated

Material Reviewed:

Submission Date: August 13, 2001

Receipt Date: August 14, 2001

Background and Summary

In this submission the sponsor has provided proposed labeling in response to the FAX communications dated July 24 and August 9, 2001, and the telephone conversation with Dr. Chien-Hua Niu. This submission incorporated all the changes requested in these communications.

Review

The labeling with submission dated, August 13, 2001, was compared with the July 3, 2001, draft labeling and the following changes were noted:

1. In the **DESCRIPTION** section, "nasal spray" was removed from the name "desmopressin acetate nasal spray."
2. Under **CLINICAL PHARMACOLOGY**, the following section has been revised to read:

CLINICAL PHARMACOLOGY

Desmopressin acetate nasal spray contains as active substance 1-(3-mercaptopropionic acid)-8-D-arginine vasopressin, which is a synthetic analogue of the natural hormone arginine vasopressin. One mL (0.1 mg) of intranasal desmopressin acetate nasal spray has an antidiuretic activity of about 400 IU; 10 µg of desmopressin acetate is equivalent to 40 IU.

The change in structure of arginine vasopressin to desmopressin acetate has resulted in a decreased vasopressor action and decreased actions on visceral smooth muscle relative to the enhanced antidiuretic activity, so that clinically effective antidiuretic doses are usually below threshold levels for effects on vascular or visceral smooth muscle.

3 Page(s) Withheld

 § 552(b)(4) Trade Secret / Confidential

 4 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

Withheld Track Number: Administrative-

CONCLUSIONS:

The labeling dated August 13, 2001, was compared with the draft labeling dated July 3, 2001. The August 13, 2001, incorporated all the labeling changes requested by FDA. However, the following change should be requested:

On August 13, 2001, Dr. Johnson reviewed the revised CLINICAL PHARMACOLOGY section and found it acceptable with one change. The phrase "nasal spray" should be deleted from the second sentence of the Pharmacokinetics subsection. The sentence describes the active moiety, not the final dosage form.

REGULATORY RECOMMENDATIONS:

Pending the agreement of the applicant for changes described above, the draft labeling is acceptable.

Steve McCort
Project Manager, HFD-510

Supervisory Comment/Concurrence:

Enid Galliers
Chief, Project Management Staff, HFD-510

Drafted: Smm/August 14, and August 21, and August 27, 2001

Final: smm/August 28, 2001

Intialed by E Galliers 8/24 and 8-28/01

Filename: n21333la2.doc

Cc:

HFD-510:/NDA 21-333

HFD-510/DivFile

HFD-510/S McCort/E Galliers

CSO LABELING REVIEW 2

42 Page(s) Withheld

 § 552(b)(4) Trade Secret / Confidential

 6 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

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

/s/

Stephen McCort
8/28/01 04:05:07 PM
CSO

Enid Galliers
8/28/01 05:01:56 PM
CSO

9

8/20/01

**Division of Metabolic and Endocrine Drug Products
CONSUMER SAFETY OFFICER
LABELING REVIEW #1**

Application Number: 21-333

Name of Drug: Desmopressin Acetate Nasal Spray, 0.1 mg/mL

Sponsor: Ferring Pharmaceuticals Incorporated

Material Reviewed:

Submission Date: July 3, 2001

Receipt Date: July 5, 2001

Background and Summary

On October 27, 2000, Ferring submitted a new drug application (NDA) for a refrigerated formulation of desmopressin acetate nasal spray. Currently Ferring is approved to manufacture the identical refrigerated product under NDA 17-922 which is owned by Aventis. At this time Aventis does not market the refrigerated formulation but only the room temperature product.

In this NDA Ferring submitted draft labeling for a refrigerated formulation of desmopressin acetate nasal spray, with the proposed trade name, *Minirin*TM. The draft labeling for this NDA was the same as the currently approved labeling for NDA 17-922 for *DDAVP*® *Nasal Spray* (*desmopressin acetate 0.01% NASAL SOLUTION*), except for differences from the approved proprietary name, revisions to the vial and carton label (NDC #, *Caution* statement and manufacturer changes), revisions to the *How Supplied* section of the package insert (name of manufacturer), revisions to the Patient Instruction Guide and the differences in storage conditions between the room temperature and refrigerated formulations. In an April 12, 2001, submission to the NDA, the firm withdrew the trade name *Minirin*TM, and proposed instead the generic name, *Desmopressin Acetate Nasal Spray*. The July 3, 2001, submission deleted "0.01% NASAL SOLUTION" from vial and carton labels and made other changes for those labels.

A consult was sent to the Office of Post-Marketing Drug Risk Assessment (OPDRA) which included both the original submission dated October 27, 2000, with proposed labeling and the submission dated April 12, 2001. The April 12, 2001, submission included withdrawal of the name, *Minirin*TM *Nasal Spray* (*desmopressin acetate*) and a proposed new name, *Desmopressin Acetate Nasal Spray*. While the new name did not require a nomenclature review, the labeling for this new submission was reviewed and assessed by OPDRA. The completed review dated June 21, 2001, was returned to the Division with specific recommendations regarding the container label and carton labeling.

