

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**202211s000**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

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.	
<b>PATENT INFORMATION SUBMITTED WITH THE FILING          OF AN NDA, AMENDMENT, OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation and Composition)          and/or Method of Use</i>		NDA NUMBER 202-211	
		NAME OF APPLICANT/NDA HOLDER MSD Consumer Care, Inc.	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME) OXYTROL® For Women			
ACTIVE INGREDIENT(S) Oxybutynin		STRENGTH(S) 3.9 mg/day	
DOSAGE FORM Transdermal Patch			
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 5,601,839		b. Issue Date of Patent February 11, 1997	c. Expiration Date of Patent April 26, 2015
d. Name of Patent Owner Watson Laboratories, Inc.		Address (of Patent Owner) 577 Chipeta Way	
		City/State Salt Lake City, Utah	
		ZIP Code 84108	FAX Number (if available)
		Telephone Number 801-588-6654	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<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:**

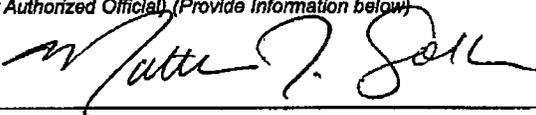
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Claims 1-4	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.) See Attachment 1
---	--

**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

<b>6. Declaration Certification</b>	
<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><b>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)</b></p> 	<p>Date Signed</p> <p>3/16/12</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><b>Check applicable box and provide information below.</b></p>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<p>Name</p> <p>Matthew J. Golden</p>	
<p>Address</p> <p>126 E. Lincoln Avenue</p>	<p>City/State</p> <p>Rahway, NJ</p>
<p>ZIP Code</p> <p>07065</p>	<p>Telephone Number</p> <p>732-594-0587</p>
<p>FAX Number (if available)</p> <p>732-594-2300</p>	<p>E-Mail Address (if available)</p> <p>matthew.golden@merck.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>	

Form FDA 3542a  
OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 5,601,839

## **ATTACHMENT 1**

Item 4.2a

### ***Use***

- treats overactive bladder in women
- you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:
  - urinary frequency (the need to urinate more often than usual; typically more than 8 times in 24 hours)
  - urinary urgency (a strong need to urinate right away)
  - urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)

### ***Directions***

women 18 years of age and older:

#### **How to use the patch:**

- open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.
- wear patch under clothing, do not expose the patch to sunlight
- do not cut the patch into smaller pieces
- wear only 1 patch at a time for 4 days in a row
- after 4 days, remove the used patch and apply a new one
- continue to change the patch every 4 days for as long as you use this product
- each time you put on a new patch, you should change the place where you put it (*i.e.*, *abdomen, hips or buttocks*) to avoid possible skin irritation

#### **How to dispose of a used patch:**

- when you take off a used patch, fold it in half with the sticky sides together
- throw it away so that it cannot be worn or swallowed by another person, especially a child, or a pet

**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

202-211

NAME OF APPLICANT/NDA HOLDER

MSD Consumer Care, Inc.

*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)

OXYTROL® For Women

ACTIVE INGREDIENT(S)

Oxybutynin

STRENGTH(S)

3.9 mg/day

DOSAGE FORM

Transdermal Patch

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

5,834,010

b. Issue Date of Patent

November 10, 1998

c. Expiration Date of Patent

April 26, 2015

d. Name of Patent Owner

Watson Laboratories, Inc.

