CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-503

ADMINISTRATIVE DOCUMENTS/CORRESPONDENCE

Section 14: Patent Information Under 21 U.S.C. § 355(b)(2)

The undersigned declares that the investigations described in clause (A) of 21 U.S.C. § 355(b)(1) (i.e., investigations that were made to show whether the drug for which approval is sought by this application is safe for and effective in use) and are relied upon by applicant for approval of this application were conducted by or for the applicant or are investigations for which the applicant has obtained a right of reference or use from the person by or for whom the investigations were conducted. Consequently, a certification providing patent information described at 21 U.S.C. § 355(b)(2)(A) is not required.

The undersigned further declares that, with respect to the drug for which the investigations described in clause (A) of 21 U.S.C. § 355(b)(1) were conducted, the method-of-use patents identified in Section 13--U.S. Patent Nos. 5,952,343 and 6,162,812--do not claim any use for which the applicant is not seeking approval. Consequently, the statement described at 21 U.S.C. § 355(b)(2)(B) is not required.

Jeffrey W. Rennecker
Patent Counsel
Agouron Pharmaceuticals, Inc., A Pfizer Company

Date: June 28, 2002

APPEARS THIS WAY
ON ORIGINAL

Section 13: Patent Information Under 21 U.S.C. § 355(b)(1)

The following information and declarations are provided in accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53(c):

U.S. Patent Number:	5,484,926
Expiration Date:	October 7, 2013
Type of Patent:	drug substance
Assignee:	Agouron Pharmaceuticals, Inc.

U.S. Patent Number:	5,952,343
Expiration Date:	October 7, 2013
Type of Patent:	drug substance, drug product, and method of use
Assignee:	Agouron Pharmaceuticals, Inc.

U.S. Patent Number:	6,162,812
Expiration Date:	October 7, 2013
Type of Patent:	drug product and method of use
Assignee:	Agouron Pharmaceuticals, Inc.

The undersigned declares that U.S. Patent No. 5,484,926 covers the drug substance (ingredient or compound) in the drug (Viracept® formulation) that is the subject of this application under Section 505 of the Federal Food, Drug, and Cosmetic Act for which approval is sought.

The undersigned further declares that U.S. Patent No. 5,952,343 covers the drug substance (ingredient or compound), drug product (formulation or composition), and method of use of the drug that is the subject of this application under Section 505 of the Federal Food, Drug, and Cosmetic Act for which approval is sought.

The undersigned further declares that U.S. Patent No. 6,162,812 covers the drug product (formulation or composition) and method of use of the drug that is the subject of this application under Section 505 of the Federal Food, Drug, and Cosmetic Act for which approval is sought.

Jeffrey W. Rennecker
Patent Counsel
Agouron Pharmaceuticals, Inc., A Pfizer Company

APPEARS THIS WAY
ON ORIGINAL

Date: June 28, 2002

EXCLUSIVITY SUMMARY for NDA # 21-503 SUPPL # N/A

Trade Name: Viracept® Generic Name nelfinavir mesylate

Applicant Name Agouron Pharmaceuticals, Inc. HFD-530

Approval Date May 1, 2003

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/ X / NO /__/

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

   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 / x /

   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.

   N/A

   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:

   N/A

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 /__/ NO /__X__/

If yes, NDA # _____ Drug Name _____

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 /__X__/

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 / **X** / NO /___/

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

NDA # **20-778** **Viracept 250 mg Tablets**

NDA # **20-779** **Viracept 50 mg Powder**

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 /__/

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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: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

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 /X/ 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 /__X__/ 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 /__X__/

(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: _____

_____

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(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 /X/

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 # AG1343-503

Investigation #2, Study # AG1343-510

Investigation #3, Study # AG1343-511

Investigation #4, Study # AG1343-542

Investigation #5, Study # M/3331/0073A

Investigation #6, Study # M/3331/0073B

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 /X/ NO /__/

Investigation #2 YES /X/ NO /__/

Investigation #3 YES /X/ NO /__/

Investigation #4 YES /X/ NO /__/

Investigation #5 YES /X/ NO /__/

Investigation #6 YES /X/ 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 # 20-778 Study # AG1343-503

NDA # 20-778 Study # AG1343-510

NDA # 20-778 Study # AG1343-511

NDA # 20-778 Study # AG1343-542

NDA # 20-705 Study # M/3331/0073A

NDA # 20-705 Study # M/3331/0073B

(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: _____

_____

_____

Jeff O'Neill
Signature of Preparer
Jeff O'Neill, ACRN
Regulatory Project Manager
Division of Antiviral Drug Products

April 29, 2003
Date

Jeff Murray for Debra Birnkrant
Signature of Office or Division Director

April 30, 2002
Date

Debra Birnkrant, M.D.
Division Director
Division of Antiviral Drug Products

cc:
Archival NDA 21-503
HFD-530/Division File
HFD-530/RPM/O'Neill
HFD-530/CRPM/DeCicco
HFD-530/DivDir/Birnkrant
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

Section 16: Debarment Certification

The undersigned certifies that Agouron Pharmaceuticals, Inc. personnel have reviewed a current list of individuals that have received debarment notices or have been debarred from activities regulated by the Food and Drug Administration against a list of individuals under the employment of Agouron, key preclinical contract personnel, and clinical investigators listed in **Section 6 Human Pharmacokinetics and Bioavailability** and have not found the names of debarred individuals associated with this new drug application. The debarment list, dated May 7, 2002, was provided to Agouron by the Food and Drug Administration, pursuant to the Freedom of Information Act.

Marie-Do Mompas, Pharm.D.
Director, Regulatory Strategy - VIRACEPT®

28 June 2002
Date

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BEST POSSIBLE COPY

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA/BLA # : 21-503 Supplement Type (e.g. SE5): N/A Supplement Number: N/A

Stamp Date: July 1, 2002 Action Date: May 1, 2003

HFD-530 Trade and generic names/dosage form: Viracept® (nelfinavir mesylate) Tablets

Applicant: Agouron Pharmaceuticals, Inc. Therapeutic Class: Antiviral

Indication(s) previously approved: VIRACEPT in combination with other antiretroviral agents is indicated for the treatment of HIV infection.

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): One

Indication #1: VIRACEPT in combination with other antiretroviral agents is indicated for the treatment of HIV infection

Is there a full waiver for this indication (check one)?

☐ Yes: Please proceed to Section A.

