

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204655Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

**PATENT INFORMATION SUBMITTED WITH THE FILING  
OF AN NDA, AMENDMENT, OR SUPPLEMENT**

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

NDA NUMBER

204-655

NAME OF APPLICANT/NDA HOLDER

AstraZeneca LP

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

TRADE NAME (OR PROPOSED TRADE NAME)

NEXIUM 24HR esomeprazole magnesium Delayed-Release Capsule

ACTIVE INGREDIENT(S)

esomeprazole magnesium

STRENGTH(S)

20 mg (equivalent to 22.3 mg Esomeprazole Magnesium Trihydrate)

DOSAGE FORM

Oral

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).

Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

**For hand-written or typewriter versions (only) 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 submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.**

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

**1. GENERAL**

a. United States Patent Number

5,690,960

b. Issue Date of Patent

November 25, 1997

c. Expiration Date of Patent

November 25, 2014

d. Name of Patent Owner

AstraZeneca AB

Address (of Patent Owner)

Karlebyhus, Astraallén

City/State

Södertälje

ZIP Code

SE-151 85

FAX Number (if available)

Telephone Number

011 46 (0)8 553 260 00

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)

Steve Mohr, Deputy General Counsel, North American and US General Counsel

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

1800 Concord Pike

City/State

Wilmington, DE

ZIP Code

19803

FAX Number (if available)

1 302-886-1578

Telephone Number

(800) 456-3669

E-Mail Address (if available)

Steve.Mohr@astrazeneca.com

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 the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**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 pending NDA, amendment, 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 pending NDA, amendment, or supplement?  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 active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending 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

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  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

**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

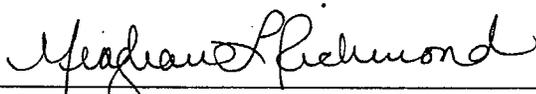
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) 17, 18 Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)  
Use for treatment of frequent heartburn  
Drug Facts; Use-treats frequent heartburn (occurs 2 or more days a week)  
Package Insert; How NEXIUM 24HR Treats Your Frequent Heartburn-NEXIUM 24HR stops acid production at the source – the pumps that release acid into the stomach. NEXIUM 24HR is clinically proven to treat frequent heartburn.

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and 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	
<p><b>6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending 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.</b></p> <p><b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b></p>	
<p>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)</p> 	<p>Date Signed</p> <p>May 6, 2013</p>
<p><b>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).</b></p>	
<p>Check applicable box and provide information below.</p>	
<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
<p>Name</p> <p>Meaghan L. Richmond, Ph.D.</p>	
<p>Address</p> <p>35 Gatehouse Drive</p>	<p>City/State</p> <p>Waltham, MA</p>
<p>ZIP Code</p> <p>02451</p>	<p>Telephone Number</p> <p>781-839-4054</p>
<p>FAX Number (if available)</p> <p>781-839-4121</p>	<p>E-Mail Address (if available)</p> <p>meaghan.richmond@astrazeneca.com</p>
<p>The public reporting burden for this collection of information has been estimated to average 20 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:</p> <p style="text-align: center;">           Department of Health and Human Services            Food and Drug Administration            Office of Chief Information Officer            1350 Piccard Drive, Room 400            Rockville, MD 20850         </p> <p style="text-align: center;"><i>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.</i></p>	

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**1. GENERAL**

a. United States Patent Number

5,714,504

b. Issue Date of Patent

February 3, 1998

c. Expiration Date of Patent

February 3, 2015

d. Name of Patent Owner

AstraZeneca AB

Address (of Patent Owner)

Karlebyhus, Astraallén

City/State

Södertälje

ZIP Code

SE-151 85

FAX Number (if available)

Telephone Number

011 46 (0)8 553 260 00

E-Mail Address (if available)

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

Yes  No

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

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

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**4. Method of Use**

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4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

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4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the proposed labeling.) Use for treatment of frequent heartburn Drug Facts; Use-treats frequent heartburn (occurs 2 or more days a week) Package Insert; How NEXIUM 24HR Treats Your Frequent Heartburn-NEXIUM 24HR stops acid production at the source – the pumps that release acid into the stomach. NEXIUM 24HR is clinically proven to treat frequent heartburn.
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**5: No Relevant Patents**

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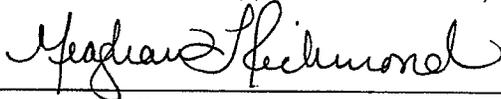
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**6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)**

Date Signed



May 6, 2013

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**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

Meaghan L. Richmond, Ph.D.

Address

35 Gatehouse Drive

City/State

Waltham, MA

ZIP Code

02451

Telephone Number

781-839-4054

FAX Number (if available)

781-839-4121

E-Mail Address (if available)

meaghan.richmond@astrazeneca.com

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Department of Health and Human Services  
Food and Drug Administration  
Office of Chief Information Officer  
1350 Piccard Drive, Room 400  
Rockville, MD 20850

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**I. GENERAL**

a. United States Patent Number

5,877,192

b. Issue Date of Patent

March 2, 1999

c. Expiration Date of Patent

May 27, 2014

d. Name of Patent Owner

AstraZeneca AB

Address (of Patent Owner)

Karlebyhus, Astraallén

City/State

Södertälje

ZIP Code

SE-151 85

FAX Number (if available)

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011 46 (0)8 553 260 00

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Steve.Mohr@astrazeneca.com

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Yes

No

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

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**4. Method of Use**

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4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) 1, 2, 5-7, 10, 11, 23 Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)  
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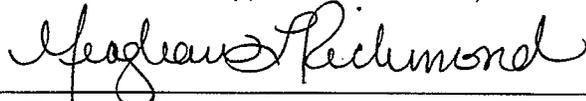
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**Check applicable box and provide information below.**

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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

Meaghan L. Richmond, Ph.D.

