

APPLICATION NUMBER:
22-417

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

**PATENT INFORMATION SUBMITTED UPON AND
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation or
Composition) and/or Method of Use*

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/10
See OMB Statement on Page 3.

NDA NUMBER

22-417

NAME OF APPLICANT/NDA HOLDER

Abbott Laboratories

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

ritonavir

STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

5,541,206

b. Issue Date of Patent

July 30, 1996

c. Expiration Date of Patent

July 30, 2013

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

FAX Number (if available)

Telephone Number

(847) 938-3508

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.37? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) claims 18-19 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Treatment of HIV-infection in combination with other antiretroviral agents in accordance with the approved labeling including the Drug Interactions, Indications and Usage, Clinical Studies, and Dosage and Administration sections.

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
Treatment of HIV infection in combination with other antiretroviral agents.

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)

Date Signed

3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Paul D. Yasger

Address

Dept. D377, Bldg. AP6A-1
100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

Telephone Number

(847) 938-3508

FAX Number (if available)

E-Mail Address (if available)

paul.yasger@abbott.com

The public reporting burden for this collection of information has been estimated to average 5 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 Services
Food and Drug Administration
Office of Chief Information Officer (HFA-710)
5600 Fishers Lane
Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542
PATENT INFORMATION SUBMITTED UPON AND AFTER
APPROVAL OF AN NDA OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/10
See OMB Statement on Page 3.

**PATENT INFORMATION SUBMITTED UPON AND
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22-417

NAME OF APPLICANT/NDA HOLDER

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TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

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STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

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For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

5,635,523

b. Issue Date of Patent

June 3, 1997

c. Expiration Date of Patent

June 3, 2014

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

FAX Number (if available)

Telephone Number

(847) 938-3508

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) claims 1-10 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Treatment of HIV-infection in combination with other antiretroviral agents in accordance with the approved labeling including the Drug Interactions, Indications and Usage, and Clinical Studies sections.

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
 Treatment of HIV-Infection in combination with other antiretroviral agents

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)



Date Signed: 3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Paul D. Yasger	
Address Dept. D377, Bldg. AP6A-1 100 Abbott Park Road	City/State Abbott Park, IL
ZIP Code 60064	Telephone Number (847) 938-3508
FAX Number (if available)	E-Mail Address (if available) paul.yasger@abbott.com

The public reporting burden for this collection of information has been estimated to average 5 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 Services
 Food and Drug Administration
 Office of Chief Information Officer (HFA-710)
 5600 Fishers Lane
 Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542

PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services
Food and Drug Administration

**PATENT INFORMATION SUBMITTED UPON AND
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NAME OF APPLICANT/NDA HOLDER

Abbott Laboratories

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TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

ritonavir

STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

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1. GENERAL

a. United States Patent Number

5,648,497

b. Issue Date of Patent

July 15, 1997

c. Expiration Date of Patent

July 15, 2014

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

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FAX Number (if available)

Telephone Number

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E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)



Date Signed: 3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Paul D. Yasger	
Address Dept. D377, Bldg. AP6A-1 100 Abbott Park Road	
City/State Abbott Park, IL	
ZIP Code 60064	Telephone Number (847) 938-3508
FAX Number (if available)	E-Mail Address (if available) paul.yasger@abbott.com

The public reporting burden for this collection of information has been estimated to average 5 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 Services
 Food and Drug Administration
 Office of Chief Information Officer (HFA-710)
 5600 Fishers Lane
 Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542

PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/10
See OMB Statement on Page 3.

**PATENT INFORMATION SUBMITTED UPON AND
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation or
Composition) and/or Method of Use*

NDA NUMBER

22-417

NAME OF APPLICANT/NDA HOLDER

Abbott Laboratories

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

ritonavir

STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

5,674,882

b. Issue Date of Patent

October 7, 1997

c. Expiration Date of Patent

October 7, 2014

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

FAX Number (if available)

Telephone Number

(847) 938-3508

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) claims 1-3 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Treatment of HIV-infection in combination with other antiretroviral agents in accordance with the proposed labeling including the Drug Interactions, Indications and Usage, Clinical Studies, and Dosage and Administration sections.

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
 Treatment of HIV-infection in combination with other antiretroviral agents

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

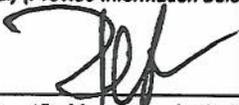
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below) Date Signed

 3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Paul D. Yasger	
Address Dept. D377, Bldg. AP6A-1 100 Abbott Park Road	
City/State Abbott Park, IL	
ZIP Code 60064	Telephone Number (847) 938-3508
FAX Number (if available)	E-Mail Address (if available) paul.yasger@abbott.com

The public reporting burden for this collection of information has been estimated to average 5 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 Services
 Food and Drug Administration
 Office of Chief Information Officer (HFA-710)
 5600 Fishers Lane
 Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542
PATENT INFORMATION SUBMITTED UPON AND AFTER
APPROVAL OF AN NDA OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

**PATENT INFORMATION SUBMITTED UPON AND
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation or
Composition) and/or Method of Use*

NDA NUMBER

22-417

NAME OF APPLICANT/NDA HOLDER

Abbott Laboratories

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

ritonavir

STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

6,037,157

b. Issue Date of Patent

March 14, 2000

c. Expiration Date of Patent

June 26, 2016

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

FAX Number (if available)

Telephone Number

(847) 938-3508

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) claims 1-16 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Treatment of HIV-infection in combination with other antiretroviral agents in accordance with the proposed labeling including the Drug Interactions, Indications and Usage, and Dosage and Administration sections.

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
 Treatment of HIV-infection in combination with other antiretroviral agents

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below) Date Signed



3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Paul D. Yasger	
Address Dept. D377, Bldg. AP6A-1 100 Abbott Park Road	City/State Abbott Park, IL
ZIP Code 60064	Telephone Number (847) 938-3508
FAX Number (if available)	E-Mail Address (if available) paul.yasger@abbott.com

The public reporting burden for this collection of information has been estimated to average 5 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 Services
 Food and Drug Administration
 Office of Chief Information Officer (HFA-710)
 5600 Fishers Lane
 Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542

PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/10
See OMB Statement on Page 3.

**PATENT INFORMATION SUBMITTED UPON AND
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation or
Composition) and/or Method of Use*

NDA NUMBER

22-417

NAME OF APPLICANT/NDA HOLDER

Abbott Laboratories

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

ritonavir

STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

6,703,403

b. Issue Date of Patent

March 9, 2004

c. Expiration Date of Patent

June 26, 2016

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

FAX Number (if available)

Telephone Number

(847) 938-3508

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes."
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) 21-47, 66-92 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Treatment of HIV-infection in combination with other antiretroviral agents in accordance with the proposed labeling including the Drug Interactions, Indications and Usage, and Dosage and Administration sections.

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
 Treatment of HIV-infection in combination with other antiretroviral agents.

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)



Date Signed: 3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Paul D. Yasger	
Address Dept. D377, Bldg. AP6A-1 100 Abbott Park Road	City/State Abbott Park, IL
ZIP Code 60064	Telephone Number (847) 938-3508
FAX Number (if available)	E-Mail Address (if available) paul.yasger@abbott.com

The public reporting burden for this collection of information has been estimated to average 5 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 Services
 Food and Drug Administration
 Office of Chief Information Officer (HFA-710)
 5600 Fishers Lane
 Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542
PATENT INFORMATION SUBMITTED UPON AND AFTER
APPROVAL OF AN NDA OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/10
See OMB Statement on Page 3.

**PATENT INFORMATION SUBMITTED UPON AND
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation or
Composition) and/or Method of Use*

NDA NUMBER

22-417

NAME OF APPLICANT/NDA HOLDER

Abbott Laboratories

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

ritonavir

STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

7,148,359

b. Issue Date of Patent

December 12, 2006

c. Expiration Date of Patent

July 19, 2019

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

FAX Number (if available)

Telephone Number

(847) 938-3508

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)

Date Signed



3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Paul D. Yasger

Address

Dept. D377, Bldg. AP6A-1
100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

Telephone Number

(847) 938-3508

FAX Number (if available)

E-Mail Address (if available)

paul.yasger@abbott.com

The public reporting burden for this collection of information has been estimated to average 5 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 Services
Food and Drug Administration
Office of Chief Information Officer (HFA-710)
5600 Fishers Lane
Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542

PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/10
See OMB Statement on Page 3.

**PATENT INFORMATION SUBMITTED UPON AND
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation or
Composition) and/or Method of Use*

NDA NUMBER

22-417

NAME OF APPLICANT/NDA HOLDER

Abbott Laboratories

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME

Norvir

ACTIVE INGREDIENT(S)

ritonavir

STRENGTH(S)

100 mg

DOSAGE FORM

tablet; oral

APPROVAL DATE OF NDA OR SUPPLEMENT

February 10, 2010

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

7,364,752

b. Issue Date of Patent

April 29, 2008

c. Expiration Date of Patent

November 10, 2020

d. Name of Patent Owner

Abbott Laboratories

Address (of Patent Owner)

100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

FAX Number (if available)

Telephone Number

(847) 938-3508

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

4. Method of Use

Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more approved methods of using the approved drug product? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) Claim 9 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? Yes No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Treatment of HIV-infection in combination with other antiretroviral agents in accordance with the proposed labeling including the Drug Interactions, Indications and Usage, Clinical Studies, and Dosage and Administration sections.

4.2b If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.

Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)

Treatment of HIV-infection in combination with other antiretroviral agents.

FDA will not list the patent in the Orange Book as claiming the method of use if:

- the answer to question 4.1 or 4.2 is "No," or
- if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.

5. No Relevant Patents

For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed

3/4/10

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Paul D. Yasger

Address

Dept. D377, Bldg. AP6A-1
100 Abbott Park Road

City/State

Abbott Park, IL

ZIP Code

60064

Telephone Number

(847) 938-3508

FAX Number (if available)

E-Mail Address (if available)

paul.yasger@abbott.com

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First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

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- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
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5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

EXCLUSIVITY SUMMARY

NDA # 22-417

SUPPL # 000

HFD # 530

Trade Name NORVIR Tablets

Generic Name Ritonavir

Applicant Name Abbott Laboratories

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy 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 a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

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.

The sponsor (Abbott) concurs that the information submitted were from bioavailability studies. Abbott submitted this application to evaluate the bioequivalence of the two ritonavir formulations: comparing the bioavailability of ritonavir tablets (new formulation) to the bioavailability of ritonavir capsules (approved formulation). Data submitted and reviewed by FDA were from the bioequivalence and ritonavir tablet food effect trials.

The previously reviewed clinical data support the safety of the greater exposures (26-40%) achieved with the Norvir tablet formulation compared to the marketed Norvir SGC (soft gelatin capsule) formulation at the approved 600 mg dose. Efficacy was not needed as

exposures achieved with the new tablet were equal to or greater than those achieved with the previously approved SGC and therefore there was no need to look at any new efficacy data.