In addition, a separate consult was sent to the Division of Reproductive and Urologic Drug Products, HFD-580, for comment.

Review

The labeling with submission dated July 3, 2001, which included the new proposed name and dosage strength, "*Desmopressin Acetate Nasal Spray 0.1 mg/mL*" for this NDA, was compared to Aventis's currently approved labeling, for "*DDAVP Nasal Spray (desmopressin acetate) 0.01% NASAL SOLUTION*," (NDA 17-922/S-023, approved on August 7, 1996). The following differences are noted below:

9 Page(s) Withheld

 § 552(b)(4) Trade Secret / Confidential

b § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

Withheld Track Number: Administrative-

REGULATORY RECOMMENDATIONS:

The labeling revisions described above in "CONCLUSIONS" should be communicated to the sponsor.

Steve McCort
Project Manager, HFD-510

Supervisory Comment/Concurrence:

Enid Galliers
Chief, Project Management Staff, HFD-510

Drafted: Smm/June 22, 2001
Revised/Initialed: Egalliers/July 5, 2000/SmcCort July 6, 2001
Finalized: smm/August 10, 2001
Filename: n21333lab.doc

CSO LABELING REVIEW

34 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

0 § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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

/s/

Stephen McCort
8/28/01 03:54:50 PM
CSO

Enid Galliers
8/28/01 04:56:35 PM
CSO

DUPLICATE

FERRING
PHARMACEUTICALS

August 13, 2001

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrine Drug products (HFD-510)
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857



N 000 BL

Attention: Steve McCort, Regulatory Project Manager

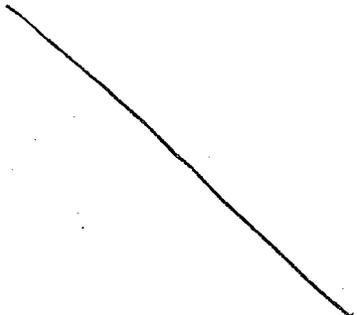
**Re: NDA #21-333, Desmopressin Acetate Nasal Spray
Labeling**

Dear Mr McCort:

This labeling amendment is submitted in response to several communications (fax of August 9 from you, fax of July 24 from Enid Galliers, and a telephone conversation on July 9 with Dr Chein-Hua Niu) concerning the labeling text pertaining to Desmopressin Acetate Nasal Spray (NDA 21-333).

For the reviewer's convenience, please find the proposed labeling for Desmopressin Acetate Nasal Spray submitted in the labeling amendment of July 3, 2001, in which the latest revisions are indicated (Appendix 1). The revisions are summarized below.

The following revisions have been made to the package insert:



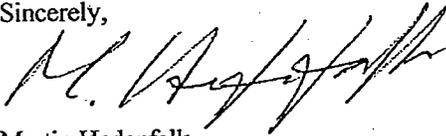
Finally, please find the final revised text sections for the vial label, the carton labeling and the package insert in Appendix 2.

Steve McCort
August 13, 2001
Page 2

This submission contains an application form FDA 356h, both an archival copy and a review copy, and as required by CFR 314.50, a field copy of this amendment has been provided to the NY District Office.

I can be contacted at (914) 333 8929 or via fax (914) 631 5120 if you have any immediate questions or need additional information.

Sincerely,



Martin Hedenfalk
Regulatory Manager



NDA 21-333

DISCIPLINE REVIEW LETTER

Ferring Pharmaceuticals Inc.
Attention: Martin Hedenfalk
Regulatory Manager
120 White Plains Road, Suite 400
Tarrytown, NY 10591

Dear Mr. Hedenfalk:

Please refer to your October 27, 2000, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Desmopressin Acetate Nasal Spray, 0.01%.

We also acknowledge receipt of your submissions dated April 12 and July 3, 2001.

Our reviews of the Clinical; Biopharmaceutics; and Chemistry, Manufacturing, and Controls sections of your submission are complete, and we have identified the following deficiencies:

1. Underlined text should be added to labeling and ~~strikeout~~ text should be deleted from labeling.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

NDA 21-333

Page 3

If you have any questions, call me at (301) 827-6429. After July 31, 2001, call Steve McCort, Regulatory Project Manager, at (301) 827-6415 if you have questions.