Address

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Waltham, MA

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Telephone Number

781-839-4054

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E-Mail Address (if available)

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Department of Health and Human Services Food and Drug Administration		Form Approved: OMB No. 0910-0513 Expiration Date: 10/31/2013 See OMB Statement on Page 3.	
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DOSAGE FORM Oral			
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the <i>only</i> information relied upon by FDA for listing a patent in the Orange Book.			
<b>For hand-written or typewriter versions (only) of this report:</b> 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.			
<b>FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number 5,900,424		b. Issue Date of Patent May 4, 1999	c. Expiration Date of Patent May 4, 2016
d. Name of Patent Owner AstraZeneca AB		Address (of Patent Owner) Karlebyhus, Astraallén	
		City/State Södertälje	
		ZIP Code SE-151 85	FAX Number (if available)
		Telephone Number 011 46 (0)8 553 260 00	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)  Steve Mohr, Deputy General Counsel, North America and US General Counsel		Address (of agent or representative named in 1.e.) 1800 Concord Pike	
		City/State Wilmington, DE	
		ZIP Code 19803	FAX Number (if available) 1 302 886 1578
		Telephone Number (800) 456-3669	E-Mail Address (if available) Steve.Mohr@astrazeneca.com
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input type="checkbox"/> No	

**For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**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 pending NDA, amendment, or supplement?	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> 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).	<input type="checkbox"/> Yes	<input type="checkbox"/> 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 active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
2.6 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> 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.)	<input type="checkbox"/> Yes	<input type="checkbox"/> No

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
3.2 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> 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.)	<input type="checkbox"/> Yes	<input type="checkbox"/> No

**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
4.2 Patent Claim Number(s) (as listed in the patent) 21, 22	Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the proposed labeling.) Use for treatment of frequent heartburn Drug Facts; Use-treats frequent heartburn (occurs 2 or more days a week) Package Insert; How NEXIUM 24HR Treats Your Frequent Heartburn-NEXIUM 24HR stops acid production at the source – the pumps that release acid into the stomach. NEXIUM 24HR is clinically proven to treat frequent heartburn.
---	---

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and 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.	<input type="checkbox"/> Yes
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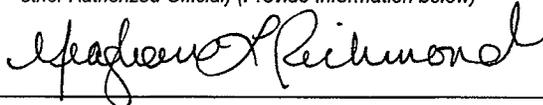
**6. Declaration Certification**

**6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending 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



May 6, 2013

**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

Meaghan L. Richmond, Ph.D.

Address

35 Gatehouse Drive

City/State

Waltham, MA

ZIP Code

02451

Telephone Number

781-839-4054

FAX Number (if available)

781-839-4121

E-Mail Address (if available)

meaghan.richmond@astrazeneca.com

The public reporting burden for this collection of information has been estimated to average 20 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  
 1350 Piccard Drive, Room 400  
 Rockville, MD 20850

*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.*

**PATENT INFORMATION SUBMITTED WITH THE FILING  
OF AN NDA, AMENDMENT, OR SUPPLEMENT**

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

NDA NUMBER

204-655

NAME OF APPLICANT/NDA HOLDER

AstraZeneca LP

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

TRADE NAME (OR PROPOSED TRADE NAME)

NEXIUM 24HR esomeprazole magnesium Delayed-Release Capsule

ACTIVE INGREDIENT(S)

esomeprazole magnesium

STRENGTH(S)

20 mg (equivalent to 22.3 mg Esomeprazole Magnesium Trihydrate)

DOSAGE FORM

Oral

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

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

**1. GENERAL**

a. United States Patent Number

6,369,085

b. Issue Date of Patent

April 9, 2002

c. Expiration Date of Patent

May 25, 2018

d. Name of Patent Owner

AstraZeneca AB

Address (of Patent Owner)

Karlebyhus, Astraallén

City/State

Södertälje

ZIP Code

SE-151 85

FAX Number (if available)

Telephone Number

011 46 (0)8 553 260 00

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)

Steve Mohr, Deputy General Counsel, North America and US General Counsel

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

1800 Concord Pike

City/State

Wilmington, DE

ZIP Code

19803

FAX Number (if available)

1 302 886 1578

Telephone Number

(800) 456-3669

E-Mail Address (if available)

Steve.Mohr@astrazeneca.com

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 the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**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 pending NDA, amendment, or supplement?	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> 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).	<input type="checkbox"/> Yes	<input type="checkbox"/> 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 active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
2.6 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> 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.)	<input type="checkbox"/> Yes	<input type="checkbox"/> No

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
3.2 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> 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.)	<input type="checkbox"/> Yes	<input type="checkbox"/> No

**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
4.2 Patent Claim Number(s) (as listed in the patent)	Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?	
12	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the proposed labeling.) Use for treatment of frequent heartburn Drug Facts; Use-treats frequent heartburn (occurs 2 or more days a week) Package Insert; How NEXIUM 24HR Treats Your Frequent Heartburn-NEXIUM 24HR stops acid production at the source – the pumps that release acid into the stomach. NEXIUM 24HR is clinically proven to treat frequent heartburn.	

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and 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.	<input type="checkbox"/> Yes
---	------------------------------

**6. Declaration Certification**

**6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending 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.**

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

Date Signed



May 6, 2013

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**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

Meaghan L. Richmond, Ph.D.

Address

35 Gatehouse Drive

City/State

Waltham, MA

ZIP Code

02451

Telephone Number

781-839-4054

FAX Number (if available)

781-839-4121

E-Mail Address (if available)

meaghan.richmond@astrazeneca.com

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Department of Health and Human Services  
Food and Drug Administration  
Office of Chief Information Officer  
1350 Piccard Drive, Room 400  
Rockville, MD 20850

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**PATENT INFORMATION SUBMITTED WITH THE FILING  
OF AN NDA, AMENDMENT, OR SUPPLEMENT**

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

NDA NUMBER

204-655

NAME OF APPLICANT/NDA HOLDER

AstraZeneca LP

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

TRADE NAME (OR PROPOSED TRADE NAME)

NEXIUM 24HR esomeprazole magnesium Delayed-Release Capsule

ACTIVE INGREDIENT(S)

esomeprazole magnesium

STRENGTH(S)

20 mg (equivalent to 22.3 mg Esomeprazole Magnesium Trihydrate)

DOSAGE FORM

Oral

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**1. GENERAL**

a. United States Patent Number

6,428,810

b. Issue Date of Patent

August 6, 2002

c. Expiration Date of Patent

November 3, 2019

d. Name of Patent Owner

AstraZeneca AB

Address (of Patent Owner)

Karlebyhus, Astraallén

City/State

Södertälje

ZIP Code

SE-151 85

FAX Number (if available)

Telephone Number

011 46 (0)8 553 260 00

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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)

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FAX Number (if available)

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Steve.Mohr@astrazeneca.com

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 the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**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 pending NDA, amendment, 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 pending NDA, amendment, or supplement?  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 active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending 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

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  Yes  No

3.2 Does the patent claim only an intermediate?  Yes  No

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**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) 11 Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

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

Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)  
 Use for treatment of frequent heartburn  
 Drug Facts; Use-treats frequent heartburn (occurs 2 or more days a week)  
 Package Insert; How NEXIUM 24HR Treats Your Frequent Heartburn-NEXIUM 24HR stops acid production at the source – the pumps that release acid into the stomach. NEXIUM 24HR is clinically proven to treat frequent heartburn.