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

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

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

No

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

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

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (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# 20945 (NORVIR Capsule)

NDA# 20659 (NORVIR Oral Solution)

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 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs 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 8.

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.

(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 8:

(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:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

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

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

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

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

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"):

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:

Title: Director, Division of Antiviral Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	Ritonavir Tablet

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

/s/

AMALIA C HIMAYA
02/01/2010

JEFFREY S MURRAY
02/01/2010

(AL) 1 page of Admin has been withheld in full immediately following this page as B4 CCI/TS



1.3.3 Debarment Certification

Certification Requirement for Approval of a Drug Product Concerning Using Services of Debarred Persons

Any applicant for approval of a new drug product submitted on or after June 1, 1992 per Section 306(k)(1) of the Federal Food, Drug, and Cosmetic Act must include:

- (1) A certification that the applicant did not and will not use in any capacity the services of any person debarred under Section 306, subsection (a) and (b), in connection with such application.

Abbott Laboratories certifies that it did not, and will not use in any capacity the services of any person debarred under Section 306, subsection (a) and (b), in connection with this application.

Mary Konkowski
Manager
Global Pharmaceutical Regulatory Affairs
Abbott Laboratories

Document Approval

Debarment Certification - 2008-sep-16

Version: 1.0

Date: 16-Sep-2008 06:10:12 PM

Abbott ID: 09162008-00AB619C33B241-00001-en

Signed by:	Date:	Meaning Of Signature:
Konkowski_Mary_S	16-Sep-2008 06:10:04 PM	Approver

(F) 1 page of faxcover withheld in full immediately following this page as B4 CCI/TS

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 22-417 BLA #	NDA Supplement # 000 BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: NORVIR Established/Proper Name: Ritonavir Dosage Form: Tablet		Applicant: Abbott Laboratories Agent for Applicant (if applicable):
RPM: Amalia Himaya		Division: DAVP
<p>NDAs: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p> <p>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</p>
❖ User Fee Goal Date Action Goal Date (if different)		2/11/10 2/10/10
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (<i>specify type and date for each action taken</i>)		<input type="checkbox"/> None CR on 10/16/09
❖ Promotional Materials (<i>accelerated approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		<input type="checkbox"/> Received

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

❖ Application Characteristics ²	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC Comments: _____	
❖ Date reviewed by PeRC (required for approvals only) If PeRC review not necessary, explain: _____	9/2/09
❖ BLAs only: RMS-BLA Product Information Sheet for TBP has been completed and forwarded to OBPS/DRM (approvals only)	<input type="checkbox"/> Yes, date
BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Press Office notified of action (by OEP)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information dissemination are anticipated	<input type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other: Outreach Program

All questions in all sections pertain to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new RMS-BLA Product Information Sheet for TBP must be completed.

Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLA: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (Summary Reviews)).</i> 	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for each paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
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CONTENTS OF ACTION PACKAGE

Copy of this Action Package Checklist ³	Included
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Officer/Employee List

❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included

Action Letters

❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Approval 2/10/10 CR 10/16/09 Fileable 2/18/09
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Labeling

❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	1/20/10
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	n/a
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	12/19/08
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
❖ Medication Guide/Patient Package Insert/Instructions for Use (<i>write submission/communication date at upper right of first page of each piece</i>)	<input type="checkbox"/> Medication Guide <input checked="" type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> None

³ Fill in blanks with dates of reviews, letters, etc.
Version: 8/26/09

<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	1/20/10
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	n/a
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	12/19/08
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	n/a
❖ Labels (full color carton and immediate-container labels) (write submission/communication date on upper right of first page of each submission)	
<ul style="list-style-type: none"> • Most-recent division proposal for (only if generated after latest applicant submission) 	n/a
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	9/29/09
❖ Proprietary Name	
<ul style="list-style-type: none"> • Review(s) (indicate date(s)) • Acceptability/non-acceptability letter(s) (indicate date(s)) 	n/a
❖ Labeling reviews (indicate dates of reviews and meetings)	<input checked="" type="checkbox"/> RPM 2/2/10 <input checked="" type="checkbox"/> DMEPA 9/4/09 <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC 7/2/09 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
Administrative Reviews (e.g., RPM Filing Review ⁴ /Memo of Filing Meeting) (indicate date of each review)	RPM 3/25/09
❖ NDAs only: Exclusivity Summary (signed by Division Director)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<ul style="list-style-type: none"> • Applicant in on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (indicate date) ○ If yes, OC clearance for approval (indicate date of clearance communication) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatric Page (approvals only, must be reviewed by PERC before finalized)	<input checked="" type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (include certification)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications (letters (except previous action letters), emails, faxes, telecons)	Included
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
<ul style="list-style-type: none"> • PeRC (indicate date of mtg; approvals only) 	<input type="checkbox"/> Not applicable 9/2/09
<ul style="list-style-type: none"> • Pre-Approval Safety Conference (indicate date of mtg; approvals only) 	<input checked="" type="checkbox"/> Not applicable
<ul style="list-style-type: none"> • Regulatory Briefing (indicate date of mtg) 	<input checked="" type="checkbox"/> No mtg

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 8/26/09

• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg 10/22/08
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other (e.g., EOP2a, CMC pilot programs)	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 2/4/10
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 10/15/09
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	
• Clinical review(s) (<i>indicate date for each review</i>)	1/4/10 9/29/09 1/29/09 (Filing)
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Safety update review(s) (<i>indicate location/date if incorporated into another review</i>)	
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	p. 10 of the 9/29/09 review
❖ Clinical reviews from other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Risk Management <ul style="list-style-type: none"> • REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>) • REMS Memo (<i>indicate date</i>) • Review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	n/a n/a <input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 1/13/10
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 2/2/10 (Filing) 8/24/09
Biostatistics <input checked="" type="checkbox"/> None	
Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None

⁵ Filing reviews should be filed with the discipline reviews.

Statistical Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None 10/14/09
Clinical Pharmacology review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None 1/13/10 9/23/09 2/6/09 (Filing)
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None 7/27/09
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 3/30/09 1/30/09 (Filing)
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input checked="" type="checkbox"/> No carc
ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Product quality review(s) (indicate date for each review)	<input type="checkbox"/> None 1/14/10 10/15/09 1/29/09 (Filing)
• ONDQA Biopharmaceutics review (indicate date for each review)	
• BLAs only: Facility information review(s) (indicate dates)	<input type="checkbox"/> None
❖ Microbiology Reviews	
• NDAs: Microbiology reviews (sterility & pyrogenicity) (indicate date of each review)	<input checked="" type="checkbox"/> Not needed
• BLAs: Sterility assurance, product quality microbiology (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)	10/15/09 (p. 127)
<input type="checkbox"/> Review & FONSI (indicate date of review)	

<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<ul style="list-style-type: none"> • NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) 	Date completed: 12/18/09 <input checked="" type="checkbox"/> Acceptable (see 1/14/10 Product Quality Review) <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> • BLAs: <ul style="list-style-type: none"> ○ TBP-EER ○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) (<i>date completed must be within 60 days prior to AP</i>) 	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation Date completed: <input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed

Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's CIRA.



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 10, 2010

TO: Mary Konkowski, Associate Director
Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: Advice on Merging of Norvir Labels for NDAs 22-417 (Tablets),
20-659 (Oral Solution) and 20-945 (Capsule)

Reference is made to your September 25, 2009 electronic mail correspondence and the September 28, 2009 teleconference between Abbott and FDA. Specifically, you requested FDA's opinion on the following.

Since the Norvir Capsule formulation will remain on the market after the approval of Norvir Tablet, Abbott would like to get FDA's opinion on the acceptability of adding the capsule formulation information into the tablet and oral solution PLR-formatted labeling as a prior approval supplement after the approval of NDA 22-417 and NDA 20-659/S-045.

Upon further review and consideration, we recommend *separate* labeling for the Norvir capsule/oral solution and the Norvir tablet/oral solution. We will reevaluate this recommendation upon receipt of your residual demand assessment for the capsule. From our understanding of the September 28, 2009 teleconference, you will assess capsule residual demand after one year of Norvir tablet approval. Please provide this assessment to the FDA when it becomes available.

Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ See appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	Ritonavir Tablet
NDA-20945	ORIG-1	ABBOTT LABORATORIES	NORVIR(RITONAVIR)SEC CAPS 100/200MG
NDA-20659	ORIG-1	ABBOTT LABORATORIES PHARMACEUTICA L PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION

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

/s/

AMALIA C HIMAYA
02/10/2010



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: January 20, 2010

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-417 and 20-659 S-045 (Norvir)

Reference is made to your January 18, 2010 submission. We have the following labeling comments:

1) In Section 15, the footnote for reference #2 was based on the following sentence in the ritonavir capsule label that has been deleted from the ritonavir tablet label: (b) (4)

[REDACTED] Therefore, reference #2 in section 15 should be deleted.

2) The revision date at the end of highlights replaces the “revision” or “issued” date at the end of the labeling. The revision date should not appear in both places. Therefore, the revision date “Rev. 01/2010” at the end of the package insert should be deleted.

Please provide your response by January 22, 2010. If you agree to the above comments, the final label will reflect these changes. Please feel free to contact me at (301) 796-3391 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
01/20/2010



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: January 13, 2010

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-417 and 20-659 S-045 (Norvir)

Reference is made to your December 11, 2009 resubmission. We have the following labeling comments:

- 1) In Table 1, there is a superscripted "1". It is unclear what the superscripted "1" represents. Please clarify this issue.

- 2) In Table 2, please correct the wording for the sildenafil-ritonavir drug-drug interaction clinical comment. It should read: A safe and effective dose has not been established when used with ritonavir. There is an increased potential for sildenafil-associated adverse events, including visual abnormalities, hypotension, prolonged erection, and syncope.

Please provide your response by January 18, 2010. Submission of the amended label is not necessary at this time. Please feel free to contact me at (301) 796-3391 if you have any questions regarding the contents of this transmission.

{ see appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION

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/s/

AMALIA C HIMAYA
01/13/2010



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: January 8, 2010

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-417 and 20-659 S-045 (Norvir)

Reference is made to your December 11, 2009 resubmission. We propose the following label revision:

In Section 12.4, under Resistance subsection, please amend the second sentence of the paragraph as follows:

Genotypic analysis of these isolates showed mutations in the HIV-1 protease gene leading to (b) (4)-amino acid substitutions (b) (4) I84V, V82F, A71V, and M46I.

Please provide your response by January 13, 2010. Submission of the amended label is not necessary at this time. Please feel free to contact me at (301) 796-3391 if you have any questions regarding the contents of this transmission.