☒ No: Please check all that apply: ___Partial Waiver __x__Deferred __x__Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver: N/A

☐ Products in this class for this indication have been studied/labeled for pediatric population
☐ Disease/condition does not exist in children
☐ Too few children with disease to study
☐ There are safety concerns
☐ Other:_____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived: N/A

Min____ kg____ mo.____ yr.____ Tanner Stage____
Max____ kg____ mo.____ yr.____ Tanner Stage____

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Reason(s) for partial waiver:

☐ Products in this class for this indication have been studied/labeled for pediatric population
☐ Disease/condition does not exist in children
☐ Too few children with disease to study
☐ There are safety concerns
☐ Adult studies ready for approval
☐ Formulation needed
☐ Other:_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min ____ **kg**____ **mo.** 0 **yr.**____ **Tanner Stage**____
Max____ **kg**____ **mo.**____ **yr.** <2 **Tanner Stage**____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☒ **Other: Per the sponsor, the studies have been completed but not yet submitted. The sponsor plans to submit the studies by July 1, 2003.**

Date studies are due (mm/dd/yy): July 1, 2003

studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min ____ **kg**____ **mo.**____ **yr.** >2 **Tanner Stage**____
Max____ **kg**____ **mo.**____ **yr.** 13 **Tanner Stage**____

Comments:

Study AG1343-524, evaluating the use of nelfinavir in children aged 2 to 13 years was completed, and safety data and dosing recommendations derived from this study were incorporated into the product label.

This page was completed by:

{See appended electronic signature page}

Jeff O'Neill, ACRN
Regulatory Project Manager
&
Katherine Laessig, M.D.
Medical Team Leader

cc: NDA
HFD-950/ Terrie Crescenzi
HFD-960/ Grace Carmouze
(revised 9-24-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

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

/s/

Kathrine Laessig
4/30/03 11:38:48 AM

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NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information

NDA 21-503	**Efficacy Supplement Type: N/A**	**Supplement Numbers: N/A**	
Drug: Viracept® (nelfinavir mesylate)		**Applicant: Agouron Pharmaceuticals, Inc.**	
RPM: **Jeff D. O'Neill, ACRN**		**HFD-530**	Phone # **301-827-2362**
Application Type: **(X)** 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	**May 1, 2003**
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	N/A
• OC clearance for approval	N/A
❖ 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.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (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).	( ) Verified
❖ Exclusivity Summary (approvals only)	**Completed**
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	**Rev. of Action Package-04/28/03**

General Information	
Actions	
• Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	N/A
• Status of advertising (approvals only)	(X) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	(X) Yes ( ) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	( ) None (X) Press Release ( ) Talk Paper (X) 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)	N/A
• Most recent applicant-proposed labeling	Included
• Original applicant-proposed labeling	Included
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	N/A
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	Included
• Reviews	Included in chemistry review
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	No new requests for applicant
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	Included in Action Package
❖ Memoranda and Telecons	Included in Action Package
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	Included-February 22, 2002
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	N/A
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Clinical and Summary Information	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(12/24/02)*	**Medical Team Leader Review Included**
❖ Clinical review(s) *(01/03/03)*	**Draft Included**
❖ Microbiology (efficacy) review(s) *(11/27/02)*	**Draft included**
❖ Safety Update review(s) *(01/03/03)*	**Included in clinical review**
❖ Pediatric Page(12/24/02)	**Included**
❖ Statistical review(s) *(01/03/03)*	**Draft included**
❖ Biopharmaceutical review(s) *(12/17/02)*	**Draft included**
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	**N/A**
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	**N/A**
• Bioequivalence studies	**N/A**
CMC Information	
❖ CMC review(s) *(01/23/03)*	**Draft included**
❖ Environmental Assessment	
• Categorical Exclusion *(01/23/03)*	**Included**
• Review & FONSI *(indicate date of review)*	**N/A**
• Review & Environmental Impact Statement *(01/23/03)*	**Included**
Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	**N/A**
❖ Facilities inspection (provide EER report)	Date completed: 4/14/2003 **(X)** Acceptable ( ) Withhold recommendation
❖ Methods validation	**(X)** Completed: See NDA 20-779 ( ) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(12/13/02)*	**Included**
❖ Nonclinical inspection review summary	**N/A**
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	**N/A**
❖ CAC/ECAC report	**N/A**

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: April 16, 2003

To: Marie-Do Mompas, Director, Regulatory Strategy
Agouron Pharmaceuticals, Inc., a Pfizer Company

From: Jeff D. O'Neill, Regulatory Project Manager, HFD-530

Through: Lisa Naeger, Ph.D., Microbiology Reviewer, HFD-530
Jules O'Rear, Ph.D., Microbiology Team Leader, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530
Stephen P. Miller, Ph.D., Chemistry Team Leader, HFD-530
Ita Yuen, Ph.D., Pharmacology/Toxicology Reviewer, HFD-530
James Farrelly, Ph.D., Pharmacology/Toxicology Team Leader, HFD-530
Robert Kumi, Ph.D., Pharmacokinetics Reviewer, HFD-530
Kellie Reynolds, Pharm.D., Pharmacokinetics Team Leader, HFD-530
Susan Zhou, Ph.D., Statistical Reviewer, HFD-530
Greg Soon, Ph.D., Statistical Reviewer Team Leader, HFD-530
Neville Gibbs, M.D., Medical Officer, HFD-530
Katherine Laessig, M.D., Ph.D., Medical Team Leader, HFD-530

NDA: 21-503

Drug: Viracept (nelfinavir)

Subject: Suggested revisions for the Viracept PI

The Division of Antiviral Drug Products recommends the following revisions to the Viracept package insert (a copy of the PI is attached):

On page 2:

Line 56, add "the HIV-1 of" before >10%.

Line 58, add "isolates (n=157)" before "from patients" and delete "(n=157)" before "receiving nelfinavir monotherapy".

Line 64, delete — after patients and add "isolate" before possessed.

On page 4:

Line numbers 135-143 have been removed and replaced by wording in line numbers 144-149.

Line numbers 151-153, add "In healthy volunteers receiving a single 750 mg dose under fed conditions, nelfinavir concentrations were similar following administration of the 250 mg tablets and the oral powder."

On page 14:

[redacted] has been deleted.

On page 25:

Line 631, add "the 250 or 625 mg" before tablets.

Line 632, add "may" before dissolve and add the following statement to lines 632-635: "the tablets in a small amount of water. Once dissolved, patients should mix the cloudy liquid well, and consume it immediately. The glass should be rinsed with water and the rinse swallowed to ensure the entire dose is consumed."

Lines 635-638, delete information that begins with [redacted] and ends with [redacted]

On page 26:

Line 660, add "(nelfinavir mesylate)" after VIRACEPT.

Line 664, add "(nelfinavir mesylate)" after VIRACEPT.

The final change has been made to the entire document:

Replace CYP3A4 with CYP3A throughout the document. Newer scientific information indicates that CYP3A4 and CYP3A5 are both important, but it is difficult to tell which is responsible for specific interactions (a lot of overlap). So, we prefer the more general term, CYP3A.