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**6. Declaration Certification**

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Date Signed



May 6, 2013

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**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

Meaghan L. Richmond, Ph.D.

Address

35 Gatehouse Drive

City/State

Waltham, MA

ZIP Code

02451

Telephone Number

781-839-4054

FAX Number (if available)

781-839-4121

E-Mail Address (if available)

meaghan.richmond@astrazeneca.com

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OF AN NDA, AMENDMENT, OR SUPPLEMENT**

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

NDA NUMBER

204-655

NAME OF APPLICANT/NDA HOLDER

AstraZeneca LP

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

TRADE NAME (OR PROPOSED TRADE NAME)

NEXIUM 24HR esomeprazole magnesium Delayed-Release Capsule

ACTIVE INGREDIENT(S)

esomeprazole magnesium

STRENGTH(S)

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DOSAGE FORM

Oral

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**1. GENERAL**

a. United States Patent Number 6,875,872	b. Issue Date of Patent April 5, 2005	c. Expiration Date of Patent May 27, 2014
d. Name of Patent Owner AstraZeneca AB	Address (of Patent Owner) Karlebyhus, Astraallén	
	City/State Södertälje	
	ZIP Code SE-151 85	FAX Number (if available)
	Telephone Number 011 46 (0)8 553 260 00	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)  Steve Mohr, Deputy General Counsel, North America and US General Counsel	Address (of agent or representative named in 1.e.) 1800 Concord Pike	
	City/State Wilmington, DE	
	ZIP Code 19803	FAX Number (if available) 1 302 886 1578
	Telephone Number (800) 456-3669	E-Mail Address (if available) Steve.Mohr@astrazeneca.com
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		
<input type="checkbox"/> Yes <input type="checkbox"/> No		

**For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**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 pending NDA, amendment, 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 pending NDA, amendment, or supplement?  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 active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending 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

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  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

**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

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

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and 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

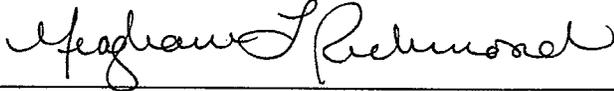
**6. Declaration Certification**

**6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending 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



May 6, 2013

**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

Meaghan L. Richmond, Ph.D.

Address

35 Gatehouse Drive

City/State

Waltham, MA

ZIP Code

02451

Telephone Number

781-839-4054

FAX Number (if available)

781-839-4121

E-Mail Address (if available)

meaghan.richmond@astrazeneca.com

The public reporting burden for this collection of information has been estimated to average 20 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  
 1350 Piccard Drive, Room 400  
 Rockville, MD 20850

*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.*

**PATENT INFORMATION SUBMITTED WITH THE FILING  
OF AN NDA, AMENDMENT, OR SUPPLEMENT**  
*For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation and Composition)  
and/or Method of Use*

NDA NUMBER  
204-655  
NAME OF APPLICANT/NDA HOLDER  
AstraZeneca LP

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

TRADE NAME (OR PROPOSED TRADE NAME)

NEXIUM 24HR esomeprazole magnesium Delayed-Release Capsule

ACTIVE INGREDIENT(S)

esomeprazole magnesium

STRENGTH(S)

20 mg (equivalent to 22.3 mg Esomeprazole Magnesium Trihydrate)

DOSAGE FORM

Oral

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

**For hand-written or typewriter versions (only) 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 submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.**

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

**1. GENERAL**

a. United States Patent Number 7,411,070	b. Issue Date of Patent August 12, 2008	c. Expiration Date of Patent May 25, 2018
d. Name of Patent Owner AstraZeneca AB	Address (of Patent Owner) Karlebyhus, Astraallén	
	City/State Södertälje	
	ZIP Code SE-151 85	FAX Number (if available)
	Telephone Number 011 46 (0)8 553 260 00	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)  Steve Mohr, Deputy General Counsel, North America and US General Counsel	Address (of agent or representative named in 1.e.) 1800 Concord Pike	
	City/State Wilmington, DE	
	ZIP Code 19803	FAX Number (if available) 1 302 886 1578
	Telephone Number (800) 456-3669	E-Mail Address (if available) Steve.Mohr@astrazeneca.com
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?	<input type="checkbox"/> Yes <input type="checkbox"/> No	

**For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**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 pending NDA, amendment, 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 pending NDA, amendment, or supplement?  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.  
**\*\*PLEASE NOTE: Regarding Responses 2.2 to 2.4, certain claims of this patent may cover at least one additional polymorph in addition to claiming the drug substance, but the patent is not being submitted for listing on that basis .**

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending 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

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  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

**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

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

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and 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, amendment, or supplement pending 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.**

<p>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)</p> 	<p>Date Signed</p> <p>May 6, 2013</p>
--	---------------------------------------

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
<p>Name Meaghan L. Richmond, Ph.D.</p>	
<p>Address 35 Gatehouse Drive</p>	<p>City/State Waltham, MA</p>
<p>ZIP Code 02451</p>	<p>Telephone Number 781-839-4054</p>
<p>FAX Number (if available) 781-839-4121</p>	<p>E-Mail Address (if available) meaghan.richmond@astrazeneca.com</p>

The public reporting burden for this collection of information has been estimated to average 20 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  
 1350 Piccard Drive, Room 400  
 Rockville, MD 20850

*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.*

## EXCLUSIVITY SUMMARY

NDA # 204655

SUPPL # N/A

HFD # 560

Trade Name Nexium 24HR

Generic Name esomeprozole magnesium

Applicant Name AstraZeneca LP

Approval Date, If Known March 28, 2014

### 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) NDA

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

YES  NO

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

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

d) Did the applicant request exclusivity?

YES  NO

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

3 years

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?