{ See appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICA L PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION

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/s/

AMALIA C HIMAYA
01/08/2010



NDA 22-417

ACKNOWLEDGE CLASS 1 COMPLETE RESPONSE

Abbott Laboratories
Attention: Mary Konkowski
Manager, Global Pharmaceutical Regulatory Affairs
Dept. PA76/ Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

We acknowledge receipt on December 11, 2009 of your December 11, 2009 resubmission to your new drug application for NORVIR[®] (ritonavir) 100mg tablets.

We consider this a complete, class 1 response to our October 16, 2009 action letter. Therefore, the user fee goal date is February 11, 2009.

If you have any questions, call Amalia Himaya, Regulatory Project Manager, at (301) 796-3391 or 301-796-1500.

Sincerely,

{See appended electronic signature page}

Karen Winestock
Chief, Project Management Staff
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

SHERLY ABRAHAM
12/23/2009

KAREN D WINESTOCK
12/23/2009



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration Silver
Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: October 9, 2009

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-417 and 20-659 S-045 (Norvir)

Reference is made to your October 5, and October 7, 2009 label submissions. We found your response acceptable. We have one additional recommendation:

In Section 12.3, please amend the following sentence by adding the word "single" as follows:

*Under moderate fat conditions (857 kcal; 31% fat, 13% protein, 56% carbohydrates), when a **single** 100 mg NORVIR dose was administered as a tablet compared with a capsule, $AUC_{(0-\infty)}$ met equivalence criteria but mean C_{max} was increased by 26% (92.8% confidence intervals: $\uparrow 15$ - $\uparrow 39\%$).*

Reference is also made to the October 8, 2009 Information Request sent to you by ONDQA.

Please provide your response by October 13, 2009 to include this and the ONDQA Information Request dated October 8, 2009. Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ See appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
10/09/2009



NDA 22-417

INFORMATION REQUEST LETTER

Abbott Laboratories
Attention: Mary Konkowski, Manager
Global Pharmaceutical Regulatory Affairs
Dept. PA76, Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your December 19, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norvir (ritonavir) (100 mg) Tablet.

We also refer to your submissions dated January 29, 2009, March 31, 2009, April 27, 2009, June 3, 2009, July 17, 2009, August 5, 2009, and September 22, 2009.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA:

- Regarding your response to comment 20 in the amendment dated September 22, 2009, please note that FDA finds unsuitable for regulatory purposes the NMT ^(b)₍₄₎ relative standard deviation (RSD) exception to the 25 mg/25% threshold. Accordingly, for those items below the 25 mg/25% threshold, testing by Content Uniformity should be performed. Please revise your proposed drug product specification to include the Uniformity of Dosage Units testing by Content Uniformity only.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Amalia Himaya, Regulatory Project Manager the Office of New Drugs (Amalia.Himaya@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Norman Schmuff, Ph.D.
Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

STEPHEN P MILLER

10/08/2009

I concur, as Acting Branch Chief



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: October 2, 2009

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-147 and 20-659 S-045

Reference is made to your October 1, 2009, submissions to NDAs 22-147 and 20-659 S-045. We have the following recommendation:

In the Boxed Warning, please delete the phrase [REDACTED] (b) (4) because astemizole and terfenadine were deleted in Section 4, Contraindications.

Reference is also made to the voice message and electronic mail correspondence sent to you today regarding the FDA comments sent on October 1, 2009. We requested [REDACTED] (b) (4) be replaced with "meal" in the following revision: "Norvir should be taken twice daily with meal [REDACTED] (b) (4)"

If possible, please include these revisions in your October 5, 2009 response. Otherwise, we request response by October 7, 2009. Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ See appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
10/02/2009



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: October 1, 2009

TO: Mary Konkowski, Associate Director
Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories (Abbott)

SUBJECT: NDA 22-417 and 20-659 S-45 (NORVIR)

Reference is made to your submission dated September 29, 2009 in response to DMEPA comments sent on September 23 and 24, 2009. Your response is acceptable with one additional recommendation.

1. Throughout the label, please change the statement (b) (4) to "Norvir should be taken **twice daily** with food."

Please include this revision in your October 5, 2009 response. Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ See appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
10/01/2009

From: Greeley, George
Sent: Wednesday, September 30, 2009 5:03 PM
To: Himaya, Amalia
Cc: Stowe, Ginneh D.
Subject: NDA 22-417 Norvir

Importance: High

Hi Amalia,

The Norvir (ritonavir) partial waiver and appropriately labeled application was reviewed by the PeRC PREA Subcommittee on September 02, 2009. The Division recommended a partial waiver because there are too few children with disease/condition to study and because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

The PeRC agreed with the Division to grant a partial waiver from 0<1 month because there are too few children with disease/condition and that the product is appropriately labeled from 1 month to 16 years of age.

Thank you.

George Greeley
Regulatory Health Project Manager
Pediatric and Maternal Health Staff
Office of New Drugs
FDA/CDER
10903 New Hampshire Ave.
Bldg #22, Room 6467
Silver Spring, MD 20993-0002
301.796.4025

Please consider the environment before printing this e-mail.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
10/09/2009
PeRC Meeting Minutes

From: Himaya, Amalia
Sent: Tuesday, September 29, 2009 11:37 AM
To: 'Mary S Konkowski'
Subject: RE: NORVIR - Labeling and PMC Questions

Mary, please see response below in red font:

Amalia

From: Mary S Konkowski [mailto:mary.konkowski@secure.abbott.com]
Sent: Friday, September 25, 2009 9:27 AM
To: Himaya, Amalia
Subject: NORVIR - Labeling and PMC Questions

Hi Amalia,

As discussed, here are the labeling questions regarding NORVIR Tablets, Oral Solution and Capsules:

1. During the September 23, 2008 NORVIR Tablet pre-NDA meeting, FDA mentioned there may be a need for a Medication Guide. Will a Medication Guide be required for Norvir? **No**
2. The action date for Norvir Tablet NDA and the PLR conversion for Norvir Oral Solution (NDA 20-659/S-045) is October 19, 2009. As background, the PLR-formatted labeling will be used for both Norvir Tablets and Norvir Oral Solution. On May 29, 2009, a prior approval labeling supplement (PAS) was submitted for NDAs 20-659 and 20-945 to add new contraindications for salmeterol and sildenafil for pulmonary arterial hypertension where the labeling submitted was in the legacy USPI format. The projected action date for these pending safety update labeling supplements for NDA 20-659 and 20-945 is ~November 29, 2009. As background, these same safety update changes were submitted for Kaletra in a CBE-0 (submitted on April 28, 2009 for NDA 21-906/S-022 and NDA 21-251/S-029) but FDA re-categorized the supplement to a PAS since it impacted the contraindications. For Norvir, since the labeling will be identical to the labeling approved for the legacy-formatted USPI for Norvir capsule and oral solution, we believe the CBE-0 would be the most effective way to implement the change into the PLR-formatted USPI for Norvir tablets and oral solution. Once the safety update labeling supplements are approved, will it be acceptable to incorporate the approved safety changes into the approved PLR-formatted Norvir Tablet and Norvir Oral Solution USPI via CBE-0 supplement? **You can submit the safety changes via CBE supplement for Norvir Tablet and Oral Solution only after the approval of pending safety update labeling supplements (PAS) in Norvir.** Alternatively, if the review of the labeling PAS is ahead of schedule, can the proposed changes be incorporated into the draft Norvir Tablet and Norvir Oral Solution PLR-formatted labeling prior to the Norvir Tablet action date? **We do not anticipate the PAS will be ahead of schedule to be incorporated into the draft Norvir Tablet and Oral Solution.**
3. Since the Norvir Capsule formulation will remain on the market after the approval of Norvir Tablet, Abbott would like to get FDA's opinion on the acceptability of adding the capsule formulation information into the tablet and oral solution PLR-formatted labeling as a prior approval supplement after the approval of NDA 22-417 and NDA 20-659/S-045. **This will be addressed after action on NDA 22-417 is taken.**
4. Additionally, Abbott would like to know if there will be any post-marketing commitments resulting from the Norvir Tablet, NDA 22-417, review? **There will be no PMC for 22-417.**

Thank you for assistance with these questions. Please feel free to call me if you have any questions.

Kind regards,

Mary

Mary S Konkowski
Associate Director,
GPRA North America
Antiviral & Anti-Infective Products Abbott Laboratories
200 Abbott Park Road
AP30-1E, Dept PA76
Abbott Park, IL 60064-6157 Tel: (847) 938-3063
Cell: (224) 217-7663
mary.konkowski@abbott.com

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-20659	SUPPL-47	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-20945	SUPPL-26	ABBOTT LABORATORIES	NORVIR(RITONAVIR)SEC CAPS 100/200MG
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
09/29/2009

In Response to Abbott's question on Norvir; correspondence via email.



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration Silver
Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: September 28, 2009

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-417 and 20-659 S-045 (Norvir)

Reference is made to your September 24, 2009 submission containing your response to our September 15, 2009 and September 22, 2009 labeling comments. We have the following recommendations.

1. The information in Section 4 (Contraindication) pertaining to St John's Wort and Norvir was modified to provide language consistent with the information from the atazanavir and darunavir labels:

Voriconazole and St. John's Wort are exceptions in that co-administration of NORVIR with voriconazole results in a significant decrease in plasma concentration of voriconazole, and co-administration of NORVIR with St. John's Wort may result in (b) (4) decreased ritonavir (b) (4) plasma concentrations (b) (4)

2. Please delete the following sentence from Section 2 (Dosage and Administration) because the information does not reflect the current treatment practice for combination antiretroviral treatment:

(b) (4)

Please provide your response by October 2, 2009. Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ see appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
09/28/2009



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: September 24, 2009

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories (Abbott)

SUBJECT: NDA 22-417 (Norvir Tablets)

Reference is made to your submission dated December 19, 2008, for NORVIR[®] (ritonavir) 100mg tablets and our comments sent to you on September 23, 2009. As mentioned, we intend to provide you the container label comments separately. Hence, on behalf of the Division of Medication Error Prevention and Analysis (DMEPA), we have the following recommendations:

Container Label

1. Relocate the net quantity away from the product strength to ensure that that the net quantity statement can be readily identified when dispensing the products.
2. Revise the labels to include an alert on the principle display panel. This alert should notify practitioners and patients of the new storage requirement and new dosing with respect to food in order to avoid confusion with the introduction of the new tablets. We recommend this alert be implemented for the first six months of new product marketing.

We request your September 29, 2009 response address this and the September 23, 2009 comments . Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ see appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
09/24/2009



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: September 23, 2009

TO: Mary Konkowski, Associate Director
Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories (Abbott)

SUBJECT: NDA 22-417 (Norvir Tablets)

Reference is made to your submission dated December 19, 2008, for NORVIR[®] (ritonavir) 100mg tablets. On behalf of the Division of Medication Error Prevention and Analysis (DMEPA), we have the following recommendations. Please note we will also provide you separate comments on the container label as soon as possible.