Sincerely yours,

{See appended electronic signature page}

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Enid Galliers

7/24/01 11:09:07 AM

FERRING

PHARMACEUTICALS

July 3, 2001

Food and Drug Administration
 Center for Drug Evaluation and Research
 Division of Metabolism and Endocrine Drug products (HFD-510)
 Attention: Division Document Room, 14B-19
 5600 Fishers Lane
 Rockville, MD 20857

N-000-BL
NDA ORIG AMENDMENT



Attention: Steve McCort, Regulatory Project Manager

**Re: NDA #21-333, Minirin™ Nasal Spray (desmopressin acetate)
 Labeling**

Dear Mr McCort:

This labeling amendment is submitted in response to several communications (fax of June 25, 2001 and follow-up telephone conversations on June 25, 26 and July 2) with Dr Chein-Hua Niu concerning the labeling text pertaining to Desmopressin Acetate Nasal Spray (NDA 21-333).

Please find the proposed revised text sections for the vial label, the carton labeling and the package insert (Appendix 2). For the reviewer's convenience, please also find the proposed labeling for Desmopressin Acetate Nasal Spray submitted in the labeling amendment of April 12, 2001, in which the latest changes are indicated (Appendix 1). Please note that the text that has been removed in the proposed labeling of April 12, 2001 is written in strikethrough and is replaced by wording in *Italics* immediately after.

We have considered the comments and think that the proposed changes resolve the concerns the Agency has at this time. Please note that we have removed the recommendation _____ since stability studies performed to confirm the shelf life of the product do not indicate that this is a concern.

This submission contains an application form FDA 356h, both an archival copy and a review copy, and as required by CFR 314.50, a field copy of this amendment has been provided to the NY District Office.

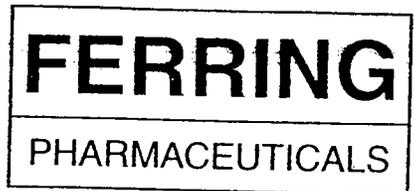
I can be contacted at (914) 333 8929 or via fax (914) 631 5120 if you have any immediate questions or need additional information.

Sincerely,

Martin Hedenfalk
 Regulatory Manager

CC (fax) Dr Chein-Hua Niu
 301-443-9282

ORIGINAL

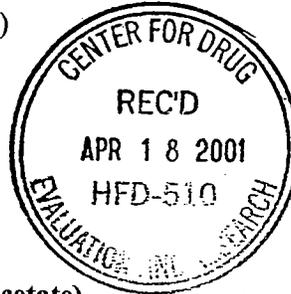


April 12, 2001

NDA SUPPL. AMENDMENT

N-000-BL

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrine Drug products (HFD-510)
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857



Attention: Steve McCort, Regulatory Project Manager

Re: NDA #21-333, Minirin™ Nasal Spray (desmopressin acetate)
Labeling

Dear Steve McCort:

This responds to our telephone conversation of February 8, 2001 concerning your request for mock-ups of the labeling for Minirin™ Nasal Spray (desmopressin acetate).

We have encountered major obstacles when trying to register the tradename "Minirin" and have decided to use the generic name "Desmopressin Acetate Nasal Spray" for the time being.

NDA #21-333 cross-references the approved NDA #17-922 for all clinical, toxicology, CMC information, and the proposed labeling for NDA #21-333 is based on the approved labeling for DDAVP® Nasal Spray (desmopressin acetate) in NDA 17-922.

Enclosed please find mock-ups of the draft generic labeling for Desmopressin Acetate Nasal Spray (Appendix 3 to 5), in which "Minirin™", in the previously submitted labeling, has been replaced by "Desmopressin Acetate". For the reviewer's convenience please also find the current labeling text for Desmopressin Acetate Nasal Spray approved under NDA #17-922, in which all proposed changes are indicated (Appendix 1), and the proposed draft labeling text for Desmopressin Acetate Nasal Spray (Appendix 2).

This submission contains an application form FDA 356h, both an archival copy and a review copy, and as required by CFR 314.50, a field copy of this amendment has been provided to the NY District Office.

I can be contacted at (914) 333 8929 or via fax (914) 631 5120 if you have any immediate questions or need additional information.

Sincerely,

Martin Hedenfalk
Regulatory Manager

REVIEWS COMPLETED	
GSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
GSO INITIALS	DATE

42 Page(s) Withheld

 § 552(b)(4) Trade Secret / Confidential

6 § 552(b)(4) Draft Labeling

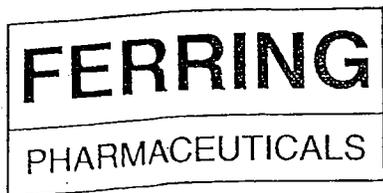
 § 552(b)(5) Deliberative Process

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

/s/

Stephen McCort
8/28/01 03:54:50 PM
CSO

Enid Galliers
8/28/01 04:56:35 PM
CSO



January 10, 2001

NEW CORRESP

Chien Hua Niu, Ph.D.
Food & Drug Administration
CDER/OPD/DNDCII (HFD-510)
Parklwan Building
5600 Fishers Lane (Rm. 14B04)
Rockville, Maryland 20857



RE: MINIRN Nasal Spray
NDA 21, 333

ORIGINAL

Dear Dr Nui:

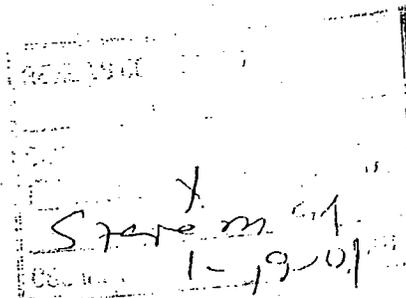
As per our telephone conversation this morning, following please find the address for

Please contact me at 914-333-8929 if you require additional information.