Address (of Patent Owner)

577 Chipeta Way

City/State

Salt Lake City, Utah

ZIP Code

84108

FAX Number (if available)

Telephone Number

801-588-6654

E-Mail Address (if available)

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

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

City/State

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FAX Number (if available)

Telephone Number

E-Mail Address (if available)

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

Yes

No

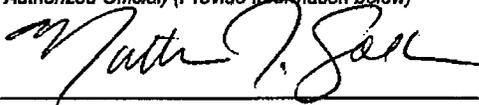
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

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

<b>2. Drug Substance (Active Ingredient)</b>	
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 type="checkbox"/> Yes <input checked="" 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	
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<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
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<input type="checkbox"/> Yes <input type="checkbox"/> No	
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<b>4. Method of Use</b>	
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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?	
<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?
Claims 1-5	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
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<b>5. No Relevant Patents</b>	
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<input type="checkbox"/> Yes	

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<p>Name</p> <p>Matthew J. Golden</p>	
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OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 5,834,010

## **ATTACHMENT 1**

Item 4.2a

### ***Use***

- treats overactive bladder in women
- you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:
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  - urinary urgency (a strong need to urinate right away)
  - urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)

### ***Directions***

women 18 years of age and older:

#### **How to use the patch:**

- open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.
- wear patch under clothing, do not expose the patch to sunlight
- do not cut the patch into smaller pieces
- wear only 1 patch at a time for 4 days in a row
- after 4 days, remove the used patch and apply a new one
- continue to change the patch every 4 days for as long as you use this product
- each time you put on a new patch, you should change the place where you put it (*i.e.*, *abdomen, hips or buttocks*) to avoid possible skin irritation

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- when you take off a used patch, fold it in half with the sticky sides together
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**1. GENERAL**

a. United States Patent Number 6,743,441 B2	b. Issue Date of Patent June 1, 2004	c. Expiration Date of Patent April 26, 2020
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d. Name of Patent Owner Watson Laboratories, Inc.	Address (of Patent Owner) 577 Chipeta Way	
	City/State Salt Lake City, Utah	
	ZIP Code 84108	FAX Number (if available)
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**3. Drug Product (Composition/Formulation)**

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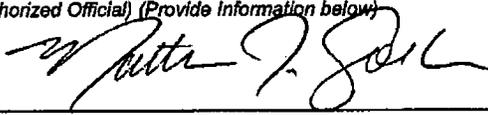
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4.2 Patent Claim Number(s) (as listed in the patent) Claims 1-14,39,40,42,44-57,60-62	Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
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<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><b>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)</b></p> 	<p>Date Signed</p> <p>3-16-12</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><b>Check applicable box and provide information below.</b></p>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<p>Name</p> <p>Matthew J. Golden</p>	
<p>Address</p> <p>126 E. Lincoln Avenue</p>	<p>City/State</p> <p>Rahway, NJ</p>
<p>ZIP Code</p> <p>07065</p>	<p>Telephone Number</p> <p>732-594-0587</p>
<p>FAX Number (if available)</p> <p>732-594-2300</p>	<p>E-Mail Address (if available)</p> <p>matthew.golden@merck.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>	

Form FDA 3542a  
OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 6,743,441 B2

## **ATTACHMENT 1**

Item 4.2a

### ***Use***

- treats overactive bladder in women
- you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:
  - urinary frequency (the need to urinate more often than usual; typically more than 8 times in 24 hours)
  - urinary urgency (a strong need to urinate right away)
  - urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)

### ***Directions***

women 18 years of age and older:

#### **How to use the patch:**

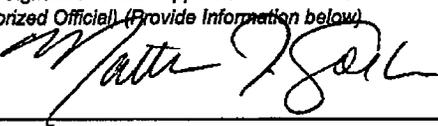
- open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.
- wear patch under clothing, do not expose the patch to sunlight
- do not cut the patch into smaller pieces
- wear only 1 patch at a time for 4 days in a row
- after 4 days, remove the used patch and apply a new one
- continue to change the patch every 4 days for as long as you use this product
- each time you put on a new patch, you should change the place where you put it (*i.e.*, *abdomen, hips or buttocks*) to avoid possible skin irritation

#### **How to dispose of a used patch:**

- when you take off a used patch, fold it in half with the sticky sides together
- throw it away so that it cannot be worn or swallowed by another person, especially a child, or a pet