A. General Information

Abbott should implement an outreach program to inform patients and practitioners about the introduction of the new Norvir tablet formulation. The communications developed should focus on three pertinent factors highlighting the differences between Norvir tablet and capsule: the change in storage requirements; the change from capsule to tablet; and the differences in administration with respect to food. In addition, patients and practitioners should be made aware that the frequency of mild to moderate gastrointestinal side effects such as nausea, vomiting, abdominal pain or diarrhea as well as parestheias may increase when switching from the capsule to the tablet formulation although this is expected to diminish over time.

B. Package Insert

1. The Dosage and Administration and Patient Counseling Section (Sections 2.1 and 17) should clarify the titration regimen by explicitly stating the maximum dose of 600 mg twice daily should not be exceeded upon completion of the titration.

Please provide your response by September 29, 2009. Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ See appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22417

ORIG-1

ABBOTT
LABORATORIES

RITONAVIR

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/s/

AMALIA C HIMAYA
09/23/2009



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: September 22, 2009

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-417 and 20-659 S-045 (Norvir)

Reference is made to our comments sent to you on September 15, 2009. We propose this additional revision in the label.

In Section 8.4, please change 18 years of age to 21 years of age:

8.4 Pediatric Use

In HIV-infected patients age greater than 1 month to 21^{(b) (4)} years, the antiviral activity and adverse event profile seen during clinical trials and through postmarketing experience were similar to that for adult patients.

Please include this revision in your September 24, 2009 response. Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{ see appended electronic signature page }

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20659	SUPPL-45	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	NORVIR (RITONAVIR) ORAL SOLUTION
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

AMALIA C HIMAYA
09/22/2009



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: September 15, 2009

TO: Mary Konkowski, Associate Director, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDAs 22-147 and 20-659 S-045

Reference is made to your September 11, 2009, submissions to NDAs 22-145 and 20-659 S-045. We agree with your proposed microbiology labeling comments. However, we have listed below additional labeling comments and proposed revisions. These listed revisions are not all inclusive as other labeling revisions have been made directly to the label. The word version of the label will be provided to you via electronic mail. Please review the entire label and make note of all the content changes section by section.

1. In Sections 2 and 17, we have replaced [REDACTED] (b) (4) to "Take NORVIR with meals." because the increase in ritonavir concentrations following administration of the tablet compared to the capsule is greater under fasted conditions than under fed conditions. The increase in concentrations may be clinically significant. Because ritonavir tablets were not evaluated with a light meal or snack, the label should instruct patients to take the tablet with a full meal.
2. In Table 2, we revised the Voriconazole clinical comments to specify the ritonavir dose.
3. In Table 5, we added voriconazole in Antifungal drug class.
4. In Section 12.1, we deleted the following statement because this information is adequately conveyed in the other sections of the label as drug-drug interaction information. Additionally, including this information in the Mechanism of Action section conveys a potential off-label use.

[REDACTED] (b) (4)

5. Throughout the label, we deleted the dosing instruction to take [REDACTED] (b) (4)

Please provide your response by September 24, 2009. Please feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22417

ORIG-1

ABBOTT
LABORATORIES

RITONAVIR

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/s/

Robert G Kosko
09/15/2009

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: September 10, 2009
TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs
SPONSOR: Abbott Laboratories
SUBJECT: NDA 22-417 Label Comments

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22-417.

Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

(b) (4)

We are providing this above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me at 301-796-0783 if you have any questions regarding the contents of this transmission

Paras M. Patel, R.Ph.
Regulatory Project Manager
Division of Antiviral Products

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22417

ORIG-1

ABBOTT
LABORATORIES

RITONAVIR

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/s/

PARAS M PATEL

09/10/2009



NDA 22-417

INFORMATION REQUEST LETTER

Abbott Laboratories
Attention: Mary Konkowski, Manager
Global Pharmaceutical Regulatory Affairs
Dept. PA76, Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your December 19, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norvir (ritonavir) (100 mg) Tablet.

We also refer to your submissions dated January 29, 2009, March 31, 2009, April 27, 2009, June 3, 2009, July 17, 2009, and August 5, 2009.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Please provide your response no later than September 22, 2009:

I. NIR methods (Assay, ID (b) (4))

We have completed the review of updated near infrared spectroscopic methods proposed in your application and find them un-acceptable to use for regulatory purposes. The major deficiencies are listed below. The document titled "Note for guidance on the use of near infrared spectroscopy by the pharmaceutical industry and the data requirements for new submissions and variations" (EMA, February 20, 2003) supports the assessment. It is referred to as "the guidance" through the rest of this communication.

(b) (4)

(AM) 2 pages of Admin has been withheld in full immediately following this page as B4 CCI/TS

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Paras Patel, Regulatory Project Manager the Office of New Drugs (Paras.Patel@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Norman Schmuff, Ph.D.
Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR
NDA-22417	ORIG-1	ABBOTT LABORATORIES	RITONAVIR

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/s/

NORMAN R SCHMUFF
09/08/2009

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: August 31, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417-Labeling Comments

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the labeling comments below from DAVP (Division of Antiviral Products) pertaining to the Dosage and Administration Section and Mechanism of Action Section of the package insert. Please respond via email correspondence and send an archival copy of your response to your NDA.

Labeling Comments:

Package Insert (PI) Comments:

Based on our recent discussion with FDA lawyers, we have further revisions to the Dosage and Administration and Mechanism of Action section. These changes are to avoid potential off label claims.

Dosage and Administration:

Please revise the current draft labeling from:

Current draft labeling:

(b) (4)

TO:

Dose reduction of Norvir is necessary when used with the following HIV-1 protease inhibitors: atazanavir, darunavir, fosamprenavir, saquinavir, and tipranavir. Prescribers should consult the full prescribing information and clinical study information of these protease inhibitors if they are co-administered with a reduced dose of ritonavir [see *Warnings and Precautions (5) and Table 5, Established and Other Potentially Significant Drug Interactions*].

Additionally, please delete the following text from Section 12.1 Mechanism of Action. This information is adequately conveyed in other sections of the label.

(b) (4)

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Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

RASHMI KALLA
08/31/2009

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: August 25, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417-Labeling Comments

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the labeling comments below from DAVP (Division of Antiviral Products) pertaining to section **12.4 Microbiology** of the package insert. Please respond via email correspondence and send an archival copy of your response to your NDA.

Microbiology Labeling Comments:

Package Insert (PI) Comments:

Please change section 12.4 Microbiology so that it reads as follows:

12.4 Microbiology

Mechanism of Action

Ritonavir is a peptidomimetic inhibitor of the HIV-1 protease. Inhibition of HIV protease renders the enzyme incapable of processing the *gag-pol* polyprotein precursor which leads to production of non-infectious immature HIV particles.

Antiviral Activity in Cell Culture

The activity of ritonavir was assessed in acutely infected lymphoblastoid cell lines and in peripheral blood lymphocytes. The concentration of drug that inhibits 50% (EC₅₀) of viral replication ranged from 3.8 to 153 nM depending upon the HIV-1 isolate and the cells employed. The average EC₅₀ value for low passage clinical isolates was 22 nM (n = 13). In MT₄ cells, ritonavir demonstrated additive effects against HIV-1 in combination with either

didanosine (ddI) or zidovudine (ZDV). Studies which measured cytotoxicity of ritonavir on several cell lines showed that > 20 µM was required to inhibit cellular growth by 50% resulting in a cell culture therapeutic index of at least 1000.

Resistance

HIV-1 isolates with reduced susceptibility to ritonavir have been selected in cell culture. Genotypic analysis of these isolates showed mutations in the HIV protease gene at amino acid positions I84V, A82F, A71V, and M46I. Phenotypic (n = 18) and genotypic (n = 44) changes in HIV-1 isolates from selected patients treated with ritonavir were monitored in phase I/II trials over a period of 3 to 32 weeks. Substitutions associated with the HIV-1 viral protease in isolates obtained from 41 patients appeared to occur in a stepwise and ordered fashion; in sequence, these substitutions were position V82A/F, I54V, A71V/T, and I36L, followed by combinations of substitutions at an additional 5 specific amino acid positions. Of 18 patients for whom both phenotypic and genotypic analysis were performed on free virus isolated from plasma, 12 showed reduced susceptibility to ritonavir in cell culture. All 18 patients possessed one or more substitutions in the viral protease gene. The V82A/F substitution appeared to be necessary but not sufficient to confer phenotypic resistance. Phenotypic resistance was defined as a ≥ 5-fold decrease in viral sensitivity in cell culture from baseline.

Cross-Resistance to Other Antiretrovirals

Among protease inhibitors variable cross-resistance has been recognized. Serial HIV-1 isolates obtained from six patients during ritonavir therapy showed a decrease in ritonavir susceptibility in cell culture but did not demonstrate a concordant decrease in susceptibility to saquinavir in cell culture when compared to matched baseline isolates. However, isolates from two of these patients demonstrated decreased susceptibility to indinavir in cell culture (8-fold). Isolates from 5 patients were also tested for cross-resistance to amprenavir and nelfinavir; isolates from 2 patients had a decrease in susceptibility to nelfinavir (12- to 14-fold), and none to amprenavir. Cross-resistance between ritonavir and reverse transcriptase inhibitors is unlikely because of the different enzyme targets involved. One ZDV-resistant HIV-1 isolate tested in cell culture retained full susceptibility to ritonavir.

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Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

RASHMI KALLA
08/27/2009

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: August 12, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417-Labeling Comments

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the labeling comments below from DAVP (Division of Antiviral Products) and DDMAC (Division of Drug Marketing, Advertising and Communications). Please note that these are our preliminary labeling comments for NDA 22417 and that additional comments will be forthcoming. Please also refer to the word document version of the NORVIR label for further recommendations. Please respond via email correspondence and send an archival copy of your response to your NDA.

Labeling Comments:

Package Insert (PI) Comments:

1. This comment is in reference to the following sentence in section 7.1 [REDACTED] (b) (4)

Based on published literature and information you submitted, ritonavir potentially induces the following enzymes that are not included in the draft ritonavir tablet label: [REDACTED] (b) (4)

[REDACTED] Please provide the following information:

- A) The rationale for removing [REDACTED] (b) (4) induction from the draft label
- B) The rationale for not including [REDACTED] (b) (4) induction in the draft label

2. Section 17.1, Information For Patients, lists some risks that should be discussed with patients. However, some important risks are not mentioned at all, such as the risk of liver dysfunction, pancreatitis and its symptoms, changes in blood glucose or lipids, immune reconstitution syndrome, and allergic reactions. We recommend that this section be revised so that patients are informed of all of the major risks of the product as outlined in the Warnings/Precautions section.
3. Please review post-marketing AEs section and remove duplicate AEs that occurred during clinical trials and are covered in other sections such as Adverse Reactions, etc.