Best regards,

Martin Hedenfalk
Regulatory Manager

MH: jac



MEMORANDUM OF MEETING MINUTES

DATE OF MEETING: December 4, 2000
TIME: 2:00 PM
LOCATION: 14B-45
APPLICATION: Minirin Nasal Spray
TYPE OF MEETING: Filing Meeting
MEETING CHAIR: David Orloff, M.D., Division Director
MEETING RECORDER: Steve McCort, Project Manager

FDA ATTENDEES, TITLES, AND OFFICE/DIVISION

<u>Name of FDA Attendee</u>	<u>Title</u>	<u>Division Name & HFD#</u>
David Orloff, M.D.	Division Director	DMEDP, HFD-510
Mary Parks, M.D.,	Medical Team Leader	DMEDP, HFD-510
Hae Young Ahn, Ph.D.	Biopharm Team Leader	DMEDP, HFD-510
Karen Davis-Bruno	Pharmacology Team Leader	DMEDP, HFD-510
Chien-Hua Niu, Ph.D	Chemistry Reviewer	DMEDP, HFD-510
Steve McCort	Project Manager	DMEDP, HFD-51

BACKGROUND: This NDA being submitted is the same as the identical product marketed under NDA 17-522 currently marketed as desmopressin acetate nasal solution. The indications are currently for both Central Diabetes Incipidus and Primary Nocturnal Enuresis. Advantis the parent company currently markets on the drug with the room temperate condition. This application is for the refrigerated condition.

CONCLUSIONS:

1. All disciplines recommended filing the NDA.
2. The only reviews need will be a chemistry review and a Nomenclature review of the name by OPTRA.
3. A consult will be sent to HFD-50 for review of the labeling.

ACTION:

The NDA is filed.

Minutes Preparer: Steve McCort

Steve McCort, Project Manager

Chair Concurrence: David Orloff

David Orloff, M.D., Div. Director

cc: Original

HFD-NDA 21-133/Div. Files

HFD-510/RPM/SMcCort

HFD-510/Mparks/Smoore.Cniu/Kdavis/Hahn/STJohnson

MINUTES

**RECORD OF TELEPHONE
CONVERSATION/MEETING**

Date: October 17, 2000

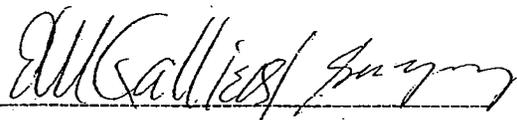
Dr. Nardi and Mr. Hedenfalk of the Ferring Pharmaceuticals Inc. initiated this t/con to get a regulatory guidance on NDA submission of an approved but not presently marketed drug product named Desmopressin (DDAVP) Acetate Nasal Spray (refrigerated product). Although Ferring developed DDAVP, Aventis owns the drug under NDA 17-922. Dr. Nardi said that Ferring has a cross reference right to the clinical data on DDAVP Nasal Spray owned by Aventis. Ferring plans to submit a NDA under 505 (b)(1) and will have the same indications (Diabetes Insipidus and Primary Nocturnal Enuresis) as Aventis' NDA 17-922.

Ferring was advised that they can submit an NDA by providing following information:

- 1) NDA Application (356H) with a cover letter
- 2) A complete right of reference by Aventis
- 3) All clinical data on DDAVP Nasal Spray (Refrigerated)
- 4) DMF
- 5) Patent information
- 6) Financial disclosure (Debarment)
- 7) Original (approved) and proposed labels
- 8) User Fee # and cover sheet

Dr. Nardi and Mr. Hedenfalk verbalized the understanding of the above requirements and said that they will submit the NDA by the end of October 2000.

cc: Original Subject File



Name: Enid Galliers/ Su Yang

Pre-NDA

Telecon/Meeting

initiated by:

Ferring Pharm

By: Telephone

Product Name:

Desmopressin Acetate
(DDAVP) Nasal Spray-
Refrigerated Product

Firm Name: Ferring Pharm

Name and Title of Person
with whom conversation
was held: Dr. Ronald
Nardi, Vice President,
Scientific and Regulatory
Affairs and Mr. Martin
Hedenfalk, Regulatory
Manager

Phone(914) 333-8929

Fax (914) 631-5120

DSJ



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-333

NOV 27 2000

Ferring Laboratories, Inc.
Attention: Ronald V. Nardi, Ph.D.
Vice President, Scientific & Regulatory Affairs
120 White Plains Road
Suite 400
Tarrytown, NY 10591

Dear Dr. Nardi:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Minirin (desmopressin acetate) Nasal Spray, 5.0 ml/0.1mg/ml
Review Priority Classification:	Standard (S)
Date of Application:	October 27, 2000
Date of Receipt:	November 3, 2000
Our Reference Number:	NDA 21-333

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on January 2, 2001, in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be September 3, 2001, and the secondary user fee goal date will be November 3, 2001.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days

from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call Steve McCort, Regulatory Project Manager, at (301) 827-6415.