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.	
<b>PATENT INFORMATION SUBMITTED WITH THE FILING          OF AN NDA, AMENDMENT, OR SUPPLEMENT</b>			
<i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation and Composition)          and/or Method of Use</i>			
NDA NUMBER		202-211	
NAME OF APPLICANT/NDA HOLDER		MSD Consumer Care, Inc.	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME)			
OXYTROL® For Women			
ACTIVE INGREDIENT(S)		STRENGTH(S)	
Oxybutynin		3.9 mg/day	
DOSAGE FORM			
Transdermal Patch			
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		b. Issue Date of Patent	c. Expiration Date of Patent
7,081,249 B2		July 25, 2006	April 26, 2020
d. Name of Patent Owner		Address (of Patent Owner)	
Watson Laboratories, Inc.		577 Chipeta Way	
		City/State	
		Salt Lake City, Utah	
		ZIP Code	FAX Number (if available)
		84108	
		Telephone Number	E-Mail Address (if available)
		801-588-6654	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<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	

<b>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.</b>		
<b>2. Drug Substance (Active Ingredient)</b>		
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 type="checkbox"/> Yes	<input checked="" 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
<b>3. Drug Product (Composition/Formulation)</b>		
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
<b>4. Method of Use</b>		
<i>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:</i>		
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?	
Claims 1-5,7-15,17,39	<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.) See Attachment 1	
<b>5. No Relevant Patents</b>		
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

<b>6. Declaration Certification</b>	
<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><b>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)</b></p> 	<p>Date Signed</p> <p>3-16-12</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><b>Check applicable box and provide information below.</b></p>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<p>Name</p> <p>Matthew J. Golden</p>	
<p>Address</p> <p>126 E. Lincoln Avenue</p>	<p>City/State</p> <p>Rahway, NJ</p>
<p>ZIP Code</p> <p>07065</p>	<p>Telephone Number</p> <p>732-594-0587</p>
<p>FAX Number (if available)</p> <p>732-594-2300</p>	<p>E-Mail Address (if available)</p> <p>matthew.golden@merck.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>	

Form FDA 3542a  
OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 7,081,249 B2

## **ATTACHMENT 1**

Item 4.2a

<p><b>Use</b></p> <ul style="list-style-type: none"><li>• treats overactive bladder in women</li><li>• you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:<ul style="list-style-type: none"><li>• urinary frequency (the need to urinate more often than usual; typically more than 8 times in 24 hours)</li><li>• urinary urgency (a strong need to urinate right away)</li><li>• urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)</li></ul></li></ul>
<p><b>Directions</b> women 18 years of age and older.</p> <p><b>How to use the patch:</b></p> <ul style="list-style-type: none"><li>• open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.</li><li>• wear patch under clothing, do not expose the patch to sunlight</li><li>• do not cut the patch into smaller pieces</li><li>• wear only 1 patch at a time for 4 days in a row</li><li>• after 4 days, remove the used patch and apply a new one</li><li>• continue to change the patch every 4 days for as long as you use this product</li><li>• each time you put on a new patch, you should change the place where you put it (<i>i.e., abdomen, hips or buttocks</i>) to avoid possible skin irritation</li></ul> <p><b>How to dispose of a used patch:</b></p> <ul style="list-style-type: none"><li>▪ when you take off a used patch, fold it in half with the sticky sides together</li><li>▪ throw it away so that it cannot be worn or swallowed by another person, especially a child, or a pet</li></ul>

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.	
<b>PATENT INFORMATION SUBMITTED WITH THE FILING          OF AN NDA, AMENDMENT, OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation and Composition)          and/or Method of Use</i>		NDA NUMBER 202-211	
		NAME OF APPLICANT/NDA HOLDER MSD Consumer Care, Inc.	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME) OXYTROL® For Women			
ACTIVE INGREDIENT(S) Oxybutynin		STRENGTH(S) 3.9 mg/day	
DOSAGE FORM Transdermal Patch			
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.			
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<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 7,081,250 B2		b. Issue Date of Patent July 25, 2006	c. Expiration Date of Patent April 26, 2020
d. Name of Patent Owner Watson Laboratories, Inc.		Address (of Patent Owner) 577 Chipeta Way	
		City/State Salt Lake City, Utah	
		ZIP Code 84108	FAX Number (if available)
		Telephone Number 801-588-6654	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<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:**