We are providing this information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Jeff D. O'Neill, ACRN
Regulatory Project Manager
Division of Antiviral Drug Products

APPEARS THIS WAY
ON ORIGINAL

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: April 16, 2003

To: Marie-Do Mompas, Director, Regulatory Strategy	**From:** Jeff D. O'Neill Regulatory Project Manager
Company: Hoffman-La Roche	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2523
Phone number: 858-622-7360	**Phone number:** 301-827-2362

Subject: NDA 21-503 Labeling revisions

Total no. of pages including cover:30

Comments: These are DAVDP's preliminary revisions for the Viracept (nelfinavir)PI.

Document to be mailed: ☐ YES ☑ NO

APPEARS THIS WAY
ON ORIGINAL

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: April 14, 2003

To: Marie-Do Mompas, Director, Regulatory Strategy	**From:** Jeff D. O'Neill Regulatory Project Manager
Company: Hoffman-La Roche	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2523
Phone number: 858-622-7360	**Phone number:** 301-827-2362

Subject: NDA 21-503 Labeling revisions

Total no. of pages including cover:9

Comments: These are DAVDP's preliminary revisions for the Viracept (nelfinavir)PPI.

Document to be mailed: ☐ YES ☑ NO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: April 14, 2003

To: Marie-Do Mompas, Director, Regulatory Strategy
Agouron Pharmaceuticals, Inc., a Pfizer Company

From: Jeff D. O'Neill, Regulatory Project Manager, HFD-530

Through: Lisa Naeger, Ph.D., Microbiology Reviewer, HFD-530
Jules O'Rear, Ph.D., Microbiology Team Leader, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530
Stephen P. Miller, Ph.D., Chemistry Team Leader, HFD-530
Ita Yuen, Ph.D., Pharmacology/Toxicology Reviewer, HFD-530-
James Farrelly, Ph.D., Pharmacology/Toxicology Team Leader, HFD-530-
Robert Kumi, Ph.D., Pharmacokinetics Reviewer, HFD-530
Kellie Reynolds, Pharm.D., Pharmacokinetics Team Leader, HFD-530
Susan Zhou, Ph.D., Statistical Reviewer, HFD-530-
Greg Soon, Ph.D., Statistical Reviewer Team Leader, HFD-530
Neville Gibbs, M.D., Medical Officer, HFD-530
Katherine Laessig, M.D., Ph.D., Medical Team Leader, HFD-530

NDA: 21-503

Drug: Viracept (nelfinavir)

Subject: Suggested revisions for the Viracept PPI

The Division of Antiviral Drug Products recommends the following revisions to the Viracept patient package insert:

On page 2, lines 73-77 should be changed to read: "If you are unable to swallow the 250 mg tablets, dissolve in a small amount of water. Once dissolved, mix the cloudy liquid well, and consume immediately. The glass should be rinsed with water and the rinse swallowed to insure the entire dose is consumed."

On page 2, remove the sentence that corresponds with line numbers 85-87,

On page 5, lines 242-243 should be changed to read: "Diarrhea may be more common in patients receiving the 625 mg formulation."

On page 6, under the section "How should VIRACEPT be stored? ", please add the bulleted statement ' ———— in original container."

A copy of the revised Patient Package Insert in attached.

We are providing this information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Jeff D. O'Neill, ACRN
Regulatory Project Manager
Division of Antiviral Drug Products

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APPEARS THIS WAY
ON ORIGINAL

MEMORANDUM

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

DATE: 04-13-03

FROM: Katherine A. Laessig, M.D.
Division of Antiviral Drug Products, HFD-530

TO: Division File

SUBJECT: Group Leader Memo for NDA 21-503 Viracept (nelfinavir mesylate) 625-mg tablets

1.0 Background

Viracept is a member of the antiretroviral class of protease inhibitors and is indicated for the treatment of HIV-1 infection in combination with other antiretroviral agents. This NDA submission contains data to support the marketing approval for an alternate dosing formulation, the 625-mg tablet. The 250-mg tablet and oral powder received marketing approval in 1997, based on substantive evidence of efficacy and safety. Because results of the bioequivalence study of the 250-mg tablet and the 625-mg tablet revealed increased bioavailability with the 625-mg formulation, the sponsor has submitted clinical safety and pharmacokinetic data in this NDA to provide evidence that the higher exposures do not pose a safety risk. No efficacy information is contained in this submission because it is unlikely that a more bioavailable formulation would be less efficacious. The efficacy of nelfinavir has been previously demonstrated and reviewed in NDAs 20778/9.

2.0 Summary of Study Results

In order to provide evidence that the increased bioavailability of the 625 mg formulation does not have a worse toxicity profile than the 250 mg formulation, the sponsor pooled and reanalyzed data from previously reported and reviewed study results. The previously reported studies included 4 phase 2 studies (503, 510, 0073A, and 0073B), and 2 phase 3 studies (511 and 542). These studies were chosen because they included pharmacokinetic assessments and were therefore amenable to exposure response analysis. Subjects from studies 503, 510, 511, and 542 were pooled into Pooled Population 1 (PPE1), and subjects from studies 0073A and B were pooled into Pooled Population 2 (PPE2). Subjects in PPE 2 were analyzed separately since they received delavirdine in

addition to nelfinavir and had nelfinavir exposures 2-3X that of nelfinavir administered alone.

The sponsor grouped the adverse events from these studies based on the range of AUC_{24} values expected after exposure to a single dose of nelfinavir. The lowest quartile included values <41 mg*hr/L, the middle 2 quartiles of 41-61 mg*hr/L, and the upper quartile of >61 mg*hr/L. The median expected AUC_{24} for the 625 mg tablet is approximately 58 mg*hr/L. Review of the frequency of AEs categorized by AE exposure revealed a trend toward increased frequency of diarrhea at higher exposures of nelfinavir. To confirm these findings, a pharmacometrics consult was obtained in order to conduct a formal exposure response analysis. As reported by Jenny J. Zheng, Ph.D., the probability of diarrhea based on mean AUC_{24} values for both the 250 and 625-mg tablets revealed an increase of 6% for the 625-mg tablet compared to the 250 mg tablet. The point estimate for the probability of developing diarrhea with the 250-mg tablet is 31%, while the point estimate for the 625-mg tablet is 37%. Rates of other adverse events did not appear to be consistently increased with higher exposures of nelfinavir.

3.0 **Recommendation**

The results of the sponsor's analysis and the FDA reviews support the safety of nelfinavir 625-mg tablets for the treatment of HIV-1 infection. Because of the potential for rates of diarrhea to be increased with treatment using the 625-mg tablet, language to this effect will be added to the product labeling. I concur with the findings of the medical officer review by Neville Gibbs, M.D., M.P.H., that this application should be approved.