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# 21153

Nexium (esomeprazole magnesium) 20 and 40 mg capsules

NDA#

NDA#

2. Combination product.

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

YES  NO

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

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 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:

D961RC00001: double-blind, randomized, placebo, parallel group multicenter  
D961RC00002: double-blind, randomized, placebo, parallel group multicenter

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"):

D961RC00001: double-blind, randomized, placebo, parallel group multicenter  
 D961RC00002: double-blind, randomized, placebo, parallel group multicenter

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 # 111185 YES  ! NO   
 ! Explain:

Investigation #2 !  
 !  
 IND # 111185 YES  ! NO   
 ! Explain:



Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/  
-----

DANIEL BRUM  
03/27/2014

THERESA M MICHELE  
03/27/2014

### 1.3.3 DEBARMENT CERTIFICATION

**Re: NDA 204-655**

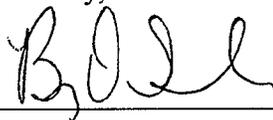
**NEXIUM® (esomeprazole magnesium) Delayed-Release Capsules Over the Counter (OTC)**

**Debarment Certification Statement**

---

In response to the requirements of the Generic Drug Enforcement Act of 1992, I hereby certify on behalf of AstraZeneca LP (AstraZeneca), that we did not use and will not use in connection with this New Drug Application, the services of any person in any capacity debarred under section 306 (a) or (b).

Sincerely,



---

Barry Sickels, Vice President  
Regulatory Affairs  
AstraZeneca

**From:** [Buchanan, Jeffrey A.](mailto:Jeffrey.A.Buchanan@astrazeneca.com)  
**To:** [angela.vickers@astrazeneca.com](mailto:angela.vickers@astrazeneca.com)  
**Cc:** [Firor, Judy W \(judy.firor@astrazeneca.com\)](mailto:Firor, Judy W (judy.firor@astrazeneca.com)); [christine.chirido@pfizer.com](mailto:christine.chirido@pfizer.com); [Buchanan, Jeffrey A.](mailto:Jeffrey.A.Buchanan@astrazeneca.com)  
**Subject:** NDA 204655 Nexium 24HR capsules - information  
**Date:** Tuesday, March 25, 2014 11:50:35 AM  
**Importance:** High

---

Hello Ms. Vickers,

See the information below:

- 1) It is acceptable to use the term Pharmaceutical Ink on the labels without listing the ingredients of the ink, since this product is a solid oral dosage form.
- 2) To be consistent with the Rx labeling, the trade name followed by the established name should be :

Nexium 24HR (esomeprazole magnesium)

Delayed-Release Capsules

- 3) For all labeling, to be consistent with the labeling of the Rx capsules, the strength of the OTC capsules should be depicted as 20 mg with a notation, as in the Rx labeling, that 20 mg of esomeprazole corresponds to 22.3 mg of esomeprazole magnesium trihydrate. In this connection, note the following wording taken from the approved labeling of the Nexium Rx product:

Each delayed-release capsule contains 20 mg, or  
40 mg of esomeprazole

(NEXIUM is supplied in delayed-release capsules  
and in packets for a delayed-release oral present  
as 22.3 mg, or 44.5 mg esomeprazole magnesium  
trihydrate)

- 4) In order to facilitate an accurate review of labeling, AstraZeneca should submit labeling as it is produced, rather than waiting until COB Thursday to submit *all* labeling.

***Jeff Buchanan***

*Regulatory Health Project Manager*

~~~~~

Division of Nonprescription Clinical Evaluation (DNCE)

FDA/OMPT/CDER/OND/ODE IV

10903 New Hampshire Avenue, WO22/Room 5461

Silver Spring, MD 20903

Phone: 301-796-1007 Fax: 301-796-9899

[jeffrey.buchanan@fda.hhs.gov](mailto:jeffrey.buchanan@fda.hhs.gov)

**Confidentiality Notice:** This message is private and may contain confidential and proprietary information. If you have received this message in error, please notify me immediately, remove the message from your system, and note that you must not copy, distribute, or take any action in reliance on it. Any unauthorized use or disclosure of the contents of this message is not permitted and may be unlawful.

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

/s/  
-----

JEFFREY A BUCHANAN  
03/25/2014

## Stewart, Sherry

---

**From:** Salvatore, Alina  
**Sent:** Tuesday, February 18, 2014 2:39 PM  
**To:** judy.firor@astrazeneca.com  
**Cc:** angela.vickers@astrazeneca.com; Stewart, Sherry; Salvatore, Alina; Buchanan, Jeffrey A.  
**Subject:** NDA 204655 Nexium 24H capsules- information request

Hi Judy,

Please see the information request below and submit the revised drug product specification section to reflect the change or submit your commitment by February 20, 2014. Also, please email me and Jeff Buchanan a copy of your response.

### Biopharmaceutics Information Request:

Your proposed dissolution acceptable criterion of  $Q = \frac{(b)}{(4)}\%$  at 30 min is NOT acceptable since esomeprazole dissolved  $\frac{(b)}{(4)}\%$  at 30 min in the buffer stage. The Agency's recommendations of  $Q = \frac{(b)}{(4)}\%$  at 30 min should be implemented.

Thank you,  
Alina

Alina W. Salvatore, R.Ph., M.S.  
CDR, United States Public Health Service  
Regulatory Project Manager  
Division of Nonprescription Clinical Evaluation  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research  
Phone: 240-402-0379

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

SHERRY A STEWART  
02/18/2014

**PeRC PREA Subcommittee Meeting Minutes**  
**January 22, 2014**

**PeRC Members Attending:**

Rosemary Addy

George Greeley

Jane Inglese

Hari Cheryl Sachs (did not review [REDACTED] (b) (4))

Wiley Chambers

Karen Davis-Bruno (only reviewed [REDACTED] (b) (4))

Colleen LoCicero

Peter Starke

Andrew Mulberg

Daiva Shetty (only reviewed [REDACTED] (b) (4))

Lily Mulugeta

Barbara Buch (only reviewed [REDACTED] (b) (4))

Rachel Witten (only reviewed [REDACTED] (b) (4))

Robert Nelson

Dianne Murphy

William Rodriiguez

Eleanor Mayer (only reviewed [REDACTED] (b) (4))

**Agenda**

**PREA**



NDA 204655      Nexium 24HR (esomeprazole)      Frequent heartburn  
Full Waiver



**Nexium 24HR (esomeprazole) Full Waiver**

- NDA 204655 seeks marketing approval for Nexium 24HR (esomeprazole) for the treatment of frequent heartburn.
- The application has a PDUFA goal date of March 30, 2014.
- The application triggers PREA as directed to a new indication.
- *PeRC Recommendations:*
  - The PeRC agreed with a full waiver because the product would be ineffective and/or unsafe for pediatric patients (a learned intermediary is needed). Labeling will reflect the need to consult a doctor.

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/s/  
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JANE E INGLESE  
02/03/2014

**From:** [Buchanan, Jeffrey A.](#)  
**To:** [Firor, Judy W \(judy.firor@astrazeneca.com\)](#)  
**Cc:** [angela.vickers@astrazeneca.com](#); [Buchanan, Jeffrey A.](#)  
**Subject:** NDA 204655 Nexium 24HR capsules - information request  
**Date:** Tuesday, January 28, 2014 12:28:01 PM  
**Importance:** High

---

Hi Judy,

Please see the information request below and respond with a formal submission to your application by close of business Monday, February 3, 2014. If you have questions, please contact me. Thank you.

*During the review of NDA 204655 Nexium 24HR delayed-release capsules, we note that some subjects in studies D961RC00001 and D961RC00002 received more than 280 mg of esomeprazole magnesium (20 mg x 14) over the course of the study. Please clarify the reason as to why and how this occurred.*

***Jeff Buchanan***

*Regulatory Health Project Manager*