Patient Package Insert (PPI) Comments:

1. **“What is NORVIR and How Does it work?”**

“NORVIR is for adults and for children age > 1 month and older.”

The symbol “>” may not be understood by the typical consumer. Please revise and state greater than 1 month and older.

2. **“How Should I take NORVIR?”**

“Children from > 1 month to (b) (4) years of age can also take NORVIR.”

Please see comment above. Also please change (b) (4) of age to 18 years of age. Eighteen years of age and older are considered adults and not children.

3. **What is NORVIR and How Does it work?”**

(b) (4)

This statement is absolute and implies that the reduction in viral load is guaranteed with Norvir. Please revise to state, “When used with other anti-HIV medicines, NORVIR may reduce the amount of HIV in your blood and increase the number of CD4+ cells.”

4. **“Can I Take NORVIR With Other Medications?”**

“NORVIR oral solution contains alcohol. Talk with your doctor if you are taking or planning to take metronidazole or disulfiram. Severe nausea and vomiting can occur” (added emphasis).

Please consider including both the brand and generic names to facilitate better communication for the consumer.

5. **“What Are the Possible Side Effects of NORVIR?”**

(b) (4)

Please consider revising this statement to clearly convey to consumers that patients with hemophilia have a risk of increased bleeding with protease inhibitors, including Norvir (added emphasis).

6. **“What Are the Possible Side Effects of NORVIR?”**

(b) (4)

According to the WARNINGS and PRECAUTIONS, Allergic Reactions section of the draft PI, “Allergic reactions including urticaria, mild skin eruptions, bronchospasm, and angioedema have been reported... anaphylaxis and Stevens-Johnson syndrome have also been reported.” **We recommend revising the risk of allergic reactions in the draft PPI to convey the potential severity of this risk in consumer-friendly language.**

7. **“What Should I Tell My Doctor Before Taking NORVIR?”**

(b) (4)

The draft PPI does not make patients aware of the Antiretroviral Pregnancy Registry. According to the PREGNANCY, Antiretroviral Pregnancy Registry section of the draft PI, “To monitor maternal-fetal outcomes of pregnant women exposed to NORVIR, an Antiretroviral Pregnancy Registry has been established. Physicians are encouraged to register patients by calling 1-800-258-4263.” We note that the PPIs for numerous antiretroviral agents encourage patients to speak with their doctor about being included in the Antiretroviral Pregnancy Registry. Please revise as follows: “It is not known if NORVIR can harm your unborn baby. You and your healthcare professional will need to decide if NORVIR is right for you. If you take NORVIR while you are pregnant, talk to your healthcare professional about how you can be in the Antiretroviral Pregnancy Registry” (added emphasis).

8. **“What Should I Tell My Doctor Before Taking NORVIR?”**

(b) (4)

This above paragraph omits material information that in addition to the risk of HIV transmission, women taking Norvir should not breastfeed due to the potential of serious

adverse reactions to the baby in breastfeeding mothers who take Norvir. According to the NURSING MOTHERS section of the draft PI, “The Centers for Disease Control and Prevention recommend that HIV-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV. It is not known whether ritonavir is secreted in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions in nursing infants, mothers should be instructed not to breast-feed if they are receiving NORVIR” (added emphasis). **Please revise the draft PPI to include this material information.**

9. The draft PPI does not include Aptivus (tipranavir) on the list of drugs that have established and other potentially significant drug interactions with Norvir. According to Table 5 in the draft PI, with the co-administration of tipranavir 500 mg b.i.d with ritonavir 200 mg b.i.d., “there have been reports of clinical hepatitis and hepatic decompensation including some fatalities. Due to increased risk of hepatotoxicity, extra vigilance is warranted in patients with chronic hepatitis B or hepatitis C co-infection.” **Please add risk information pertaining to Aptivus in the section of the draft PPI which discusses drug interactions information pertinent to Norvir.**

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Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

RASHMI KALLA
08/17/2009

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: July 21, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Pharmacology Information Request

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please further refer to the amendment submitted on May 14, 2009 in response to FDA facsimile dated May 4, 2009 requesting clinical pharmacology supporting information in regards to the dosing recommendations for protease inhibitors coadministered with the proposed ritonavir tablets. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA **by close of business August 4, 2009**.

Clinical Pharmacology Comments:

1. In the data that was previously submitted to DAVP, the saquinavir pharmacokinetic information indicates that when the dose of ritonavir was increased from 100 to 200 mg once daily with saquinavir 1200 mg once daily, the saquinavir $AUC_{(0-24h)}$, C_{max} , and C_{min} geometric mean values decreased by approximately 40%, 30%, and 40%, respectively with a doubling of ritonavir doses.

Please provide published or presented information available to the general public to demonstrate that the new ritonavir tablets do not cause a clinically significant change in the pharmacokinetics of saquinavir.

We are providing this above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me at 301-796-3931 if you have any questions regarding the contents of this transmission

Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

Rashmi Kalla
7/21/2009 03:26:30 PM
CSO

Rashmi Kalla
7/21/2009 03:27:24 PM
CSO



NDA 22-417

INFORMATION REQUEST LETTER

Abbott Laboratories
Attention: Mary Konkowski, Manager
Global Pharmaceutical Regulatory Affairs
Dept. PA76, Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your December 19, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norvir (ritonavir) (100 mg) Tablet.

We also refer to your submissions dated January 29, 2009, and March 31, 2009.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Please provide your response no later than August 3, 2009:

(b) (4)

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Rashmi Kalla, Regulatory Project Manager the Office of New Drugs (Rashmi.Kalla@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Norman Schmuff, Ph.D.
Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Norman Schmuff
7/17/2009 01:09:49 PM

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: July 10, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Pharmacology Information Request

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the comments below pertaining to the ritonavir bioanalytical methods and bioanalysis from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

Clinical Pharmacology Comments:

- 1) For the ritonavir reference standard, the interval retest date was August 21, 2007 and samples were analyzed from March through June 2008 for the M10-235 and M10-307 protocols. Please clarify whether the ritonavir reference standard was recertified before August 21, 2007.
- 2) If the ritonavir reference standard was not recertified, please clarify how Abbott verified that there are no stability or purity issues with the ritonavir reference standard used in analyzing samples for the M10-235 and M10-307 protocols.
- 3) For the ritonavir method validation, please clarify if the experiments were conducted before the interval retest date for the ritonavir reference standard (no COA was provided with the ritonavir method validation report).
- 4) If there is no certificate of analysis for the internal standard (b)(4) please clarify how Abbott verified that there are no stability or purity issues with the (b)(4) reference standard used in analyzing samples for the M10-235 and M10-307 protocols or for ritonavir method validation.

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Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

Rashmi Kalla
7/17/2009 01:30:28 PM
CSO
Fax already sent on 07.10.09 but unable to DFS

Rashmi Kalla
7/17/2009 01:33:10 PM
CSO



NDA 22-417

INFORMATION REQUEST LETTER

Abbott Laboratories
Attention: Mary Konkowski, Manager
Global Pharmaceutical Regulatory Affairs
Dept. PA76, Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your December 19, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norvir (ritonavir) (100 mg) Tablet.

We also refer to your submissions dated January 29, 2009 and March 31, 2009.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

(b) (4)

(AN) 1 page of Admin has been withheld in full immediately following this page as B4 CCI/TS

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Rashmi Kalla, Regulatory Project Manager the Office of New Drugs (Rashmi.Kalla@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Norman Schuff, Ph.D.
Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Norman Schmuff
5/19/2009 09:53:27 AM

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: May 4, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Pharmacology Information Request

We refer to your submission dated December 18, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA. Please note that in order to complete our review the following information is needed by close of business May 15, 2009.

Clinical Pharmacology Comments:

DAVP is requesting additional supporting information in regards to dosing recommendations for protease inhibitors coadministered with the proposed ritonavir tablets:

- 1) To evaluate the impact of increased ritonavir exposures on the pharmacokinetics of coadministered protease inhibitors, please provide information either from FDA approved prescribing information or from published or presented information available to the general public (e.g. published journal articles) for the following protease inhibitors: atazanavir (for a 300/100 mg atazanavir/ritonavir dosage regimen), tipranavir, darunavir, and saquinavir.
- 2) In Table 6 in the Summary of Clinical Pharmacology Studies, information is presented on the pharmacokinetics of protease inhibitors coadministered with ritonavir pharmacokinetic boosting doses. Please clarify the source(s) of information for the atazanavir, tipranavir, and darunavir pharmacokinetic data.

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Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

Rashmi Kalla
5/12/2009 12:32:18 PM
CSO
Fax sent may 4, 2009

Rashmi Kalla
5/12/2009 12:33:27 PM
CSO

NDA/BLA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

Application Information		
NDA # 22417 BLA#	NDA Supplement #:S- BLA STN #	Efficacy Supplement Type SE-
Proprietary Name: Norvir Established/Proper Name: Ritonavir Dosage Form: Tablets Strengths: 100mg		
Applicant: Abbott Agent for Applicant (if applicable):		
Date of Application: 12/19/08 Date of Receipt: 12/19/08 Date clock started after UN:		
PDUFA Goal Date: 10/19/09		Action Goal Date (if different):
Filing Date: 02/17/09 Date of Filing Meeting: 01/29/09		
Chemical Classification: (1,2,3 etc.) (original NDAs only) 3		
Proposed Indication(s): use in combination with other antiretroviral agents for the treatment of HIV-infection		
Type of Original NDA: AND (if applicable)		<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
Type of NDA Supplement:		<input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<i>Refer to Appendix A for further information.</i>		
Review Classification:		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
<i>If the application includes a complete response to pediatric WR, review classification is Priority.</i>		
<i>If a tropical disease Priority review voucher was submitted, review classification defaults to Priority.</i>		<input type="checkbox"/> Tropical disease Priority review voucher submitted
Resubmission after withdrawal? <input type="checkbox"/>		
Resubmission after refuse to file? <input type="checkbox"/>		
Part 3 Combination Product? <input type="checkbox"/>		<input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Drug/Device <input type="checkbox"/> Biologic/Device
<i>Not a combination product</i>		
<input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation		<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR
<input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC		
Other:		

601.42)	
Collaborative Review Division (if OTC product):	
List referenced IND Number(s): IND 43,718 ritonavir (ABT-378)	
PDUFA and Action Goal dates correct in tracking system? <i>If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are the proprietary, established/proper, and applicant names correct in tracking system? <i>If not, ask the document room staff to make the corrections. Also, ask the document room staff to add the established name to the supporting IND(s) if not already entered into tracking system.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are all classification codes/flags (e.g. orphan, OTC drug, pediatric data) entered into tracking system? <i>If not, ask the document room staff to make the appropriate entries.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Application Integrity Policy	
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at:</i> http://www.fda.gov/ora/compliance_ref/aiplist.html If yes, explain: If yes, has OC/DMPQ been notified of the submission? Comments:	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
User Fees	
Form 3397 (User Fee Cover Sheet) submitted	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
User Fee Status	<input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required
<i>Note: 505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. It is expected that all 505(b) applications, whether 505(b)(1) or 505(b)(2), will require user fees unless otherwise waived or exempted (e.g., business waiver, orphan exemption).</i>	
Exclusivity	

<p>Does another product have orphan exclusivity for the same indication? <i>Check the Electronic Orange Book at: http://www.fda.gov/cder/ob/default.htm</i></p> <p>If yes, is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?</p> <p><i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES <input checked="" type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? (<i>NDAs/NDA efficacy supplements only</i>)</p> <p><i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES # years requested: <input checked="" type="checkbox"/> NO</p>
<p>If the proposed product is a single enantiomer of a racemic drug previously approved for a different therapeutic use (<i>NDAs only</i>):</p> <p>Did the applicant (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b) request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?</p> <p><i>If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.</i></p>	<p><input checked="" type="checkbox"/> Not applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
505(b)(2) (NDAs/NDA Efficacy Supplements only)	
<p>1. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</p> <p>2. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (see 21 CFR 314.54(b)(1)).</p> <p>3. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug (see 21 CFR 314.54(b)(2))?</p>	<p><input checked="" type="checkbox"/> Not applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>

Note: If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).

4. Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? **Check the Electronic Orange Book at:** <http://www.fda.gov/cder/ob/default.htm>

YES
 NO

If yes, please list below:

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 108(b)(2). Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.

Format and Content

Do not check mixed submission if the only electronic component is the content of labeling (COL).

Comments:

All paper (except for COL)
 All electronic
 Mixed (paper/electronic)

CTD
 Non-CTD
 Mixed (CTD/non-CTD)

If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?

If electronic submission: paper forms and certifications signed (non-CTD) or electronic forms and certifications signed (scanned or digital signature)(CTD)?

YES
 NO

Forms include: 356h, patent information (3542a), financial disclosure (3454/3455), user fee cover sheet (3542a), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.

Comments:

If electronic submission, does it follow the eCTD guidance? (<http://www.fda.gov/cder/guidance/7087rev.pdf>)

YES
 NO

If not, explain (e.g., waiver granted):

<p>Form 356h: Is a signed form 356h included?</p> <p><i>If foreign applicant, both the applicant and the U.S. agent must sign the form.</i></p> <p>Are all establishments and their registration numbers listed on the form?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Index: Does the submission contain an accurate comprehensive index?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including:</p> <p><input checked="" type="checkbox"/> legible <input checked="" type="checkbox"/> English (or translated into English) <input checked="" type="checkbox"/> pagination <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Controlled substance/Product with abuse potential:</p> <p>Abuse Liability Assessment, including a proposal for scheduling, submitted?</p> <p>Consult sent to the Controlled Substance Staff?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>BLAs/BLA efficacy supplements only:</p> <p>Companion application received if a shared or divided manufacturing arrangement?</p> <p>If yes, BLA #</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
Patent Information (NDAs/NDA efficacy supplements only)	
<p>Patent information submitted on form FDA 3542a?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Debarment Certification	
<p>Correctly worded Debarment Certification with authorized signature?</p> <p><i>If foreign applicant, both the applicant and the U.S. Agent must</i></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p>sign the certification.</p> <p><i>Note: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., “[Name of applicant] 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.” Applicant may not use wording such as, “To the best of my knowledge...”</i></p> <p>Comments:</p>	
Field Copy Certification (NDAs/NDA efficacy supplements only)	
<p>Field Copy Certification: that it is a true copy of the CMC technical section (<i>applies to paper submissions only</i>)</p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>	<p><input checked="" type="checkbox"/> Not Applicable (<i>electronic submission or no CMC technical section</i>)</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
Financial Disclosure	
<p>Financial Disclosure forms included with authorized signature?</p> <p><i>Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an Agent.</i></p> <p><i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i></p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
Pediatrics	
<p><u>PREA</u></p>	
<p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p>	
<p>Are the required pediatric assessment studies or a full waiver of pediatric studies included?</p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p>If no, is a request for full waiver of pediatric studies OR a request for partial waiver/deferral and a pediatric plan included?</p> <ul style="list-style-type: none"> • <i>If no, request in 74-day letter.</i> • If yes, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3) 	<p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p>Comments:</p>	

BPCA (NDAs/NDA efficacy supplements only):	
Is this submission a complete response to a pediatric Written Request? <i>If yes, contact PMHS (pediatric exclusivity determination by the Pediatric Exclusivity Board is needed).</i> Comments:	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
Prescription Labeling	
Check all types of labeling submitted. Comments:	<input type="checkbox"/> Not applicable <input checked="" type="checkbox"/> Package Insert (PI) <input checked="" type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use <input type="checkbox"/> MedGuide <input type="checkbox"/> Carton labels <input checked="" type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)
Is electronic Content of Labeling submitted in SPL format? <i>If no, request in 74-day letter.</i> Comments:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Package insert (PI) submitted in PLR format? If no , was a waiver or deferral requested before the application was received or in the submission? If before , what is the status of the request? <i>If no, request in 74-day letter.</i> Comments:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? Comments:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
MedGuide or PPI (plus PI) consulted to OSE/DRISK? (<i>send WORD version if available</i>) Comments: Not required checked with OSE.	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
REMS consulted to OSE/DRISK? Comments:	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Carton and immediate container labels, PI, PPI, and proprietary name (if any) sent to OSE/DMEDP? Comments:	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

OTC Labeling	
<p>Check all types of labeling submitted.</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> Outer carton label <input type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify)
<p>Is electronic content of labeling submitted?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>Are annotated specifications submitted for all stock keeping units (SKUs)?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>If representative labeling is submitted, are all represented SKUs defined?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>Proprietary name, all labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEDP?</p> <p>Comments:</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
Meeting Minutes/SPA Agreements	
<p>End-of Phase 2 meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO
<p>Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES Date(s): 09/23/2008 <input type="checkbox"/> NO
<p>Any Special Protocol Assessment (SPA) agreements?</p> <p><i>If yes, distribute letter and/or relevant minutes before filing meeting.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: January 29, 2009

NDA/BLA #: 22-417

PROPRIETARY/ESTABLISHED NAMES: NORVIR® (ritonavir) 100mg tablets

APPLICANT: Abbott

BACKGROUND: Norvir (ritonavir) 100mg capsules and Norvir (ritonavir) 80 mg per ml solution already approved and this NDA is for Norvir (ritonavir) 100mg tablets. The Norvir (ritonavir) 100mg tablets will not require refrigeration and eventually the Norvir (ritonavir) 100mg capsules (which require refrigeration) will be taken off the market.

(Provide a brief background of the drug, (e.g., molecular entity is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Rashmi Kalla, PharmD	Y
	CPMS/TL:	Karen Winestock	Y
Cross-Discipline Team Leader (CDTL)	Kimberly Struble, PharmD		Y
Clinical	Reviewer:	Regina Alivisatos, MD	Y
	TL:	Kimberly Struble, PharmD	Y
Social Scientist Review (for OTC products)	Reviewer:		
	TL:		
Labeling Review (for OTC products)	Reviewer:		
	TL:		
OSE	Reviewer:		
	TL:		
Clinical Microbiology (for antimicrobial products)	Reviewer:	Narayana Battula, PhD	Y

	TL:	Julian O'Rear, PhD	Y
Clinical Pharmacology	Reviewer:	Stanley Au, PharmD	Y
	TL:	Kellie S. Reynolds, PharmD	Y
Biostatistics	Reviewer:	Wen Zeng, PhD	Y
	TL:	Greg Soon, PhD	N
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Pritam Verma, PhD	N
	TL:	Hanan Ghantous, PhD	N
Statistics, carcinogenicity	Reviewer:		
	TL:		
Product Quality (CMC)	Reviewer:	Dorota M. Matecka, PhD	Y
	TL:	Stephen Miller, PhD PAL, ONDQA	Y
Facility (<i>for BLAs/BLA supplements</i>)	Reviewer:		
	TL:		
Microbiology, sterility (<i>for NDAs/NDA efficacy supplements</i>)	Reviewer:		
	TL:		
Bioresearch Monitoring (DSI)	Reviewer:		N
	TL:		N
Other reviewers			N

OTHER ATTENDEES: Jeffrey Murray, MD, Deputy Director, DAVP
Debra Birnkrant, MD, Director, DAVP

505(b)(2) filing issues? If yes, list issues:	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Per reviewers, are all parts in English or English translation? If no, explain:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p>Electronic Submission comments</p> <p>List comments</p>	<input checked="" type="checkbox"/> Not Applicable
<p>CLINICAL</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical study site(s) inspections(s) needed? <p>If no, explain: Dosage form change relying on bioequivalence studies only. No Clinical data submitted.</p>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<ul style="list-style-type: none"> Advisory Committee Meeting needed? <p>Comments:</p> <p><i>If no, for an original NME or BLA application, include the reason. For example:</i></p> <ul style="list-style-type: none"> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>CLINICAL MICROBIOLOGY</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>CLINICAL PHARMACOLOGY</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE

<p>Comments:</p>	<input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical pharmacology study site(s) inspections(s) needed? 	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>BIOSTATISTICS</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>PRODUCT QUALITY (CMC)</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>If EA submitted, consulted to EA officer (OPS)?</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Establishment(s) ready for inspection? Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ? <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Sterile product? 	<input type="checkbox"/> YES

<p>If yes, was Microbiology Team consulted for validation of sterilization? (NDAs/NDA supplements only)</p>	<input checked="" type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>FACILITY (BLAs only)</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
REGULATORY PROJECT MANAGEMENT	
<p>Signatory Authority: Jeffrey Murray, MD, Deputy Director, DAVP</p> <p>GRMP Timeline Milestones: Issue Acknowledgement letter by January 02, 2009 Filing Meeting by February 02, 2009 Filing Letter with no issues by March 03, 2009 PDUFA IV Target Date: (for labeling/post-marketing/risk management plan discussions): June 05, 2009 Establish date for completion of Reviews: August 19, 2009 GRMP date for DIVsig NDA/BLAs: September 26, 2009 PDUFA DATE October 19, 2009</p> <p>Comments:</p>	
REGULATORY CONCLUSIONS/DEFICIENCIES	
<input type="checkbox"/>	The application is unsuitable for filing. Explain why:
<input checked="" type="checkbox"/>	The application, on its face, appears to be suitable for filing. <input checked="" type="checkbox"/> No review issues have been identified for the 74-day letter. <input type="checkbox"/> Review issues have been identified for the 74-day letter. List (optional): <input checked="" type="checkbox"/> Standard Review <input type="checkbox"/> Priority Review
ACTIONS ITEMS	
<input checked="" type="checkbox"/>	Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into tracking system.
<input type="checkbox"/>	If RTF action, notify everybody who already received a consult request, OSE PM., and Product Quality PM. Cancel EER/TBP-EER.