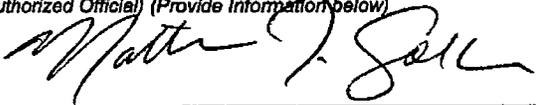
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Claims 1-5, 8	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.) See Attachment 1
---	--

**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

<b>6. Declaration Certification</b>	
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<p><b>Check applicable box and provide information below.</b></p>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<p><b>Name</b> Matthew J. Golden</p>	
<p><b>Address</b> 126 E. Lincoln Avenue</p>	<p><b>City/State</b> Rahway, NJ</p>
<p><b>ZIP Code</b> 07065</p>	<p><b>Telephone Number</b> 732-594-0587</p>
<p><b>FAX Number (if available)</b> 732-594-2300</p>	<p><b>E-Mail Address (if available)</b> matthew.golden@merck.com</p>
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Form FDA 3542a  
OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 7,081,250 B2

## **ATTACHMENT 1**

### Item 4.2a

#### **Use**

- treats overactive bladder in women
- you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:
  - urinary frequency (the need to urinate more often than usual; typically more than 8 times in 24 hours)
  - urinary urgency (a strong need to urinate right away)
  - urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)

#### **Directions**

women 18 years of age and older:

#### **How to use the patch:**

- open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.
- wear patch under clothing, do not expose the patch to sunlight
- do not cut the patch into smaller pieces
- wear only 1 patch at a time for 4 days in a row
- after 4 days, remove the used patch and apply a new one
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#### **How to dispose of a used patch:**

- when you take off a used patch, fold it in half with the sticky sides together
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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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		NAME OF APPLICANT/NDA HOLDER MSD Consumer Care, Inc.	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME) OXYTROL® For Women			
ACTIVE INGREDIENT(S) Oxybutynin		STRENGTH(S) 3.9 mg/day	
DOSAGE FORM Transdermal Patch			
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<b>1. GENERAL</b>			
a. United States Patent Number 7,081,251 B2		b. Issue Date of Patent July 25, 2006	c. Expiration Date of Patent April 26, 2020
d. Name of Patent Owner Watson Laboratories, Inc.		Address (of Patent Owner) 577 Chipeta Way	
		City/State Salt Lake City, Utah	
		ZIP Code 84108	FAX Number (if available)
		Telephone Number 801-588-6654	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<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:**

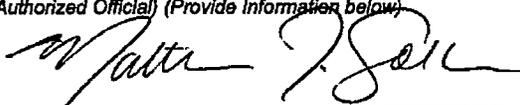
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Claims 1-6, 9	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.) See Attachment 1
---	--

**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

<b>6. Declaration Certification</b>	
<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><b>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)</b></p> 	<p>Date Signed</p> <p>3-16-12</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><b>Check applicable box and provide information below.</b></p>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<p>Name</p> <p>Matthew J. Golden</p>	
<p>Address</p> <p>126 E. Lincoln Avenue</p>	<p>City/State</p> <p>Rahway, NJ</p>
<p>ZIP Code</p> <p>07065</p>	<p>Telephone Number</p> <p>732-594-0587</p>
<p>FAX Number (if available)</p> <p>732-594-2300</p>	<p>E-Mail Address (if available)</p> <p>matthew.golden@merck.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>	

Form FDA 3542a  
OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 7,081,251 B2