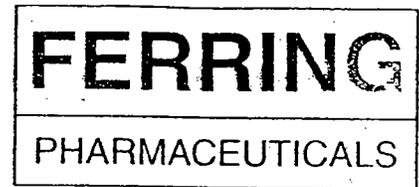
Sincerely,

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

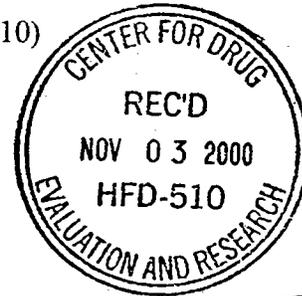
/s/

Enid Galliers
11/13/00 05:15:14 PM

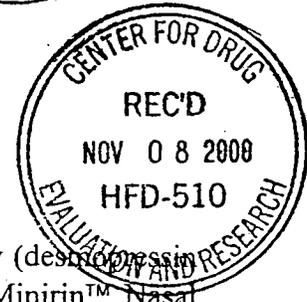
October 27, 2000



John Jenkins, M.D., Director
Center for Drug Evaluation and Research
Division of Metabolism and Endocrine Drug products (HFD-510)
Office of Drug Evaluation II
Document Control Room #14B-04
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857



Re: NDA #21-333
Minirin™ Nasal Spray (desmopressin acetate)



Dear Dr. Jenkins,

Enclosed please find a New Drug Application for Minirin™ Nasal Spray (desmopressin acetate), NDA #21-333, for your review as a 505(b)(1) application. Minirin™ Nasal Spray is a preparation of desmopressin acetate, manufactured by Ferring Pharmaceuticals, for the treatment of Primary Nocturnal Enuresis and Central Cranial Diabetes Insipidus.

The identical product manufactured by Ferring Pharmaceuticals is approved but not marketed under NDA 17-922, currently owned by Aventis Pharmaceuticals Inc. Ferring Pharmaceuticals developed the original desmopressin acetate nasal solution drug product for the indication Diabetes Insipidus and submitted the original NDA #17-922, which was approved on February 2, 1978. A supplemental application providing for a second indication, Primary Nocturnal Enuresis, was approved on November 28, 1989. More recently, the desmopressin acetate nasal spray was reformulated from a refrigerated solution to a new formula that may be stored at room temperature. The two formulations are bio-equivalent and the room temperature formulation was developed for commercial reasons unrelated to efficacy or safety of the refrigerated formulation. Aventis Pharmaceuticals Inc. currently only markets the room temperature stable desmopressin acetate nasal spray also manufactured by Ferring Pharmaceuticals under NDA #17-922. This application is for the refrigerated formulation of desmopressin acetate nasal spray.

The content and format of the attached 505(b)(1) application was discussed during a Pre-NDA telephone conference that took place on October 17, 2000 and the following was agreed upon:

- In view of the brevity of the application each color-coded binder for individual reviewing disciplines, including the field copy, should contain the complete application.

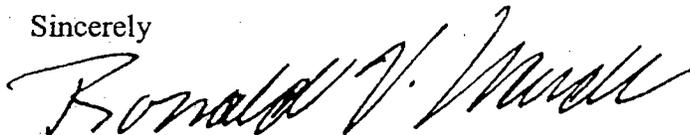
- Include a user fee cover sheet, 356H form, patent information, investigator disclosure, applicable reference letters, and additional Chemistry, Manufacturing, or Control information if different from what is approved in NDA #17-922 for the refrigerated desmopressin acetate nasal spray.
- Identify labeling changes between approved labeling for the identical product approved under NDA #17-922 and proposed labeling in the cover letter and also provide a Microsoft word file with the proposed labeling the CSO.

The application cross-references the approved NDA #17-992 for all clinical, toxicology, and CMC information except the proposed labeling and environmental assessment. Only two global changes are proposed in the labeling in this application compared to the labeling approved under NDA #17-922 for DDAVP[®] Nasal Spray (desmopressin acetate). The global changes proposed in the labeling for Minirin[™] Nasal Spray are:

- The name of the drug product has been changed from Desmopressin Acetate Nasal Spray to Minirin[™] Nasal Spray and,
- the product is manufactured for Ferring Pharmaceuticals Inc. instead of Aventis Pharmaceuticals Inc.

If you need any other information please feel free to contact me at 914-333-8932 or by fax 914-631-5120.