<input type="checkbox"/>	If filed and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
<input type="checkbox"/>	If BLA or priority review NDA, send 60-day letter.
<input checked="" type="checkbox"/>	Send review issues/no review issues by day 74
<input checked="" type="checkbox"/>	Other: Send DDMAC Consult Request by next week 02/04/09 and Finalize OSE involvement.

Appendix A (NDA and NDA Supplements only)

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

- (1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
- (2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),
- (2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.
- (3) All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely

for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),
- (2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or
- (3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your OND ADRA or OND IO.

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

/s/

Rashmi Kalla

3/25/2009 02:29:14 PM

CSO

Forgot to DFS. This was completed by 03/03/09 just not DFSd.

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: February 24, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

**SUBJECT: NDA 22417 Clinical Pharmacology Information Request Clarification-
Submission Dated February 5, 2009-Studies M10-307 and M10-235**

We refer to your submission dated February 5, 2009 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417 which provided datasets for studies M10-307 and M10-235 which included ritonavir plasma concentrations and pharmacokinetic parameters. Please also refer to FDA's facsimile dated February 20, 2009 with clinical pharmacology information request asking for a data file with ritonavir dose administration clock times for all subjects dosed in the M10-307 and M10-235 studies. Finally refer to email correspondence received from Ms. Mary Konkowski on February 20, 2009 asking for clarification of this request. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

Clinical Pharmacology Comments:

1. Please provide a data file that combines the following for the M10-307 and M10-235 studies:
 - a) The scheduled and actual clock time for when the dose was administered.
 - b) The scheduled and actual sampling times (clock times) for the pre-dose and post-dose blood samples for each subject (and each period that a subject was dosed in).
 - c) The pre-dose and the post-dose sampling times for the pre-dose and post-dose blood samples for each subject (and each period that a subject was dosed in) relative to when the dose was administered.

We are providing this above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me at 301-796-3931 if you have any questions regarding the contents of this transmission

Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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

/s/

Rashmi Kalla
3/9/2009 11:15:28 AM
CSO

Fax sent already regarding clarification of clin pharm request
sampling times

Kimberly Struble
3/11/2009 08:51:13 AM
MEDICAL OFFICER

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: February 20, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Pharmacology Information Request -Submission Dated February 5, 2009-Studies M10-307 and M10-235

We refer to your submission dated February 5, 2009 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417 which provided datasets for studies M10-307 and M10-235 which included ritonavir plasma concentrations and pharmacokinetic parameters. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

Clinical Pharmacology Comments:

- Please provide a data file with the ritonavir dose administration clock times (planned and actual) for all subjects who were dosed in the M10-307 and M10-235 studies. If this information was submitted in the NDA application, please specify the location.

We are providing this above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me at 301-796-3931 if you have any questions regarding the contents of this transmission

Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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

/s/

Rashmi Kalla

3/9/2009 11:20:19 AM

CSO

Clin pharm request for ritonavir dose admin clock times
M10-307 & M10-235 fax sent 02/20/09

Clin pharm request for ritonavir dose admin clock times
M10-307 & M10-235

Kimberly Struble

3/11/2009 08:51:37 AM

MEDICAL OFFICER



FILING COMMUNICATION

NDA 22-417

Abbott Laboratories
Attention: Mary Konkowski
Manager, Global Pharmaceutical Regulatory Affairs
Dept. PA76/ Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your new drug application (NDA) dated December 19, 2009, received December 19, 2009 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for NORVIR® (ritonavir) 100mg tablets.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Standard**. Therefore, the user fee goal date is October 19, 2009.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by June 5, 2009.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

We acknowledge your request for a waiver of the requirement that the **Highlights** of Prescribing Information be limited to no more than one-half page. We will consider your request during labeling discussions.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a (b) (4) waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the (b) (4) waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Rashmi Kalla, PharmD, Regulatory Project Manager, at (301) 796-3931.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

Debra Birnkrant
2/18/2009 03:36:33 PM
NDA 22-417

International Inspections:

(Please note: International inspections require sign-off by the ORM Division Director or DPE Division Director.)

We have requested an international inspection because:

There is a lack of domestic data that solely supports approval;

_____ Other (please explain):

Goal Date for Completion:

We request that the inspections be conducted and the Inspection Summary Results be provided by **July 31, 2009**. We intend to issue an action letter on this application by **October 19, 2009**.

Should you require any additional information, please contact Rashmi Kalla (301-796-3931).

Concurrence:

Kellie Reynolds, Pharm.D., Deputy Director, Division of Clinical Pharmacology 4

Stanley Au, Pharm.D., BCPS, Clinical Pharmacology Reviewer

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/s/

John Lazor
2/10/2009 01:45:16 PM

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: January 29, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Pharmacology Information Request

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. We also refer to FDA's facsimile dated January 26, 2009 in which we asked for ritonavir method validation report for the ritonavir bioanalysis method used to analyze samples for the M10-235 and M10-307 studies. We finally refer to Abbott's submission received on January 28, 2009 in which method validation data was provided for studies M10-235 and M10-307. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

Clinical Pharmacology Comments:

1. Please confirm that the ritonavir method validated by [REDACTED] (b) (4) was used to analyze samples for the M10-235 and M10-307 studies. An additional ritonavir method validation report by [REDACTED] (b) (4) was also submitted-please clarify the purpose of this additional report.

We are providing this above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me at 301-796-3931 if you have any questions regarding the contents of this transmission

Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

Rashmi Kalla
1/30/2009 10:01:21 AM
CSO

Fax sent 01/30/09 f/u maethod validation info req from
clin pharm

Kimberly Struble
1/30/2009 10:11:57 AM
MEDICAL OFFICER

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: January 26, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Pharmacology Information Request

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

Clinical Pharmacology Comments:

1. Please provide the ritonavir method validation report for the ritonavir bioanalysis method used to analysis samples for the M10-235 and M10-307 studies. Please provide this information by January 30, 2008.
2. Please submit the following information for the M10-235 and M10-307 studies at your earliest convenience:
 - a) Please provide both the actual sampling (clock) time and the post dose sampling time for each ritonavir plasma sample collected.
 - b) Please provide the ritonavir PK parameters data for each subject as SAS transport files.
3. Please note that if the requested information is located in the NDA supplement, please specify the location of the requested information.

We are providing this above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me at 301-796-3931 if you have any questions regarding the contents of this transmission

Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

Rashmi Kalla
1/30/2009 09:31:02 AM
CSO

Clin pharm fax sent 01/26/09 requesting method validation for
m10-235/m10-307-and other clin pharm info requested

Kimberly Struble
1/30/2009 10:12:14 AM
MEDICAL OFFICER

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: January 26, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Information Request

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

Clinical Comments:

- Please provide a table of mean and median exposures (C_{max} , AUC) by administered dose group for the four PK trials performed in HIV subjects that are referenced in the submission (Study M93-107, Study M93-112, Study M93-134, and Study M96-604).

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Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

Rashmi Kalla
1/30/2009 09:24:17 AM
CSO

Fax of cinical comments about PK trials and mean
and median exposures required

Kimberly Struble
1/30/2009 10:12:28 AM
MEDICAL OFFICER

FACSIMILE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: January 14, 2009

TO: Mary Konkowski, Manager, Global Pharmaceutical Regulatory Affairs

SPONSOR: Abbott Laboratories

SUBJECT: NDA 22417 Clinical Information Request

We refer to your submission dated December 19, 2008 for NORVIR® (ritonavir) Tablets, 100 mg under original NDA 22417. Please refer to the comments below from the review team. Please respond via email correspondence and send an archival copy of your response to your NDA.

Clinical Comments:

1. Please provide us the reasoning as to why the safety data from NV study M06-842 was not included in the integrated safety analysis of the PK study data (M10-263, M10-307, and M10-235).
2. Please provide a table of administered doses and exposures (C_{max}, AUC) for the four PK trials performed in HIV subjects that are referenced in the submission (Study M93-107, Study M93-112, Study M93-134 and Study M96-604).

We are providing this above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me at 301-796-3931 if you have any questions regarding the contents of this transmission

Rashmi Kalla, PharmD
Regulatory Project Manager
Division of Antiviral Products

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/s/

Rashmi Kalla
1/16/2009 04:06:51 PM
CSO

Kimberly Struble
1/21/2009 02:31:16 PM
MEDICAL OFFICER



NDA 22-417

NDA ACKNOWLEDGMENT

Abbott Laboratories
Attention: Mary Konkowski
Manager, Global Pharmaceutical Regulatory Affairs
Dept. PA76/ Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

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

Name of Drug Product: NORVIR[®] (ritonavir) Tablets, 100 mg

Date of Application: December 19, 2008

Date of Receipt: December 19, 2008

Our Reference Number: NDA 22-417

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 17, 2009 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, call Rashmi Kalla, PharmD, Regulatory Project Manager, at (301) 796-3931.

Sincerely,

{See appended electronic signature page}

Karen Winestock
Chief, Project Management Staff
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

Karen Winestock
1/7/2009 11:35:02 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

IND 43718

Abbott Laboratories
Attention: Mary Konkowski
Manager Global Pharmaceutical Regulatory Affairs
200 Abbott Park Road
PA76, AP30-1NE
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Norvir (ritonavir).

We also refer to the teleconference between representatives of your firm and the FDA on Tuesday, September 23, 2008. The purpose of the telephone conference was to obtain feedback and agreement on the proposed content and format of your new drug application (NDA) for Norvir (ritonavir) 100 mg tablets.

A copy of the official minutes of the telephone conference is attached for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Karen Winestock, Chief, Project Management Staff at (301) 796-0834.

Sincerely,

{See appended electronic signature page}

Jeffrey Murray, M.D., MPH
Deputy Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure - Meeting Minutes

MEMORANDUM OF MEETING MINUTES

MEETING DATE: September 23, 2008
TIME: 10:00 to 11:00 AM
LOCATION: White Oak Building 22, Silver Spring, MD
APPLICATION: IND 43,718
DRUG NAME: Norvir (ritonavir) Tablets
TYPE OF MEETING: Type B, PreNDA meeting

MEETING CHAIR: Jeffrey Murray, M.D., M.P.H.