## **ATTACHMENT 1**

Item 4.2a

<p><b>Use</b></p> <ul style="list-style-type: none"><li>• treats overactive bladder in women</li><li>• you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:<ul style="list-style-type: none"><li>• urinary frequency (the need to urinate more often than usual; typically more than 8 times in 24 hours)</li><li>• urinary urgency (a strong need to urinate right away)</li><li>• urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)</li></ul></li></ul>
<p><b>Directions</b> women 18 years of age and older:</p> <p><b>How to use the patch:</b></p> <ul style="list-style-type: none"><li>• open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.</li><li>• wear patch under clothing, do not expose the patch to sunlight</li><li>• do not cut the patch into smaller pieces</li><li>• wear only 1 patch at a time for 4 days in a row</li><li>• after 4 days, remove the used patch and apply a new one</li><li>• continue to change the patch every 4 days for as long as you use this product</li><li>• each time you put on a new patch, you should change the place where you put it (<i>i.e.</i>, <i>abdomen, hips or buttocks</i>) to avoid possible skin irritation</li></ul> <p><b>How to dispose of a used patch:</b></p> <ul style="list-style-type: none"><li>▪ when you take off a used patch, fold it in half with the sticky sides together</li><li>▪ throw it away so that it cannot be worn or swallowed by another person, especially a child, or a pet</li></ul>

**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

202-211

NAME OF APPLICANT/NDA HOLDER

MSD Consumer Care, Inc.

*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)

OXYTROL® For Women

ACTIVE INGREDIENT(S)

Oxybutynin

STRENGTH(S)

3.9 mg/day

DOSAGE FORM

Transdermal Patch

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

7,081,252 B2

b. Issue Date of Patent

July 25, 2006

c. Expiration Date of Patent

April 26, 2020

d. Name of Patent Owner

Watson Laboratories, Inc.

Address (of Patent Owner)

577 Chipeta Way

City/State

Salt Lake City, Utah

ZIP Code

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FAX Number (if available)

Telephone Number

801-588-6654

E-Mail Address (if available)

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

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

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FAX Number (if available)

Telephone Number

E-Mail Address (if available)

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

Yes

No

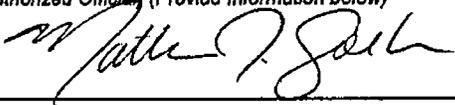
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

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

<b>2. Drug Substance (Active Ingredient)</b>	
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 type="checkbox"/> Yes <input checked="" 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	
<b>3. Drug Product (Composition/Formulation)</b>	
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?	
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<input type="checkbox"/> Yes <input type="checkbox"/> No	
<b>4. Method of Use</b>	
<b>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:</b>	
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) Claims 1-7, 9-12	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.) See Attachment 1
<b>5. No Relevant Patents</b>	
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<input type="checkbox"/> Yes	

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<p><b>Check applicable box and provide information below.</b></p>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<p>Name</p> <p>Matthew J. Golden</p>	
<p>Address</p> <p>126 E. Lincoln Avenue</p>	<p>City/State</p> <p>Rahway, NJ</p>
<p>ZIP Code</p> <p>07065</p>	<p>Telephone Number</p> <p>732-594-0587</p>
<p>FAX Number (if available)</p> <p>732-594-2300</p>	<p>E-Mail Address (if available)</p> <p>matthew.golden@merck.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>	

Form FDA 3542a  
OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 7,081,252 B2

## **ATTACHMENT 1**

Item 4.2a

<p><b>Use</b></p> <ul style="list-style-type: none"><li>• treats overactive bladder in women</li><li>• you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:<ul style="list-style-type: none"><li>• urinary frequency (the need to urinate more often than usual; typically more than 8 times in 24 hours)</li><li>• urinary urgency (a strong need to urinate right away)</li><li>• urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)</li></ul></li></ul>
<p><b>Directions</b> women 18 years of age and older:</p> <p><b>How to use the patch:</b></p> <ul style="list-style-type: none"><li>• open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.</li><li>• wear patch under clothing, do not expose the patch to sunlight</li><li>• do not cut the patch into smaller pieces</li><li>• wear only 1 patch at a time for 4 days in a row</li><li>• after 4 days, remove the used patch and apply a new one</li><li>• continue to change the patch every 4 days for as long as you use this product</li><li>• each time you put on a new patch, you should change the place where you put it (<i>i.e.</i>, <i>abdomen, hips or buttocks</i>) to avoid possible skin irritation</li></ul> <p><b>How to dispose of a used patch:</b></p> <ul style="list-style-type: none"><li>▪ when you take off a used patch, fold it in half with the sticky sides together</li><li>▪ throw it away so that it cannot be worn or swallowed by another person, especially a child, or a pet</li></ul>