Katherine Laessig, M.D.

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

/s/

Kathrine Laessig
5/7/03 09:43:59 AM
MEDICAL OFFICER

Jeffrey Murray
5/7/03 09:55:06 AM
MEDICAL OFFICER

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: April 9, 2003

To: Marie-Do Mompas, Pharm.D.	**From:** Jeff D. O'Neill, ACRN
Company: Agouron Pharmaceuticals	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2510
Phone number: 858-622-7360	**Phone number:** 301-827-2362

Subject: Clinical pharmacology comments are regarding NDA 21-503

Total no. of pages including cover: 2

Comments: The following clinical pharmacology comments for NDA 21-503 are on behalf of Robert Kumi, Ph.D.

Document to be mailed: ☐ YES ☑ NO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: April 9, 2003

To: Marie-Do Mompas, PharmD., Worldwide Regulatory Affairs

Through: Kellie S. Reynolds, Pharm.D., Clinical Pharmacology Team Leader, HFD-530
Robert Kumi, Ph.D., Clinical Pharmacology Reviewer, HFD-530

NDA: 21-503 Viracept®

Subject: Clinical pharmacology comments regarding NDA 21-503.

The following clinical comments are being provided on behalf of Robert Kumi, Ph.D.:

We have reviewed the dissolution information you submitted in NDA 21-503. We find the dissolution method acceptable, however, we think the data indicate that a dissolution specification of Q = — % in 45 minutes is more appropriate than Q = — % in 45 minutes. We are aware that a Q = — % specification may require S2 level testing on occasion and consider this approach acceptable to ensure product quality.

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Jeff D. O'Neill, ACRN
Regulatory Project Manager
Division of Antiviral Drug Products

APPEARS THIS WAY
ON ORIGINAL

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: March 28, 2003

To: Marie-Do Mompas, Director, Regulatory Strategy	**From:** Jeff D. O'Neill Regulatory Project Manager
Company: Hoffman-La Roche	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2523
Phone number: 858-622-7360	**Phone number:** 301-827-2362

Subject: NDA 21-503 Labeling revisions

Total no. of pages including cover: 30

Comments: These are DAVDP's preliminary revisions for the Viracept (nelfinavir)PI.

Document to be mailed: ☐ YES ☑ NO

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: March 26, 2003

To: Marie-Do Mompas, Director, Regulatory Strategy
Agouron Pharmaceuticals, Inc., a Pfizer Company

From: Jeff D. O'Neill, Regulatory Project Manager, HFD-530

Through: Lisa Naeger, Ph.D., Microbiology Reviewer, HFD-530
Jules O'Rear, Ph.D., Microbiology Team Leader, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530
Stephen P. Miller, Ph.D., Chemistry Team Leader, HFD-530
Ita Yuen, Ph.D., Pharmacology/Toxicology Reviewer, HFD-530
James Farrelly, Ph.D., Pharmacology/Toxicology Team Leader, HFD-530
Robert Kumi, Ph.D., Pharmacokinetics Reviewer, HFD-530
Kellie Reynolds, Pharm.D., Pharmacokinetics Team Leader, HFD-530
Susan Zhou, Ph.D., Statistical Reviewer, HFD-530
Greg Soon, Ph.D., Statistical Reviewer Team Leader, HFD-530
Neville Gibbs, M.D., Medical Officer, HFD-530
Katherine Laessig, M.D., Ph.D., Medical Team Leader, HFD-530

NDA: 21-503

Drug: Viracept (nelfinavir)

Subject: Suggested revisions for the Viracept PI

The Division of Antiviral Drug Products recommends the following revisions to the Viracept package insert (see attached pages). Recommendations for the patient package insert to follow at a later date. We have included Notes to Sponsor within the label for changes we felt require some explanation.

We are providing this information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Jeff D. O'Neill, ACRN
Regulatory Project Manager
Division of Antiviral Drug Products

APPEARS THIS WAY
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: February 6, 2003

To: Marie-Do Mompas, Pharm.D.	**From:** Jeff D. O'Neill, ACRN
Company: Agouron Pharmaceuticals	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2362
Phone number: 858-622-7360	**Phone number:** 301-827-2481

Subject: Clinical comment regarding NDA 21-503

Total no. of pages including cover: 2

Comments: The following clinical comments for NDA 21-503 are on behalf of Neville A. Gibbs, M.D., M.P.H.:

Document to be mailed: ☐ YES ☑ NO

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: February 6, 2003

To: Marie-Do Mompas, PharmD., Worldwide Regulatory Affairs

Through: Katherine A. Laessig, M.D., Medical Team Leader, HFD-530
Neville A. Gibbs, M.D., M.P.H., Medical Officer, HFD-530

NDA: 21-503 Viracept®

Subject: Clinical comment regarding NDA 21-503

The following clinical comments are being provided on behalf of Neville A. Gibbs, M.D., M.P.H.:

The Division is concerned that the episodes of QT prolongation and Torsades de Pointes reported via post-marketing surveillance may indicate a safety signal.

We are attempting to obtain all available information to make a determination about nelfinavir's role in these events. To that end, please provide detailed narratives of all subjects presenting with serious cardiac adverse events that were reported in trials submitted as part of NDA 21-503.

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Jeff D. O'Neill, ACRN
Regulatory Project Manager
Division of Antiviral Drug Products

APPEARS THIS WAY
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: November 27, 2002

To: Marie-Do Mompas, PharmD.	**From:** Sean J. Belouin, R.Ph
Company: Agouron Pharmaceuticals	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2523
Phone number: 858-622-7383	**Phone number:** 301-827-2481

Subject: Chemistry comment regarding NDA 21-503

Total no. of pages including cover: 2

Comments: The following chemistry comment for NDA 21-503 is on behalf of George Lunn, Ph.D:

Document to be mailed: ☐ YES ☑ NO

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: November 27, 2002

To: Marie-Do Mompas, PharmD., Worldwide Regulatory Affairs

Through: Steve Miller, Ph.D., Chemistry Team Leader, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530

NDA: 21-503 Viracept ®

Subject: Chemistry comment regarding NDA 21-503

The following chemistry comment for NDA 21-503 is on behalf of George Lunn, Ph.D:

CHEMISTRY

— of data are supplied for the 625 mg film-coated tablets stored at 25°C/60% RH, 30°C/60% RH, and 40°C/75% RH. The following ranges of data were observed.