~~~~~

Division of Nonprescription Clinical Evaluation (DNCE)

FDA/OMPT/CDER/OND/ODE IV

10903 New Hampshire Avenue, WO22/Room 5461

Silver Spring, MD 20903

Phone: 301-796-1007 Fax: 301-796-9899

[jeffrey.buchanan@fda.hhs.gov](mailto:jeffrey.buchanan@fda.hhs.gov)

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JEFFREY A BUCHANAN  
01/28/2014

**From:** [Buchanan, Jeffrey A.](mailto:Jeffrey.A.Buchanan@astrazeneca.com)  
**To:** [angela.vickers@astrazeneca.com](mailto:angela.vickers@astrazeneca.com)  
**Cc:** [Firor, Judy W \(judy.firor@astrazeneca.com\)](mailto:Judy.W.Firor@astrazeneca.com); [Buchanan, Jeffrey A.](mailto:Jeffrey.A.Buchanan@astrazeneca.com)  
**Subject:** NDA 204655 Nexium 24HR capsules - information request  
**Date:** Monday, November 25, 2013 3:21:39 PM  
**Importance:** High

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Hi Angela,

We are reviewing the Chemistry, Manufacturing and Control section of your NDA 204655 and have the following comments and information requests. Please respond with a formal submission to your application by COB Friday, December 20, 2013 or sooner. Feel free to contact me, if you have questions. Thank you.

1. Provide a table depicting the full current specification for your Esomeprazole drug substance.
2. Provide the name and model of (b) (4) machine used in the production of your OTC capsules
3. Provide a picture showing the colors of your proposed OTC capsules.
4. Provide the quantitative composition of the ink used for the words "NEXIUM 20 mg" and the stripes printed in yellow on the capsule, and indicate how much ink is used for the production of (b) (4) OTC capsules and how much ink is deposited on each capsule.
5. Provide the specification and acceptance tests for the above mentioned ink.
6. The substitution of the release specification of the Rx capsules for release testing of the OTC product is not acceptable unless you specify appropriate ranges for the storage times and storage conditions from the date of manufacture of the Rx capsules to the time of (b) (4).
7. Provide engineering drawings, with appropriate dimensions and tolerances, for all of your proposed packaging components (bottles and closures.)
8. Specify which (b) (4) closures are to be employed for the different bottles obtained from the various container suppliers, and indicate whether the (b) (4) closures are of the (b) (4).
9. Provide an Identification Test and the nominal weight of the filled canisters in your specification for your (b) (4).
10. You provided a Letter of Authorization (LOA) for the desiccants from (b) (4). This firm supplies both (b) (4) desiccants. If you plan to market your product with any of these desiccants, provide their specifications including Description, Appearance, Identification Tests and their Nominal Weight (and allowed weight range).

11. Specify whether or not technical batches AAAC and AAAD were manufactured in the same way as the primary stability batch of your proposed OTC capsules; if not, explain any differences.

12. Specify the attributes of the OTC capsules that are to be monitored in your primary stability program between the 12 and 36 month time points.

13. Since you provided data from stability studies on fewer than three production batches of the OTC capsules over a period that is shorter than the proposed expiry, based on the ICH Q1A(R2) Guidance, you should place at least three post-approval production batches on long term stability through the proposed shelf life and on accelerated studies for 6 months according to the protocol presented in P.8.1 of your NDA 204655.