Sincerely



Ronald V. Nardi, Ph.D.
Vice President, Scientific and Regulatory Affairs

Enclosures: NDA #21-333

Attachments: User Fee Cover Sheet

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS Ferring Pharmaceuticals Inc. 120 White Plains Road, Suite 400 Tarrytown, New York 10591	3. PRODUCT NAME Minirin™
2. TELEPHONE NUMBER (Include Area Code) (914) 333-8900	4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO <u>NDA #17-922</u> (APPLICATION NO. CONTAINING THE DATA).
5. USER FEE I.D. NUMBER 4051	6. LICENSE NUMBER / NDA NUMBER N021333

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)	

FOR BIOLOGICAL PRODUCTS ONLY

<input type="checkbox"/> WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION	<input type="checkbox"/> A CRUDE ALLERGENIC EXTRACT PRODUCT
<input type="checkbox"/> AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY	<input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT
<input type="checkbox"/> BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92	

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See reverse side if answered YES)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Vice President Scientific & Regulatory Affairs	DATE October 27, 2000
---	---	--------------------------

USER FEE VALIDATION SHEET *CSO/PM: McCort*

NDA # 21-333 Supp. Type & # UFID # 4051
 (e.g., N000, SLR001, SE1001, etc.)

1. YES NO User Fee Cover Sheet Validated? MIS Elements Screen Change(s):

2. YES NO APPLICATION CONTAINS CLINICAL DATA?
 (Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

REF IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.

3. YES NO SMALL BUSINESS EXEMPTION

4. YES NO WAIVER GRANTED

5. YES NO NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other than bundling).
 If YES, list all NDA #s, review division(s) and those for which an application fee applies.

NDA #	Division	Fee	No Fee
N _____	HFD- _____		
N _____	HFD- _____	Fee	No Fee

6. YES NO BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required
 (Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N _____	HFD- _____	N _____	HFD- _____

7. P S PRIORITY or STANDARD APPLICATION?

ewg

 PM Signature / Date

RM Gallies 11/9/00

 CPMS Concurrence Signature / Date

HF pd #142
11/6/01

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS Ferring Pharmaceuticals Inc. 120 White Plains Road, Suite 400 Tarrytown, New York 10591	3. PRODUCT NAME Minirin TM
2. TELEPHONE NUMBER (Include Area Code) (914) 333-8900	4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO <u>NDA #17-922</u> (APPLICATION NO. CONTAINING THE DATA).
5. USER FEE I.D. NUMBER 4051	6. LICENSE NUMBER /NDA NUMBER N021333

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)	

FOR BIOLOGICAL PRODUCTS ONLY

<input type="checkbox"/> WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION	<input type="checkbox"/> A CRUDE ALLERGENIC EXTRACT PRODUCT
<input type="checkbox"/> AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY	<input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT
<input type="checkbox"/> BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92	

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
 (See reverse side if answered YES)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Vice President Scientific & Regulatory Affairs	DATE October 27, 2000
--	---	--------------------------

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

09.12.02

Application Information	
NDA 21-333	Efficacy Supplement Type SE-
Supplement Number	
Drug: Desmopressin Acetate Nasal Spray, 0.1 mg/mL	
Applicant: Ferring Pharmaceuticals	
RPM: Steve McCort	HFD- 510 Phone # 827-6415
Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)	Reference Listed Drug (NDA #, Drug name):
Application Classifications:	
• Review priority	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
• Chem class (NDAs only)	5S
• Other (e.g., orphan, OTC)	
User Fee Goal Dates	September 16, 2202
Special programs (indicate all that apply)	<input checked="" type="checkbox"/> None Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review
User Fee Information	
• User Fee	<input checked="" type="checkbox"/> Paid
• User Fee waiver	<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other
• User Fee exception	<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) <input type="checkbox"/> Other
Application Integrity Policy (AIP)	
• Applicant is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• This application is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	<input checked="" type="checkbox"/> Verified
Patent	
• Information: Verify that patent information was submitted	<input checked="" type="checkbox"/> Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> IV 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	<input type="checkbox"/> Verified <div style="text-align: center; font-size: 2em; font-family: cursive;">NA</div>
Exclusivity Summary (approvals only)	X
Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	NA

General Information	
Actions	
• Proposed action	(x) AP () TA () AE () NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	x) Materials requested in AP letter () Reviewed for Subpart H
Public communications	
• Press Office notified of action (approval only) will be notified	() Yes <input checked="" type="checkbox"/> Not applicable
• Indicate what types (if any) of information dissemination are anticipated • Not sure	<input checked="" type="checkbox"/> None () Press Release () Talk Paper () Dear Health Care Professional Letter
Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings (indicate dates of reviews and meetings)	X
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	X
• Reviews	X
Post-marketing commitments	
• Agency request for post-marketing commitments	NA
• Documentation of discussions and/or agreements relating to post-marketing commitments	NA
Outgoing correspondence (i.e., letters, E-mails, faxes)	X
Memoranda and Telecons	X
Minutes of Meetings	
• EOP2 meeting (indicate date)	NA
• Pre-NDA meeting (indicate date)	NA
• Pre-Approval Safety Conference (indicate date; approvals only)	NA
• Other	NA
Advisory Committee Meeting	
• Date of Meeting	NA
• 48-hour alert	NA
Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	NA