Test	Acceptance Criterion	25°C	30°C	40°C
—	— %	ND	ND	ND
—	%	[		]
—	%			
Total degradants	—			

APPEARS THIS WAY
ON ORIGINAL

For the 250 mg film-coated tablets in NDA 20-779 Annual Report 005 the following ranges were found for the tablets stored at 25°C/60% RH for up to —

Test	Acceptance Criterion	Marketed Batches	Registrational Batches
/	[redacted] %	[redacted]	[redacted]
	%		
	%		
Total degradants	%		

For the 250 mg uncoated tablets in NDA 20-779 Annual Report 003 the following values were found for the primary stability AND marketed product batches (under all conditions) for periods ranging up to

Test	Acceptance Criterion	Ranges of values
/	[redacted] %	[redacted]
	%	
	%	
Total degradants	%	

In view of the excellent stability of both the 250 mg and 625 mg film-coated nelfinavir tablets please consider proposing new acceptance criteria for — and total degradants to apply both to the 250 mg tablets (NDA 20-779) and the 625 mg tablets (NDA 21-503).

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Sean J. Belouin, R.Ph.
Regulatory Project Manager
Division of Antiviral Drug Products

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: November 6, 2002

To: Marie-Do Mompas, PharmD.	**From:** Sean J. Belouin, R.Ph
Company: Agouron Pharmaceuticals	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2523
Phone number: 858-622-7383	**Phone number:** 301-827-2481

Subject: Chemistry comment regarding NDA 21-503: Viracept 625mg Bottle Label

Total no. of pages including cover: 2

Comments: The following chemistry comment for NDA 21-503 is on behalf of George Lunn, Ph.D:

Document to be mailed: ☐ YES ☑ NO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: November 6, 2002

To: Marie-Do Mompas, PharmD., Worldwide Regulatory Affairs

Through: Steve Miller, Ph.D., Chemistry Team Leader, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530

NDA: 21-503 Viracept ®

Subject: Chemistry comment regarding NDA 21-503: Viracept 625mg Bottle Label

---

The following chemistry comment for NDA 21-503 is on behalf of George Lunn, Ph.D:

CHEMISTRY

1. Currently, your proposed Viracept 625mg bottle label has ——————— ——— The bottle label for the currently marketed 250mg tablets is the reverse. The review team feels the color reversal is not enough to discern between the two package strengths. Please consider selecting another color, different than ——————— for the lettering on the new Viracept 625mg bottle.

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Sean J. Belouin, R.Ph.
Regulatory Project Manager
Division of Antiviral Drug Products

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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: August 27, 2002

To: Marie-Do Mompas, PharmD.	**From:** Sean J. Belouin, R.Ph
Company: Agouron Pharmaceuticals	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2523
Phone number: 858-622-7383	**Phone number:** 301-827-2481

Subject: Microbiology comments regarding NDA 21-503

Total no. of pages including cover: 2

Comments: The following microbiology comments for NDA 21-503 are on behalf of Julian O'Rear, Ph.D:

Document to be mailed: ☐ YES ☑ NO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: August 27, 2002

To: Marie-Do Mompas, PharmD., Worldwide Regulatory Affairs

Through: Julian O'Rear, Ph.D., Microbiology Team Leader, HFD-530

NDA: 21-503 Viracept ®

Subject: Microbiology comments regarding NDA 21-503

The following microbiology comments for NDA 21-503 are on behalf of Julian O'Rear, Ph.D:

MICROBIOLOGY

1. Please determine the *in vitro* combination activity relationships of Viracept with all the drugs approved since Viracept's initial approval.

2. Please determine the cross-resistance of Viracept to isolates resistant to recently approved protease inhibitors, and determine the efficacy of recently approved protease inhibitors to isolates resistant to Viracept.

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Sean J. Belouin, R.Ph.
Regulatory Project Manager
Division of Antiviral Drug Products

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DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Antiviral Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF 45 DAY FILING MEETING MINUTES

NDA: 21-503

DATE: August 26, 2002

DRUG: Viracept® (nelfinavir mesylate)

INDICATION: Treatment of HIV-1 Infection

SPONSOR: Agouron Pharmaceuticals, Inc.

PARTICIPANTS: Jeffrey Murray, M.D., M.P.H., Deputy Division Director, HFD-530
Katherine Laessig, M.D., Medical Team Leader, HFD-530
Neville Gibbs, M.D., Medical Reviewer, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530
Ita Yuen, Ph.D., Pharmacology Reviewer, HFD-530
Kellie Reynolds, PharmD., Clinical Pharmacology Team Leader, HFD-530
Robert Kumi, Ph.D., Clinical Pharmacology Reviewer, HFD-530
Julian O'Rear, Ph.D., Microbiology Team Leader, HFD-530
Greg Soon, Ph.D., Statistical Team Leader, HFD-530
Sean Belouin, R.Ph., Regulatory Project Manager, HFD-530

Related Documents: IND 48,124

BACKGROUND:

VIRACEPT® (nelfinavir mesylate), a protease inhibitor for the treatment of HIV infection, is currently approved as a 250 mg strength (as nelfinavir free base) light blue, capsule-shaped tablet with a clear film coating (NDA 20-779) and as a 50 mg/g strength (as nelfinavir free base) oral powder (NDA 20-778). The currently recommended dose for VIRACEPT Tablets in adults is 1250 mg (five 250 mg tablets) twice daily or 750 mg (three 250 mg tablets) three-times daily in combination with nucleoside analogues.

Agouron initiated a program to develop a 625 mg strength tablet to decrease the pill burden from ten tablets to four tablets daily for HIV-infected patients using a twice daily regimen of VIRACEPT.

VIRACEPT 625 mg tablets contain the same components as the commercial VIRACEPT 250mg tablets with the addition of — , silicon dioxide and the deletion of a dye. The ratio of nelfinavir mesylate to calcium silicate is higher in the 625 mg tablet formulation — compared to that in the commercial 250 mg VIRACEPT Tablet formulation — In addition, there

are differences in the ——— manufacturing process for the 625 mg tablet versus the 250 mg tablet.

As previously agreed with FDA on June 27, 2000, two single-dose bioequivalence studies have been conducted comparing the commercially available VIRACEPT 250 mg tablets to the proposed 625 mg nelfinavir mesylate tablets in both fasted and fed conditions. In these studies, the 625 mg tablets of nelfinavir mesylate exhibited increased bioavailability versus the commercially available VIRACEPT 250 mg tablet formulation. Due to the potential for higher exposure with the 625 mg tablet dosage regimen, a retrospective assessment of safety data from studies in which patients received VIRACEPT in combination with other antiretroviral therapy has been conducted. These studies include the two VIRACEPT pivotal clinical studies (Studies 511 and 542) as well as two clinical pharmacokinetics studies in which patients received high doses of VIRACEPT (Studies 503 and 510). In addition, in response to FDA's request, 4 studies in which patients received nelfinavir and delavirdine (Studies 70, 73A, 73B, and 711) have been identified and the data from these studies have been incorporated into the overall PK and safety analysis.