***Jeff Buchanan***

*Regulatory Health Project Manager*

~~~~~

Division of Nonprescription Clinical Evaluation (DNCE)

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10903 New Hampshire Avenue, WO22/Room 5461\_ **(NOTE: New room # as of 08/30/13)**

Silver Spring, MD 20903

Phone: 301-796-1007 Fax: 301-796-9899

[jeffrey.buchanan@fda.hhs.gov](mailto:jeffrey.buchanan@fda.hhs.gov)

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JEFFREY A BUCHANAN  
11/25/2013

## Buchanan, Jeffrey A.

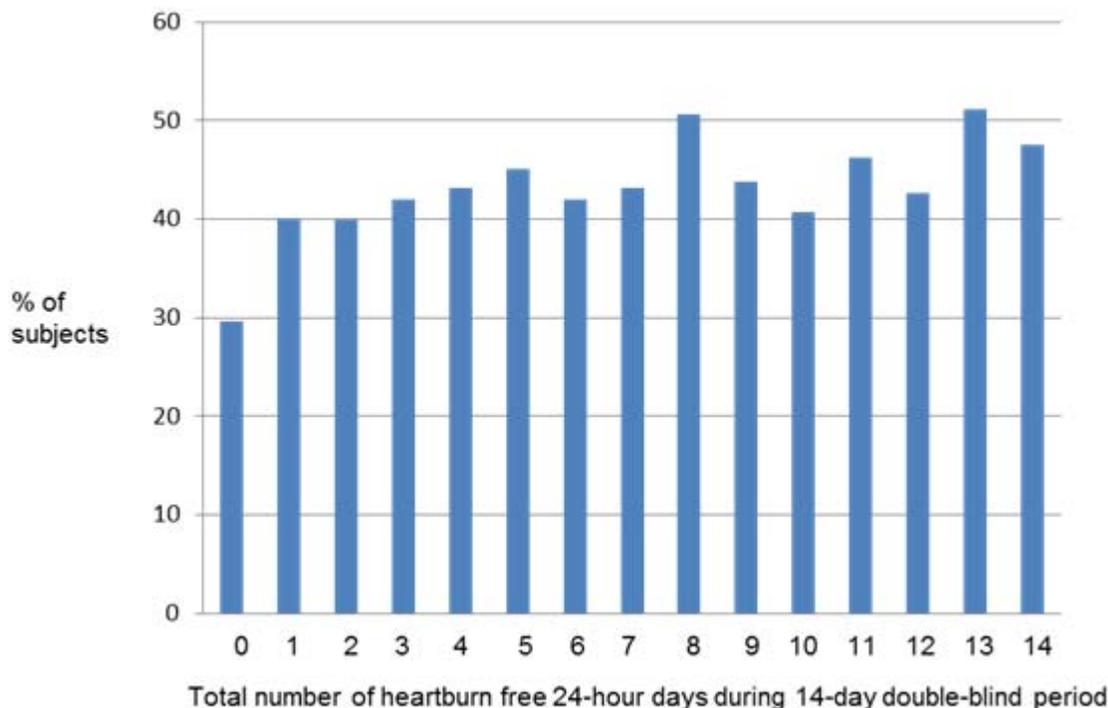
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**From:** Buchanan, Jeffrey A.  
**Sent:** Monday, November 18, 2013 12:01 PM  
**To:** angela.vickers@astrazeneca.com  
**Cc:** Firor, Judy W (judy.firor@astrazeneca.com); Buchanan, Jeffrey A.  
**Subject:** NDA 204655 Nexium 24 HR - Clinical Information Request

Hi Angela,

Please see the request for information below and respond with a formal submission to your application by COB Tuesday, December 3, 2013. If you have questions, please contact me. Thank you.

- In Table 55 of the Clinical Study Reports (CSRs) for Study D961RC00001 and Study D961RC00002, you present the percentage of subjects (by treatment arm) with heartburn free 24-hour days by diary day during the 14 days of double-blind treatment. Expand this table for each of the two studies by adding the following:*
  - The number and percentage (n/N, %) of subjects who would go on to be randomized and be included in the FAS population (by treatment arm) with heartburn free 24-hour days by diary day during the 7-day placebo run in period (days -8 to -1). Include a separate row for each day*
  - The number and percentage (n/N, %) of randomized subjects in the FAS population (by treatment arm) with a heartburn free 24-hour day on day 0 (randomization day)*
  - The number and percentage (n/N, %) of subjects in the FAS population (by treatment arm) with a heartburn free 24-hour day during each day of the 7-day placebo follow-up period (days 15 to 22). Include a separate row for each day*
- For Study D961RC00001 and Study D961RC00002, for each treatment group, provide a distribution bar graph that plots the percentage of patients (y-axis) against the total number (cumulative) of heartburn-free 24-hour days during the 14-day double blind treatment period (x-axis). The sample graph below (with arbitrary values plotted) is provided as a template.*



Also present the data in tabular format (n/N, %) for each treatment group in both studies.

**Jeff Buchanan**

*Regulatory Health Project Manager*

~~~~~

Division of Nonprescription Clinical Evaluation (DNCE)

FDA/OMPT/CDER/OND/ODE IV

10903 New Hampshire Avenue, WO22/Room 5461 **(NOTE: New room # as of 08/30/13)**

Silver Spring, MD 20903

Phone: 301-796-1007 Fax: 301-796-9899

[jeffrey.buchanan@fda.hhs.gov](mailto:jeffrey.buchanan@fda.hhs.gov)

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JEFFREY A BUCHANAN  
11/18/2013

**From:** [Vickers, Angela C](#)  
**To:** [Buchanan, Jeffrey A.](#)  
**Cc:** [Firor, Judy W](#)  
**Subject:** RE: NDA 204655 Nexium 24HR capsules - Request for guidance on updated FEI number  
**Date:** Wednesday, October 09, 2013 1:28:22 PM

---

Thanks Jeff,

For the (b) (4) facility, the current FEI # (b) (4) replaced the previous number, FEI # (b) (4).

We will submit the updated details per your advice.

*Kind regards,  
Angela*

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**From:** Buchanan, Jeffrey A. [mailto:Jeffrey.Buchanan@fda.hhs.gov]  
**Sent:** Wednesday, October 09, 2013 1:19 PM  
**To:** Vickers, Angela C  
**Cc:** Firor, Judy W; Buchanan, Jeffrey A.  
**Subject:** RE: NDA 204655 Nexium 24HR capsules - Request for guidance on updated FEI number  
**Importance:** High

Hi Angela,

It is acceptable to update the FEI number to the facility by submitting an amendment to your NDA (updated 356h and pointing the update to Module 3, Section P.3.1 will suffice). Please email to me the correct FEI number for the facility right away. Thank you.

Jeff Buchanan

---

**From:** Vickers, Angela C [mailto:Angela.Vickers@astrazeneca.com]  
**Sent:** Wednesday, October 09, 2013 10:48 AM  
**To:** Buchanan, Jeffrey A.  
**Cc:** Firor, Judy W  
**Subject:** NDA 204655 Nexium 24HR capsules - Request for guidance on updated FEI number

Hi Jeff,

We have been made aware that the FEI number for one of the manufacturing facilities (b) (4) included in our NDA has changed. Thus, the FEI number included on the 356h attachment establishment information document and in Module 3 (section P.3.1) have the older FEI number for the (b) (4) facility and not the updated FEI number.

We are seeking your guidance on handling this change in FEI number to ensure it does not impact the NDA review or cause delays with import. Would you recommend an amendment to the NDA be filed to update the 2 documents to ensure the Agency has the updated FEI information on file?

Thanks in advance for your feedback.