Clinical and Summary Information	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	X
Clinical review(s) (indicate date for each review)	X
Microbiology (efficacy) review(s) (indicate date for each review)	NA
Safety Update review(s) (indicate date or location if incorporated in another review)	NA
Pediatric Page (separate page for each indication addressing status of all age groups)	X
Statistical review(s) (indicate date for each review)	NA
Biopharmaceutical review(s) (indicate date for each review)	X
Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	NA
Clinical Inspection Review Summary (DSI)	
• Clinical studies	NA
• Bioequivalence studies	NA
CMC Information	
CMC review(s) (indicate date for each review)	X
Environmental Assessment	
• Categorical Exclusion (indicate review date)	X
• Review & FONSI (indicate date of review)	NA
• Review & Environmental Impact Statement (indicate date of each review)	NA
Micro (validation of sterilization & product sterility) review(s) (indicate date for each review)	NA
Facilities inspection (provide EER report)	Date completed: June 18, 2002 (x) Acceptable () Withhold recommendation
Methods validation	() Completed () Requested (x) Not yet requested
Nonclinical Pharm/Tox Information	
Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	NA
Nonclinical inspection review summary	NA
Statistical review(s) of carcinogenicity studies (indicate date for each review)	NA
CAC/ECAC report	NA

- ◆ Status of advertising (if AP action) Reviewed (for Subpart H – attach review) X Materials requested in AP letter

- ◆ Post-marketing Commitments N/A
 - Agency request for Phase 4 Commitments.....
 - Copy of Applicant's commitments

- ◆ Was Press Office notified of action (for approval action only)?..... Yes No
 - Copy of Press Release or Talk Paper.....

- ◆ Patent X
 - Information [505(b)(1)]
 - Patent Certification [505(b)(2)].....
 - Copy of notification to patent holder [21 CFR 314.50 (i)(4)].....

- ◆ Exclusivity Summary X

- ◆ Debarment Statement X

- ◆ Financial Disclosure X
 - No disclosable information
 - Disclosable information – indicate where review is located X (See medical review)

- ◆ Correspondence/Memoranda/Faxes X

- ◆ Minutes of Meetings X
 - Date of EOP2 Meeting _____ N/A
 - Date of pre NDA Meeting October 17, 2000 X
 - Date of pre-AP Safety Conference _____ N/A

- ◆ Advisory Committee Meeting N/A
 - Date of Meeting
 - Questions considered by the committee
 - Minutes or 48-hour alert or pertinent section of transcript

- ◆ Federal Register Notices, DESI documents N/A

- CLINICAL INFORMATION:** **Indicate N/A (not applicable), X (completed), or add a comment.**
- ◆ Summary memoranda (e.g., Office Director's memo, Division Director's memo, Group Leader's memo) N/A

 - ◆ Clinical review(s) and memoranda X

- ◆ Safety Update review(s) Not Needed
- ◆ Pediatric Information
 - Waiver/partial waiver (Indicate location of rationale for waiver) Deferred Pediatric Page.....
 - Pediatric Exclusivity requested? Denied Granted Not Applicable
- ◆ Statistical review(s) and memoranda N/A
- ◆ Biopharmaceutical review(s) and memoranda..... X
- ◆ Abuse Liability review(s) N/A
 Recommendation for scheduling
- ◆ Microbiology (efficacy) review(s) and memoranda N/A
- ◆ DSI Audits N/A
 Clinical studies bioequivalence studies

CMC INFORMATION:

Indicate N/A (not applicable), X (completed), or add a comment.

- ◆ CMC review(s) and memoranda X
- ◆ Statistics review(s) and memoranda regarding dissolution and/or stability N/A
- ◆ DMF review(s) N/A
- ◆ Environmental Assessment review/FONSI/Categorical exemption X
- ◆ Micro (validation of sterilization) review(s) and memoranda N/A
- ◆ Facilities Inspection (include EES report) X
 Date completed August 24, 2001
- ◆ Methods Validation N/A.....

Acceptable Not Acceptable
 Withhold
 Completed Not Completed

PRECLINICAL PHARM/TOX INFORMATION:

**Indicate N/A (not applicable),
X (completed), or add a
comment.**

- ◆ Pharm/Tox review(s) and memoranda X
- ◆ Memo from DSI regarding GLP inspection (if any) N/A
- ◆ Statistical review(s) of carcinogenicity studies N/A
- ◆ CAC/ECAC report N/A

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on Page 2.