A user fee was required with this application because this application requires new clinical data for approval. The appropriate user fee was paid on June 11, 2002 for this application. The user fee I.D. number assigned is 4322. The necessary financial disclosure documentation and debarment certification was included with this application. This application has been granted a standard review with an action date of May 1, 2003. This meeting was held to determine whether this application was fileable.

DISCUSSIONS:

1. **Pharmacology**

   Not applicable. No pharmacology data being reviewed for this application.

2. **Microbiology**

   Dr. O'Rear indicated that there was no data for Microbiology to review but indicated that two issues needed to be addressed by the applicant. The team agreed that the following two comments could be addressed by the applicant in this NDA application:

   a. Please determine the *in vitro* combination activity relationships of Viracept with all the drugs approved since Viracept's initial approval.

   b. Please determine the cross-resistance of Viracept to isolates resistant to recently approved protease inhibitors, and determine the efficacy of recently approved protease inhibitors to isolates resistant to Viracept.

3. **Chemistry**

   Dr. Lunn found the application fileable. Dr. Lunn indicated that several inspections were going to be necessary prior to approval given the various facilities to be used in manufacturing the new formulation. There were no comments for the applicant at this time.

4. **Clinical Pharmacology**

Dr. Kumi indicated that a pharmacometrics consult will be required to review two population pharmacokinetic study reports. Dr. Kumi found the application fileable.

5. **Statistical**

Not applicable. No statistical data being reviewed for this application.

6. **Clinical**

Dr. Gibbs found the application fileable.

CONCLUSION

The review team concluded that NDA 21-503 was fileable. The applicant will be notified of the application's filing status and ten-month PDUFA action date. Although this application allows for a decreased pill burden, that alone did not warrant a six-month PDUFA action date.

ACTION ITEMS

A facsimile with the two Microbiology comments will be faxed to the sponsor.

Signature, minutes preparer:_____

Date:_____

Concurrence:

HFD-530/DepDivDir/Murray-JSM-9/3/2002
HFD-530/MOTL/Laessig-KAL-8/28/2002
HFD-530/MO/Gibbs-NG-8/28/2002
HFD-530/Chem/Lunn-GL-8/22/2002
HFD-530/Pharmtox/Yuen-IY-8/28/2002
HFD-530/BiopharmTL/Reynolds-KSR-8/29/2002
HFD-530/Biopharm/Kumi-ROK-8/28/2002
HFD-530/Micro/O'Rear-JJO-8/28/2002
HFD-530/Stats/Soon-GS-8/28/2002
HFD-530/RPM/Belouin-SJB-9/3/2002

APPEARS THIS WAY
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: July 18, 2002

To: Marie-Do Mompas, PharmD.	**From:** Sean J. Belouin, R.Ph
Company: Agouron Pharmaceuticals	Division of Antiviral Drug Products
Fax number: 858-678-8285	**Fax number:** 301-827-2523
Phone number: 858-622-7383	**Phone number:** 301-827-2481

Subject: Chemistry comment regarding NDA 21-503

Total no. of pages including cover: 3

Comments: The following chemistry comment for NDA 21-503 is on behalf of George Lunn, Ph.D:

Document to be mailed: ☐ YES ☑ NO

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES | Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: July 18, 2002

To: Marie-Do Mompas, PharmD., Worldwide Regulatory Affairs

Through: Steve Miller, Ph.D., Chemistry Team Leader, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530

NDA: 21-503 Viracept ®

Subject: Chemistry comment regarding NDA 21-503

The following chemistry comment for NDA 21-503 is on behalf of George Lunn, Ph.D:

CHEMISTRY

1. Please confirm that the following facilities are the ONLY sites involved in the manufacturing, testing and packaging of drug product for your NDA 21-503. Please confirm that the address and the functions listed below for each site are correct, and that both facilities are ready for inspection:

[ ]

Contact: ——— Vice President, Quality Assurance/Compliance
Tel: ———
Fax : ———

CFN ———

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[redacted]

CFN [redacted]

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Sean J. Belouin, R.Ph.
Regulatory Project Manager
Division of Antiviral Drug Products

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

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pduta/default.htm

1. APPLICANT'S NAME AND ADDRESS

Agouron Pharmaceuticals, Inc.
10350 North Torrey Pines Road
La Jolla, CA 92037-1020

2. TELEPHONE NUMBER *(Include Area Code)*

(858) 622-7360

3. PRODUCT NAME

VIRACEPT®
nelfinavir mesylate

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

N021503

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☑ YES ☐ NO

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:

☑ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

4322

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

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ 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.)*

☐ 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.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☑ NO

(See item 8, reverse side if answered YES)

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:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
[signature]	Director, Regulatory Strategy	28 June 2002

FORM FDA 3397 (4/01)

Created by: PSC Media Arts (301) 443-2454 EF

APPEARS THIS WAY
ON ORIGINAL

PPG Regulatory Library
Pfizer Inc
150 East 42nd Street 3-46
New York, NY 10017
Tel 212 733 3946 Fax 212 857 3516
Email felicia.feldman@pfizer.com

Felicia A. Feldman
Director

June 4, 2002

Food and Drug Administration
Mellon Client Services Center
Room 670
500 Ross Street
Pittsburgh, PA 15262-0001

Re: Prescription Drug User Fees

Dear Sir or Madam:

As required by the Prescription Drug User Fee Act of 1997, enclosed is the entire application fee of $313,320 for Agouron Pharmaceuticals Inc. (a Pfizer company's) New Drug Application for Viracept 625mg capsule. The NDA number for this submission is 21-503 and has been assigned User Fee ID Number 4322. This submission will be filed to the Food and Drug Administration on or about June 25, 2002.

If you require further assistance, please feel free to contact me.