MEETING RECORDER: Sherly Abraham

FDA ATTENDEES:

1. Jeffrey Murray, M.D., MPH, Deputy Director, DAVP
2. Scott Proestel, M.D., Acting Clinical Team Leader, DAVP
3. Regina Alivisatos, M.D., Medical Officer, DAVP
4. Julian O'Rear, Ph.D., Microbiology Team Leader, DAVP
5. Narayana Battula, Ph.D., Microbiology Reviewer, DAVP
6. Kellie Reynolds, Pharm.D., Deputy Director, Division of Clinical Pharmacology 4, (OTS/OCP/DCP4)
7. Derek Y. Zhang, Ph.D., Clinical Pharmacology Reviewer (OTS/OCP/DCP4)
8. Stephen Miller, Ph.D., Pharmaceutical Assessment Lead, (ONDQA/DPA II)
9. Hari Sachs, M.D., Medical Team Leader, OND/PMHS
10. Alyson Karesh, M.D., Medical Reviewer, OND/PMHS
11. Karen Winestock, Chief, Project Management Staff, DAVP
12. Robert Kosko, Pharm.D., M.P.H., Regulatory Project Manager, DAVP
13. Rashmi Kalla, Pharm.D., Regulatory Project Manager, DAVP
14. Sherly Abraham, R.Ph., Regulatory Project Manager, DAVP

EXTERNAL CONSTITUENT ATTENDEES:

1. Mary Konkowski, Manager, Regulatory Affairs
2. Cheryl Dziak, Associate Director, Regulatory Affairs
3. Kevin Fitzpatrick, Director, Regulatory Affairs
4. Tom Hassall, M.S., R.Ph., Director, Regulatory Intelligence/Abbott FDA Liaison Office
5. Barry Bernstein M.D., Global Project Head
6. Tom Podsadecki, M.D., Medical Director, Antiviral Clinical Project Team
7. Denny Kim, M.D., Associate Medical Director, Antiviral Clinical Project Team
8. John Morris, Ph.D., Director, Global Pharmaceutical and Analytical Sciences
9. Cheri Enders Klein, Ph.D., Associate Director, Clinical Pharmacokinetics & Pharmacodynamics

10. Yi-Lin Chiu, P, Associate Director, Biometrics, Clinical Pharmacology & Pharmacometrics
11. Walid Awni, Ph.D., Senior Director, Clinical Pharmacology & Pharmacometrics
12. Wing Keung (Juki) Ng, Pharm.D., Ph.D., Senior Research Pharmacokineticist, Clinical Pharmacokinetics & Pharmacodynamics
13. Jeanne Fox, Divisional Vice President, Global Pharmaceutical Regulatory Affairs

BACKGROUND:

Abbott is developing Norvir (ritonavir) tablets, a peptidomimetic human immunodeficiency virus type 1(HIV-1) protease inhibitor, for the prevention and treatment of HIV-1 infection. Ritonavir is currently available as 100 mg soft gelatin capsules (SGCs) and as an 80 mg/mL oral solution. The existing SGC formulation requires refrigerated storage. Using the same melt extrusion technology used for the approved Kaletra (lopinavir/ritonavir) tablet formulations, a new 100 mg film-coated tablet formulation of ritonavir has been developed that will not require refrigeration. Abbott requested a Type B,Pre-NDA meeting to obtain feedback and agreement on the proposed content and format of their new drug application (NDA) for the new dosage form. On August 14, 2008, FDA provided preliminary comments to Abbott via facsimile. At Abbott's request, the meeting primarily focused on FDA's response to question 3. However, question 5, 10 and additional clinical pharmacology issues were discussed.

MEETING OBJECTIVES:

- Discuss and obtain feedback and agreement on the proposed content and format of the submission package for Norvir tablets.

DISCUSSION POINTS: Abbott's questions are in italics, FDA's preliminary comments are in regular font, and the discussions during September 23, 2008, teleconference are in bold.

Question 3:

The NDA will contain the information described in this briefing document to demonstrate the ritonavir pharmacokinetic profile and safety data support the risk/benefit profile of the Norvir Tablet when dosed as 600 mg twice daily. Does FDA agree the proposed information is sufficient/appropriate for the NDA filing?

Response:

As noted in the previously submitted facsimile response to question 1, the Agency has serious concerns regarding the adequacy of your proposed submission to support the use of the 100 mg tablets at the approved 600 mg dose. There are a number of reasons for these concerns, including the increased bioavailability of the new tablet formulation in the fasted state relative to the SGC, which could result in an increased frequency of adverse events.

FDA acknowledged receipt of Abbott's September 22, 2008, facsimile that provided additional information to support the 600 mg dosing regimen using the 100 mg tablets.

The FDA stated the information helped them better understand Abbott's dosing proposal. However, FDA requested Abbott provide the variability around the data presented in Table 1 and Figure 1. In addition, the FDA asked Abbott to provide some assurance that the ritonavir pharmacokinetic linearity is not formulation dependent.

Abbott agreed to provide additional information in the NDA to answer these queries.

[REDACTED] (b) (4)

[REDACTED] (b) (4)

[REDACTED] (b) (4)

The FDA stated these were review issues.

Abbott asked the FDA for guidance on how to revise the labeling.

[REDACTED] (b) (4)

[REDACTED] (b) (4)

(b) (4)

Abbott asked if they could submit a high level label proposal.

The FDA agreed to review Abbott's proposal and have a telephone conference to discuss any issues.

Question 5:

In addition to the proposed U.S. marketed packaging configuration of 30 tablets/bottle, Abbott intends to add a second packaging configuration consisting of 60 tablets in a 100 cc induction-sealed HDPE bottle with (b) (4) caps. The larger bottle/cap configuration will be of the same materials as the 30-tablet count bottle/cap configuration. The 30-tablet count bottle/cap configuration is the configuration used for the primary stability studies that were previously discussed in Abbott correspondences dated December 13, 2007 and March 10, 2008 and in FDA correspondence dated January 17, 2008 (Appendix 1). Abbott proposes to submit one-month of stability data for the new 60-tablet count package configuration in the NDA at the time of the initial submission. Abbott also proposes to update the NDA with stability data through 6 months for the new container closure during the review of the NDA at the same time the 12-month stability update is submitted for the 30-tablet count configuration as discussed in Abbott's March 10, 2008 correspondence. An expiration dating period of (b) (4) will be requested for both the 30-count and 60-count packaging configurations based on the data at the long-term storage condition for the 30-count bottle, the similarity of the packaging configuration and headspace between the packaging configurations, and the stability data of the tablets showing the same trends in both container closure systems. Providing the data presented in the NDA support a (b) (4) expiry, does FDA agree with this proposal?

Response:

This plan is acceptable from our perspective, since the stability data on the 30-count bottles includes the 30°C/75%RH long-term condition recommended for PEPFAR products. The main issue will be linking the moisture content trends between the two packaging configurations, and comparison to the moisture levels found to be acceptable via open-dish and moisture-equilibration studies. Please include the moisture permeation rate of the two bottles in the initial NDA submission. Please discuss at the September teleconference Abbott's views on the best metrics for prediction of moisture uptake by Norvir Tablets in the bottles of 30 and 60 count. Please also clarify at the September teleconference the storage recommendation that is planned for the 60-count bottle.

Abbott stated there is very little moisture permeation in either bottle and this can be compared in several ways.

The FDA requested Abbott include in the NDA Abbott's views on the best metric(s) for prediction of moisture uptake by Norvir tablets in the bottles of 30 and 60 count. (e.g. moisture permeation per tablet versus as some function of headspace, etc.)

Abbott stated the storage recommendation that is planned for the 60-count bottle would be to store at or below 30 degrees centigrade.

The FDA stated it was very useful in the Kaletra tablet NDA to have data to support a labeling statement for patients who will keep the tablets outside the bottle for a short period of time. This would probably also be appropriate for Norvir tablets, and Abbott should consider analyzing the data on exposed (b) (4) and tablets to support an analogous labeling statement.

Question 7:

Content and Format of the Application - MODULE 3

Since there were no ritonavir drug substance studies performed to support the NDA, Abbott will cross-reference the Norvir Oral Solution NDA (20-659) for all ritonavir drug substance information. Does FDA agree with this proposal?

Response:

This approach is appropriate, but please include in the Norvir Tablet NDA information on all facilities involved with commercial ritonavir drug substance manufacture and testing, and a brief summary of the significant changes made to the manufacturing and controls for ritonavir drug substance after approval of NDA 20-659.

Abbott agreed to include the facility information for ritonavir drug substance in the NDA. They asked if starting the summary of post-approval changes from the approval of the Norvir Soft Gelatin Capsule (20-945) be acceptable.

The FDA agreed with this proposal.

Question 10 Request for Priority Review

Would FDA consider granting priority review of the Norvir Tablet NDA based on the improved storage conditions associated with the tablet formulation?

Response:

A determination regarding the need for priority review will be made at the time of the submission filing.

During the telephone conference, the FDA stated if priority review is determined to be appropriate, the 12-month update for the primary stability studies (30-count bottles) would be very important for demonstrating the physical and chemical stability of the Norvir tablets. Based on the information in the briefing package, this update is planned for March

2009, approximately 4 months into the anticipated review cycle for the NDA. If this update significantly changes the stability trends seen in the 6 and 9 month datasets, or if the stability data do not support the expiration dating period, the March 2009 update would be considered a major amendment, which would extend the review cycle.

Additional CMC Information Request:

As additional background information for the September 23, 2008, Pre-NDA teleconference, please provide a summary of the early formulations of the Norvir Tablets which failed stability (b) (4) (i.e., the three tablet formulations used in BE studies M06-842 and M10-263). What has been learned from these early formulations regarding tablet attributes and/or manufacturing parameters that are important for stability under high temperature with exposure to moisture?

FDA commented that the summary presented in the September 22, 2008, amendment was useful for understanding the formulation development. The Division recommended that this information be included in the NDA submission as part of the Pharmaceutical Development section. (b) (4)

Additional Clinical Pharmacology Comments

For question 3, FDA reminded Abbott that the currently marketed soft gelatin capsules and the oral solution were not bioequivalent. The data Abbott presented in Table 2 were misleading. Abbott acknowledged the FDA's comment.

DECISIONS (AGREEMENTS) REACHED:

Abbott will update the labeling proposal (b) (4)

UNRESOLVED ISSUES OR ISSUES REQUIRING FURTHER DISCUSSION:

The data needed to support (b) (4)

ACTION ITEMS:

Abbott will submit a copy of the European package insert for Norvir
Abbott will submit a revised U.S. package insert for FDA review and feedback.

Linked Applications

Sponsor Name

Drug Name

IND 43718

ABBOTT
LABORATORIES
PHARMACEUTICAL
PRODUCTS DIV

NORVIR (RITONAVIR) SOFT ELASTIC
CAPSULES

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/s/

JEFFREY S MURRAY

10/22/2008