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE
OR AN ANTIBIOTIC DRUG FOR HUMAN USE
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

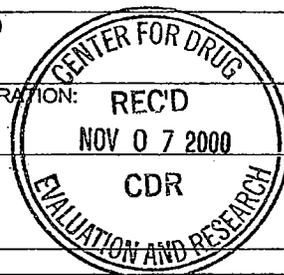
APPLICATION NUMBER **21-333**

APPLICANT INFORMATION

NAME OF APPLICANT FERRING PHARMACEUTICALS INC.	DATE OF SUBMISSION: October 27, 2000
TELEPHONE NO. (Include Area Code) (914)333-8900	FACSIMILE (FAX) NUMBER (Include Area Code) (914)631-5120
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issues): 120 White Plains Road, Suite 400 Tarrytown, NY 10591	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, Country, ZIP Code, telephone & FAX number) IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) 21-333		
ESTABLISHED NAME (e.g., Proper Name, USP/USAN name) desmopressin acetate	PROPRIETARY NAME (trade name) IF ANY Minirin™ Nasal Spray	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) n/a	CODE NAME (if any) RG 83884	
DOSAGE FORM: Nasal Solution	STRENGTHS: 5.0 mL of 0.1 mg/mL	ROUTE OF ADMINISTRATION: Nasal Spray
PROPOSED INDICATIONS FOR USE: Primary nocturnal enuresis and central cranial diabetes insipidus.		



APPLICATION INFORMATION

APPLICATION TYPE (check one)	
<input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50)	<input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21CFR 314.94)
<input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)	
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)	
IF AN ANDA, OR 505 (b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug Holder of Approved Application	
TYPE SUBMISSION (check one)	
<input checked="" type="checkbox"/> ORIGINAL APPLICATION	<input type="checkbox"/> AMENDMENT TO A PENDING APPLICATION
<input type="checkbox"/> RESUBMISSION	<input type="checkbox"/> PRESUBMISSION
<input type="checkbox"/> ANNUAL REPORT	<input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT
<input type="checkbox"/> EFFICACY SUPPLEMENT	<input type="checkbox"/> LABELING SUPPLEMENT
<input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT	<input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION:	
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)	
REASON FOR SUBMISSION: New Drug Application	
PROPOSED MARKETING STATUS (Check one)	
<input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx)	<input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED 1	THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.
See attached sheet with additional information

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, BMFs, and DMFs referenced in the current application)

NDA #17-922 Drug product
DMF _____

This application contains the following items: (Check all that apply)	
X	1. Index
X	2. Labeling (check one) <input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
X	3. Summary (21 CFR 314.50 (c))
X	4. Chemistry
X	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.20)
	B. Samples (21 CFT 314.50 (e)(1); 21 CFR 601.2(a)) (Submit only upon FDA's request)
X	C. Methods Validation Package (e.g., 21 CFR 314.50 (e) (2) (I); 21 CFR 601.2)
X	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50 (d) (2)); 21 CFR 601.2)
X	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50 (d) (3); 21 CFR 601.2)
	7. Clinical Microbiology section (e.g., 21 CFR 314.50 (d) (4))
X	8. Clinical data section (e.g., 21 CFR 314.50 (d) (5); 21 CFR 601.2))
X	9. Safety update report (e.g., 21 CFR 314.50 (d) (5) (vi) (b); 21 CFR 601.2)
X	10. Statistical section (e.g., 21 CFR 314.50 (d) (6); 21 CFR 601.2)
X	11. Case report tabulations (e.g., 21 CFR 314.50 (f) (1); 21 CFR 601.2)
X	12. Case reports forms (e.g., 21 CFR 314.50 (f) (1); 21 CFR 601.2)
X	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
X	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
X	15. Establishment description (21 CFR Part 600, if applicable)
X	16. Debarment certification (FD&C Act 306 (k)(1))
X	17. Field copy certification (21 CFR 314.50 (k)(3))
X	18. User Fee Cover Sheet (Form FDA 3397)
X	19. Financial Information (21 CFR Part 54)
	20. OTHER (Specify)

CERTIFICATION

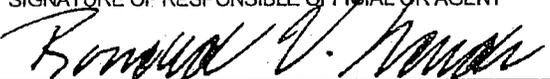
I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulation that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR PARTS 210, 211 or applicable regulations, Parts 606, and/or 820..
2. Biological establishment standards in 21 CFR part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug product or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80 and 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE Ronald V. Nardi, Ph.D. Vice President, Regulatory & Scientific Affairs	DATE 10/27/00
---	---	------------------

ADDRESS (Street, City, State, Zip Code) 120 White Plains Road, Suite 400 Tarrytown, NY 10591	TELEPHONE NO. (Include Area Code) (914) 333-8900
--	---

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Service Food and Drug Administration
Food and Drug Administration CDER, HFD-94
CBER HFM-99 12420 Parklawn Dr., Room 3046
401 Rockville Pike Rockville, MD 20852
Rockville, MD 20852-1448

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