Sincerely,

Felicia A. Feldman
Enc.

cc: John Wollebem
Terry Monk

APPEARS THIS WAY
ON ORIGINAL

BEST POSSIBLE COPY

Agouron
Pharmaceuticals, Inc.
A Pfizer Company

Agouron Pharmaceuticals
A Pfizer Company
P.O. Box 341804
Bartlett, TN 38184-1804

000001
P11171956

FOR INQUIRIES CONCERNING THIS PAYMENT
TELEPHONE (901) 215-1111

Vendor #	Voucher # Invoice #	Invoice Date	Invoice Amount	Discount	Net Amount
0000199426	0046033468 05-20-02 NDA 21-503 VIRACEPT 625MG USER FEE NUMBER 4322	05/20/02	313,320.00	0.00	313,320.00

Page 0001 of 0001

AD01 000078705 313,320.00 0.00 313,320.00

AD01000078705

Agouron
Pharmaceuticals, Inc.
A Pfizer Company

Wachovia Bank N.A.
Winston-Salem NC

61-903
531

Agouron Pharmaceuticals
P.O. Box 341804
Bartlett, TN 38184-1804

Mo	Day	Year	
05	28	02	Pay Exactly: Three Hundred Thirteen Thousand Three Hundred Twenty and NO/100 Dollars

Amount ******313,320.00

Agouron Pharmaceuticals
A Pfizer Company

Richard A. Pairn
Authorized Corporate Signatory

To the Order of FOOD AND DRUG ADMINISTRATION
0000199426 MELLON CLIENT SVCS CTR 360909
000078705 500 ROSS ST
ROOM 670
PITTSBURGH PA 15262-0001

⑈000078705⑈ ⑆053109084⑆ 8732 008940⑈

APPEARS THIS WAY
ON ORIGINAL

BEST POSSIBLE COPY

MEMORANDUM OF TELECON

DATE: March 26, 2002

APPLICATION NUMBER: IND 48,124-nelfinavir mesylate tablets

BETWEEN:
Name:

Gary Chikami, M.D., Executive Director, Clinical Dev., Antiinfectives
Alice Chu, M.S., Senior Statistician, Clinical Biostatistics
Poe Hsyu, Ph.D., Director, Clinical Research
Vicki Kelemen, Director, Strategic Business Planning
Marie-Do Mompas, PharmD., Director, Regulatory Affairs
Carolyn Petersen, M.D., Director, Medical Affairs
Siglia Piraino, M.D., Medical Monitor
Tom Thayer, Senior Clinical Research Scientist
John Tomaszewski, Director, Regulatory Affairs
Mark Longer, Ph.D., Pharmaceutical Sciences
Paul Chen, Ph.D., Director, CMC

Phone: 858-622-7360
Representing: Agouron Pharmaceuticals, Inc.

AND

Name: Jeff Murray, M.D., M.P.H., Deputy Division Director, HFD-530
Katherine Laessig, M.D., Medical Reviewer, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530
Kellie Reynolds, PharmD., Biopharm Team Leader, HFD-530
Robert Kumi, Ph.D., Biopharm Reviewer, HFD-530

Representing: Division of Antiviral Drug Products (DAVDP), HFD-530

SUBJECT: Discussion of pharmacokinetic data needed for filing of the 625mg tablet

BACKGROUND AND SUMMARY OF TELEPHONE CONVERSATION

Previously, the DAVDP review team had safety and pharmacokinetic concerns regarding the proposed filing of the 625mg tablet NDA. This teleconference is a follow-up to the February 22, 2002 teleconference held with the sponsor. The sponsor submitted a response to our February 22, 2002 teleconference request for additional safety and pharmacokinetic information in patients with higher drug exposure from studies in which the pharmacokinetics of nelfinavir was enhanced by another agent.

Discussion:

1. The sponsor was informed that, upon review of the data submitted thus far, they have enough supporting pharmacokinetic and chemistry data to submit an application for the 625mg tablet of nelfinavir mesylate. The Division has some additional comments regarding the dissolution and would provide those comments by facsimile within the next couple days.

2. DAVDP informed Agouron that because the new 625mg tablet has differences in excipients that require separate clinical studies of safety, a new NDA will be required. The need for the additional safety studies is because the new formulation is more bioavailable than the original formulation of 250mg tablets. Subsequently, because a new NDA will be required, a full USER FEE must accompany the application.

3. DAVDP requested that individual safety data be included with the NDA as line listings. **Agouron agreed to submit that data with the NDA.**

4. **The sponsor indicated that they might be filing the NDA within the next three months once they compile their data including — stability data on the new 625mg tablet formulation.**

5. **Additionally, the sponsor inquired if the NDA could be filed with — stability data for the 625mg tablet and then an amendment submitted during the review cycle when — stability data was available.** DAVDP agrees that this is acceptable under the provisions of ICH Q1C.

6. Lastly, Agouron was informed that a standard review of 10 months was anticipated for this application, noting that consideration was given to the fact that the new 625mg tablet would decrease the patient's pill burden. A final determination of the review clock would take place during the filing meeting for the NDA.

Sean J. Belouin, R.Ph
Regulatory Project Manager
Division of Antiviral Drug Products

MEMORANDUM OF TELECON

DATE: February 22, 2002

APPLICATION NUMBER: IND 48,124-nelfinavir mesylate tablets

BETWEEN:
Name:

Alice Chu, M.S., Senior Statistician, Clinical Biostatistics
Grace Furman, Ph.D., Asst. Director, Safety Evaluation (Toxicology)
Poe Hsyu, Ph.D., Director, Clinical Research
Vicki Kelemen, Director, Business Planning
Ann Kolokathis, M.D., Vice President, Medical Affairs
Mark Longer, Ph.D., Director, Regulatory CMC
Kimberly Manhard, Senior Director, Regulatory Affairs
Marie-Do Mompas, Pharm.D., Director, Regulatory Affairs
Carolyn Petersen, M.D., Director, Medical Affairs

Phone: 858-622-7360
Representing: Agouron Pharmaceuticals, Inc.

AND

Name: Grace Carmouze, Regulatory Project Manager, HFD-530
Kim Struble, PharmD., Acting Medical Team Leader, HFD-530
Katherine Laessig, M.D., Medical Reviewer, HFD-530
Steve Miller, Ph.D., Chemistry Team Leader, HFD-530
George Lunn, Ph.D., Chemistry Reviewer, HFD-530
Kellie Reynolds, PharmD., Biopharm Team Leader, HFD-530
Robert Kumi, Ph.D., Biopharm Reviewer, HFD-530

Representing: Division of Antiviral Drug Products (DAVDP), HFD-530

SUBJECT: Discussion of data needed for filing of the 625mg tablet

BACKGROUND AND SUMMARY OF TELEPHONE CONVERSATION

The DAVDP review team had concerns about several issues regarding the proposed filing of the 625mg tablet NDA. The following comments were faxed to the applicant on February 20, 2002:

Clinical Comments:

Since the results of studies 712 and 713 indicate that the 625-mg tablet is more bioavailable than the 250-mg tablet, we are requesting some additional safety information, as follows:

1. We appreciate the analysis of the safety of nelfinavir according to various exposure levels. However, we were unable to determine the number of patients who actually received each dose. Please reanalyze and submit the safety data according to the actual doses that patients received in studies 503, 510, 511, and 542. Once we have reviewed these analyses, we will be able to determine if there is enough safety information to support the filing of the 625-mg tablet.
2. Please collect and analyze any available PK and safety data for the coadministration of nelfinavir and ritonavir. Such data could be used to provide additional safety information about nelfinavir at higher exposures.