**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

202-211

NAME OF APPLICANT/NDA HOLDER

MSD Consumer Care, Inc.

*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)

OXYTROL® For Women

ACTIVE INGREDIENT(S)

Oxybutynin

STRENGTH(S)

3.9 mg/day

DOSAGE FORM

Transdermal Patch

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**1. GENERAL**

a. United States Patent Number

7,179,483 B2

b. Issue Date of Patent

February 20, 2007

c. Expiration Date of Patent

April 26, 2020

d. Name of Patent Owner

Watson Laboratories, Inc.

Address (of Patent Owner)

577 Chipeta Way

City/State

Salt Lake City, Utah

ZIP Code

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

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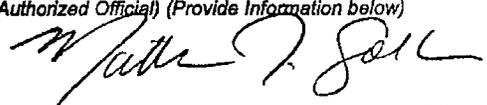
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Claims 1-17,20,21,25,27-39,41-43	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.) See Attachment 1
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**5. No Relevant Patents**

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<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
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<p>Name</p> <p>Matthew J. Golden</p>	
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<p>ZIP Code</p> <p>07065</p>	<p>Telephone Number</p> <p>732-594-0587</p>
<p>FAX Number (if available)</p> <p>732-594-2300</p>	<p>E-Mail Address (if available)</p> <p>matthew.golden@merck.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>	

Form FDA 3542a  
OXYTROL® For Women  
NDA No. 202-211  
US Patent No. 7,179,483 B2

## **ATTACHMENT 1**

Item 4.2a

### **Use**

- treats overactive bladder in women
- you may be suffering from overactive bladder if you have had 2 or more of the following symptoms for at least 3 months:
  - urinary frequency (the need to urinate more often than usual; typically more than 8 times in 24 hours)
  - urinary urgency (a strong need to urinate right away)
  - urge incontinence (leaking or wetting yourself if you cannot control the urge to urinate)

### **Directions**

women 18 years of age and older:

#### **How to use the patch:**

- open individual pouch and apply immediately to a clean, dry and smooth area of skin on your abdomen, hips or buttocks. Do not put the patch on oily, damaged (cut or scraped), or irritated (rashes) skin. Do not put the patch on skin with oils, lotions or powders because that could keep the patch from sticking to your skin.
- wear patch under clothing, do not expose the patch to sunlight
- do not cut the patch into smaller pieces
- wear only 1 patch at a time for 4 days in a row
- after 4 days, remove the used patch and apply a new one
- continue to change the patch every 4 days for as long as you use this product
- each time you put on a new patch, you should change the place where you put it (*i.e.*, *abdomen, hips or buttocks*) to avoid possible skin irritation

#### **How to dispose of a used patch:**

- when you take off a used patch, fold it in half with the sticky sides together
- throw it away so that it cannot be worn or swallowed by another person, especially a child, or a pet

## EXCLUSIVITY SUMMARY

NDA # 202211

SUPPL #

HFD #

Trade Name Oxytrol for Women

Generic Name oxybutynin transdermal system

Applicant Name Merck Consumer Care

Approval Date, If Known 01/25/13

### PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES  NO

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

505(b)(1)

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

YES  NO

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

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# 202513

NDA # 021351

NDA# 22204

NDA# 20897

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:





Investigation #2

!

YES

! NO

Explain:

! Explain:

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

YES

NO

If yes, explain:

=====

Name of persons completing form: Melissa Furness and Lesley Furlong, M.D., M.S.