*Kind regards,  
Angela*

**Angela Vickers**

Associate Director Regulatory Affairs

---

**AstraZeneca Pharmaceuticals LP**

**Global Medicines Development / Global Regulatory Affairs & Patient Safety**

C4C-302, 1800 Concord Pike, Wilmington DE 19850

Tel (302) 885-8323 Mobile (302) 981-5526

[angela.vickers@astrazeneca.com](mailto:angela.vickers@astrazeneca.com)

 Please consider the environment before printing this e-mail.

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JEFFREY A BUCHANAN  
10/09/2013

**From:** [Buchanan, Jeffrey A.](mailto:Jeffrey.A.Buchanan@astrazeneca.com)  
**To:** [angela.vickers@astrazeneca.com](mailto:angela.vickers@astrazeneca.com)  
**Cc:** [Firor, Judy W \(judy.firor@astrazeneca.com\)](mailto:Judy.W.Firor@astrazeneca.com); [Buchanan, Jeffrey A.](mailto:Jeffrey.A.Buchanan@astrazeneca.com)  
**Subject:** NDA 204655 Nexium 24HR capsules - Information Request  
**Date:** Wednesday, October 09, 2013 12:47:36 PM  
**Importance:** High

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Hi Angela,

Please see the information request below and respond with a formal submission to your application by COB Friday, November 1, 2013. Please contact me if you have questions. Thank you!

*Your 27 September 2013 amendment to NDA 204655 Nexium 24 HR capsules proposes the implementation of a microbial limits specification and test methodology consistent with current USP standards for solid oral dosage forms. However, the proposal calls for testing only one batch of drug product annually. Skip-lot testing for drug products is not allowed by regulation (21 CFR 211.165 (a) and (b).) If a drug product release specification includes tests and acceptance criteria for a given attribute, then the test must be performed on every batch.*

*However, the information provided in the 27 September 2013 supplement has provided an adequate justification for the waiver of microbial limits testing on each batch of NEXIUM® 24HR (esomeprazole magnesium) Delayed-Release Capsules Over-the-Counter, 20 mg. Microbial limits testing on stability batches should continue as a periodic check of microbiological product quality. Please provide the following information as an amendment to NDA 204655:*

- 1. A revised drug product specification that does not contain the microbial limits test method and acceptance criteria.*
- 2. A revised stability protocol with the microbial limits test method and acceptance criteria. The test methods provided in USP <61>/<62> and the acceptance criteria provided in USP <1111> are recommended.*

***Jeff Buchanan***

*Regulatory Health Project Manager*

~~~~~

Division of Nonprescription Clinical Evaluation (DNCE)

FDA/OMPT/CDER/OND/ODE IV

10903 New Hampshire Avenue, WO22/Room 5461 (NOTE: New room # as of 08/30/13)

Silver Spring, MD 20903

Phone: 301-796-1007 Fax: 301-796-9899

[jeffrey.buchanan@fda.hhs.gov](mailto:jeffrey.buchanan@fda.hhs.gov)

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JEFFREY A BUCHANAN  
10/09/2013

**From:** [Buchanan, Jeffrey A.](#)  
**To:** [angela.vickers@astrazeneca.com](mailto:angela.vickers@astrazeneca.com)  
**Cc:** [Firor, Judy W \(judy.firor@astrazeneca.com\)](#); [Buchanan, Jeffrey A.](#)  
**Subject:** NDA 204655 Nexium 24HR capsules - Information and Sample Request  
**Date:** Monday, October 07, 2013 11:49:46 AM  
**Importance:** High

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Hi Angela,

Please see the following information and sample request and respond by Monday, October 21, 2013:

We acknowledge receipt of draft labeling for a 2-count immediate container (bottle) and a 2-count sample carton on September 27, 2013. However, upon initial attempts to review the submission, neither label is readable at actual size or legible when magnified. Please submit labels that are legible for review.

We also request that you submit five immediate containers (bottles) and cartons of the actual 2-count sample carton to be marketed. You may send them directly to me at the address given below. Thank you!

Jeffrey Buchanan

Food and Drug Administration

Center for Drug Evaluation and Research

White Oak Building 22, Room 5461

10903 New Hampshire Avenue

Silver Spring, Maryland

*Use zip code 20903 if shipping via United States Postal Service (USPS).*

*Use zip code 20993 if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

***Jeff Buchanan***

*Regulatory Health Project Manager*

~~~~~

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JEFFREY A BUCHANAN  
10/07/2013



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

NDA 204655

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

AstraZeneca, LP  
1800 Concord Pike  
P.O. Box 8355  
Wilmington, DE 19803-8355

ATTENTION: Gary P. Horowitz, Ph.D.  
Executive Director, Regulatory Affairs

Dear Dr. Horowitz:

Please refer to your New Drug Application (NDA), dated and received May 30, 2013, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Esomeprazole Magnesium Capsules, 20 mg.

We also refer to your July 10, 2013, correspondence, received July 10, 2013, requesting review of your proposed proprietary name, Nexium 24HR. We have completed our review of the proposed proprietary name and have concluded that it is acceptable.

The proposed proprietary name, Nexium 24HR, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you. If **any** of the proposed product characteristics as stated in your July 10, 2013, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

Please be advised that based on FDA's review of your NDA for this OTC product, FDA may determine that a statement such as "This drug may take 1 to 4 days for full effect" must be displayed on the principal display panel of the labels and labeling of your product. If this determination is made, the acceptability of your proposed proprietary name is contingent upon you adding such a statement.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Abiola Olagundoye-Alawode, Pharm.D., Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3982. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Jeffrey Buchanan at (301) 796-1007.

Sincerely,

*{See appended electronic signature page}*

Carol Holquist, RPh  
Director  
Division of Medication Error Prevention and Analysis  
Office of Medication Error Prevention and Risk Management  
Office of Surveillance and Epidemiology  
Center for Drug Evaluation and Research

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CAROL A HOLQUIST  
09/16/2013



NDA 204655

**FILING COMMUNICATION -  
FILING REVIEW ISSUES IDENTIFIED**

AstraZeneca, LP  
Attention: Gary P. Horowitz, Ph.D.  
Executive Director, Regulatory Affairs  
1800 Concord Pike  
P.O. Box 8355  
Wilmington, DE 19803-8355

Dear Dr. Horowitz:

Please refer to your New Drug Application (NDA) dated May 30, 2013, received May 30, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Nexium® 24HR (esomeprazole magnesium) delayed-release capsules, 20 mg.