In addition, we request your response to the following:

3. Please indicate if you plan to phase out the 250-mg tablets.

Clinical Pharmacology Comment:

4. Please submit exposure-response data and analyses using the geometric mean exposure of approved nelfinavir regimens (1250 mg twice-daily and 750 mg three-times daily) as the reference exposure. These analyses should indicate the number of patients at each dose level and include patient line listings, if available.

Agouron responded with a February 21, 2002 facsimile partially addressing the questions asked by the Division. The responses from the applicant are as follows:

Clinical Comments:

1. **We appreciate the analysis of the safety of nelfinavir according to various exposure levels. However, we were unable to determine the number of patients who actually received each dose. Please reanalyze and submit the safety data according to the actual dose that patients received in studies 503, 510, 511, and 542. Once we have reviewed these analyses, we will be able to determine if there is enough safety information to support the filing of the 625-mg tablet.**

   We are providing in Attachment 1 the following information in response to the above question:

   1. A table indicating the doses and numbers of patients at each dose for each of the 4 studies.
   2. Data listings which break down the patients by dose and adverse event of ≥ grade 2 and marked changes in laboratory parameters.

2. **Please collect and analyze any available PK and safety data for the coadministration of nelfinavir and ritonavir. Such data could be used to provide additional safety information about nelfinavir at higher exposures.**

   Two studies of nelfinavir + ritonavir QD in healthy volunteers were conducted by Agouron: AG1343-708 and AG1343-711 (see attachment 2).

AG1343-708: A pharmacokinetic study of the interaction between VIRACEPT and Norvir®.

AG1343-711: A pharmacokinetic study of the interactions between VIRACEPT, ritonavir, and delavirdine.

Study reports for these two studies are under preparation. The PK and safety data from these studies will be provided to FDA as soon as they can be compiled.

We are enclosing a manuscript published in JAIDS in 2000 by Raines et al. in Attachment 2. It evaluated the combination of NVF 750 & 500 mg + RTV 400 mg BID given to HIV patients for 48 weeks. In addition, we are collecting other reports in abstract/poster form that will be provided along with the analysis of AG1343-708 and AG1343-711.

3. **Please indicate if you plan to phase out the 250-mg tablets.**

No, we do not plan to phase out the VIRACEPT 250 mg tablets currently on the market as the 250 mg tablet formulation is needed by pediatric patients as well as adult patients receiving the recommended TID regimen.

The commercial VIRACEPT 250 mg tablet and the proposed 625 mg tablet formulation of nelfinavir mesylate can be easily differentiated by their color: the currently marketed VIRACEPT 250 mg tablet is a light-blue capsule-shaped tablet. The proposed 625 mg strength formulation of nelfinavir mesylate is a white capsule-shaped tablet.

Clinical Pharmacology Comment:

4. **Please submit exposure-response data and analyses using the geometric mean exposure of approved nelfinavir regimens (1250 mg twice-daily and 750 mg three-times daily) as the reference exposure. These analyses should indicate the number of patients at each dose level and include patient line listings, if available.**

The following information is provided in Attachment 3: A description of the methodology for determining a therapeutic geometric mean from PK data for patients on approved VIRACEPT regimens. This is followed by the requested tables which mirror tables 13 and 15 from the background document submitted to FDA in January 2002. In addition, we have pooled the data for diarrhea from this second analysis and presented it in a tabular form to indicate its relationship to the analysis presented in the background document. We have provided a series of tables which report, by study, the patients with diarrhea of $\geq$ grade 2 and AUC > 61 mg*h/L with actual AUCs, CD4 counts and doses. The data presentation is followed by the data listings of patients with adverse events of $\geq$ grade 2 with dose, and AUC information.

Discussion:

1. Regarding BA data for the 625mg Tablet, DAVDP requested that the sponsor use PK modeling to simulate nelfinavir AUCs at steady state.

2. Dissolution Methodology and Dissolution Rates:
   There was an observed difference in dissolution rate between the 625 mg and 250 mg tablet formulation under the same conditions. Why? The sponsor indicated that the composition of these two strengths differed in active ingredient vs. excipient ratio: the excipient differences may affect dissolution. Additionally, the sponsor indicated that dissolution rates differ among tablets of the same strength (same formulation) because of general observed variability. It was noted that this variability is within the range typically observed with 250 mg tablets.

3. DAVDP asked the sponsor to submit PK data on nelfinavir's active metabolite, if available for the BE study. It was noted that this request is not a requirement. The sponsor agreed to submit this information.

CMC:

4. DAVDP queried the sponsor regarding what stability data were available. The sponsor indicated that they had — data on three lots and — data on two supporting batches.

Clinical:

5. DAVDP stated that they will continue to review Serial No. 472 and the NLV/RTV report for studies 708 and 711. The sponsor indicated that they had safety on NLV and DLV and will submit these data.

6. DAVDP requested that the sponsor submit all exposure-response data evaluating the safety of higher NLV exposure before submitting an NDA package for the 625mg tablet. Once these supportive data are submitted, it will be a review issue whether the data submitted are sufficient to support approval.

Conclusion:

It was agreed that after exposure-response data and the safety data on DLV and NLV are submitted, another telecon will be scheduled.

Sean J. Belouin, R.Ph
Regulatory Project Manager
Division of Antiviral Drug Products

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-503

Agouron Pharmaceuticals, Inc.
Attention: Marie-Do Mompas, PharmD
Associate Director, Worldwide Regulatory Affairs
10350 North Torrey Pines Road
La Jolla, CA 92037-1020

Dear Ms. Mompas:

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: Viracept® (nelfinavir mesylate) tablets and oral powder

Review Priority Classification: Standard (S)

Date of Application: June 8, 2002

Date of Receipt: July 1, 2002

Our Reference Number: NDA 21-503

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 August 29, 2002 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be May 1, 2003 and the secondary user fee goal date will be July 1, 2003.

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:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Drug Products, HFD-530
Attention: Division Document Room HFD-530
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Drug Products, HFD-530
Attention: Division Document Room HFD-530
9201 Corporate Blvd.
Rockville, Maryland 20850-3202

If you have any questions, call Sean J. Belouin, R.Ph, Regulatory Project Manager, at 301-827-2335.

Sincerely,

{See appended electronic signature page}

Anthony W. DeCicco, R.Ph.
Chief, Project Management Staff
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

107 Page(s) Withheld

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

____ § 552(b)(5) Deliberative Process

____ § 552(b)(5) Draft Labeling