We also refer to your amendments dated June 25 and July 10, 2013.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is Standard. Therefore, the user fee goal date is March 30, 2014.

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" located at the following web address: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079748.pdf>. 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 February 28, 2014.

During our filing review of your application, we identified the following potential review issues. We request that you submit the following information as soon as possible, and no later than September 27, 2013.

1. Please submit the information on the unit impulse response (UIR) of your IVIVC model (information obtained previously). Note that we need the UIR information to verify the IVIVC model used to generate the  $C_{max}$  and AUC data supporting your biowaiver request.
2. The justification for a waiver of microbial limits testing is not adequate.
  - a. Microbial limits testing as well as confirmation of the absence of specified microorganisms associated with the Nexium® 24HR delayed-release capsule should be provided. The test methods employed are to be identified and should conform to those described in USP <61> and <62>, respectively, or comparable standards. Please provide microbial limits acceptance criteria, a description of the methods and verification of the methods suitability for the finished drug product. The stability protocol should also be amended to include periodic microbial limits testing.
  - b. Alternatively, demonstrated process control including, but not limited to, the following may serve as an adequate justification for the elimination of microbial limits testing:
    - The identification and justification of critical control points in the manufacturing process that could affect the microbial load of the drug product.
    - A description of the microbiological monitoring and acceptance criteria for the critical control points that you have identified.
    - A description of the activities taken when microbiological acceptance criteria are not met at these control points.
    - The results of microbial limits testing performed on exhibit or stability batches of the drug product.
3. Submit a label for the 2-count sample that complies with 21 CFR 201.66 and address how the (b)(4) will be included with the 2-count sample.
4. We understand that you have submitted an analysis data set. However, the data definition file does not provide enough information for the reviewer to locate the primary and secondary endpoints. In addition, the SAS programs written in Macro codes are difficult to understand.

In order to facilitate and complete the review for Nexium 24HR, please provide the following information for both Studies D961RC00001 and D961RC00002.

- I. Please provide a new dataset in electronic format consistent with the FDA Data Specifications document:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm248635.htm>. Please note that adherence to CDISC standards are recommended, but not required.

Study number;  
Investigator or Site Number;  
Country Name (if you have collected);  
Region (if you have collected);  
Patient ID;  
Unique subject ID;  
Treatment code randomized (“ARMCD” in your dataset);  
Treatment group randomized;  
Treatment code actually received (“ARMACD” in your dataset);  
Treatment group actually received;  
All randomized subjects population (Y for yes; N for no);  
Modified Intent-to-Treat (MITT) population (Y for yes; N for no): defined as all randomized subjects who took at least one dose of randomized treatment;  
Full analysis set (Y for yes; N for no);  
Per-protocol analysis set (Y for yes; N for no);  
Missing indicator for primary endpoint (Y for missing data; N for data not missing);  
Gender;  
Age;  
Race;  
Percentage of heartburn free 24-hour days during 14 days of double-blind treatment;  
Subject reports heartburn 2 days or less during the 14-day randomized treatment period (both Weeks 1 and 2 between V3 and V4) (Y for yes; N for no);  
Subject reports heartburn 1 day or less during the final week of treatment (Y for yes; N for no);  
Subject reports heartburn 1 day or less during the second week of treatment (Y for yes; N for no);  
Subject reports heartburn 1 day or less during the first week of treatment (Y for yes; N for no);  
Percentage of days with no heartburn over Days 1-4 of treatment period;

- II. Please submit SAS programs used to perform the efficacy analyses stated in sections 5.7.1.3 “Analysis of primary efficacy variable” and 5.7.1.4 “Analysis of secondary efficacy variable” including SAS programs to generate Tables 14 to 22 presented in Sections 7.1.1 and 7.1.2.

Please modify your programs (without using macro codes) to accept the dataset described in item I. If necessary, please add additional variables as needed to the data set described in item I so that the modified SAS programs can create the analyses and tables stated above.

- III. Please perform the efficacy analyses stated in item II using the MITT population and submit the results to the Agency for review.
- IV. Please perform efficacy analysis on percentage of days with no heartburn over Days 1-4 of treatment period using FAS and MITT populations.
- V. For the primary endpoint, please perform a blocked, two-sample Wilcoxon rank sum (WRS) test (i.e., the van Elteren test), stratified by US and non-US if applicable, to assess treatment group differences and submit the results to the Agency for review.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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

If you have questions, contact Jeff Buchanan, Regulatory Project Manager, at (301) 796-1007.

Sincerely,

*{See appended electronic signature page}*

Shaw Chen, M.D., Ph.D.  
Acting Division Director  
Division of Nonprescription Clinical Evaluation  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

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SHAW T CHEN  
08/06/2013

## For Internal Use Only

### Meeting Request Withdrawal Form

(Use this form when a sponsor cancels a meeting within the first 14 days after receipt of the request **AND** before the meeting is granted.)

Complete the information below and check form into DFS.

Application Type	NDA
Application Number	204655
<b>DATE</b> Meeting Withdrawn (per communication with requester)	9/13/12
Reason for Withdrawal	Sponsor to request the same meeting under IND 111185
Project Manager	Jeff Buchanan, RPM, DNCE

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JEFFREY A BUCHANAN  
09/17/2012



NDA 204655

**NDA ACKNOWLEDGMENT**

AstraZeneca, LP  
Attention: Gary P. Horowitz, Ph.D.  
Executive Director, Regulatory Affairs  
1800 Concord Pike  
P.O. Box 8355  
Wilmington, DE 19803-8355

Dear Dr. Horowitz:

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: Nexium® 24HR (esomeprazole magnesium) delayed-release capsules, 20 mg  
Date of Application: May 30, 2013  
Date of Receipt: May 30, 2013  
Our Reference Number: NDA 204655

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 July 29, 2013, 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/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. 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 content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

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 Nonprescription Clinical Evaluation  
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/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to [SecureEmail@fda.hhs.gov](mailto:SecureEmail@fda.hhs.gov). Please note that secure email may not be used for formal regulatory submissions to applications.

If you have questions, contact me at (301) 796-1007.

Sincerely,

*{See appended electronic signature page}*

Jeffrey Buchanan  
Regulatory Health Project Manager  
Division of Nonprescription Clinical Evaluation  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JEFFREY A BUCHANAN  
06/03/2013