Title: CPMS and CDTL, respectively

Date: 01/30/13

Name of Office Directors signing form: Shaw Chen, M.D., Ph.D. and Julie Beitz, M.D.

Title: Deputy Office Director ODE IV and Office Director ODE III, respectively

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.**  
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/s/  
-----

CELIA R PEACOCK  
02/01/2013

SHAW T CHEN  
02/01/2013

JULIE G BEITZ  
02/01/2013

## 1 CLAIM FOR EXCLUSIVITY

1. Pursuant to the provisions of Sections 505(c)(3)(D)(iii) and 505(j)(4)(D)(iii) of the Food, Drug and Cosmetic Act (FDCA) and 21 CFR 314.108 (b)(4)(iv), the Sponsor claims three years of exclusivity for its nonprescription Oxytrol (Oxybutynin) Transdermal System for the relief of overactive bladder.
2. The Sponsor certifies that the clinical investigation (CL2008-13) included in the application meets the definition of "new clinical investigation" set forth in 21 CFR 314.108 (a).
3. The Sponsor certifies that the clinical investigation included in the application is essential to approval, as there is no other data that could support approval of nonprescription Oxytrol (oxybutynin) Transdermal System.

Reference is made to the October 13, 2009 End of Phase 2 meeting (minutes are included in Section 1.6.3 Correspondence Regarding Meetings), in which the Agency informed the Sponsor that an actual use study is needed for the proposed OTC product, because its use and indication differ significantly from those of existing OTC products.

4. The Sponsor of this New Drug Application, MSD Consumer Care, Inc.<sup>a</sup> is the Sponsor (Schering-Plough HealthCare Products, Inc.) named in the Form FDA 1571 for IND (b) (4) under which the new clinical investigation was conducted.

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<sup>a</sup> On April 1, 2011, Schering-Plough HealthCare Products, Inc. changed its legal entity name to MSD Consumer Care, Inc., operating under the trade name Merck Consumer Care (MCC). A notification of this change was sent to IND 74,288 on April 5, 2011, as Serial Number 013.



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



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John O'Mullane, BSc, PhD  
Group Vice President, Research and Development  
Consumer Health Care

16 February 2012  
Date



# ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # 20221 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: Oxytrol for Women Established/Proper Name: oxybutynin Dosage Form: transdermal system, 3.9mg		Applicant: Agent for Applicant (if applicable):
RPM: Melissa Furness		Division: DNCE
<p><b><u>NDA and NDA Efficacy Supplements:</u></b></p> <p>NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)            Efficacy Supplement:    <input type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p><b><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></b></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> This application does not rely upon a listed drug.  <input type="checkbox"/> This application relies on literature.  <input type="checkbox"/> This application relies on a final OTC monograph.  <input type="checkbox"/> This application relies on (explain)</p> <p><b><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b></p> <p><b><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></b></p> <p><input type="checkbox"/> No changes    <input type="checkbox"/> Updated    Date of check:</p> <p><b>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</b></p>
❖ Actions		
<ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is <u>January 26, 2013</u></li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> <li>• Previous actions (<i>specify type and date for each action taken</i>)</li> </ul>		<input checked="" type="checkbox"/> None

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

<sup>2</sup> For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a>). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics <sup>3</sup></p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch  <input type="checkbox"/> Rolling Review <input checked="" type="checkbox"/> Rx-to-OTC partial switch  <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC       </p> <p>         NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510)  <input type="checkbox"/> Restricted distribution (21 CFR 314.520)          Subpart I <input type="checkbox"/> Approval based on animal studies       </p> <p> <input type="checkbox"/> Submitted in response to a PMR  <input type="checkbox"/> Submitted in response to a PMC  <input type="checkbox"/> Submitted in response to a Pediatric Written Request       </p> <p>         BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41)  <input type="checkbox"/> Restricted distribution (21 CFR 601.42)          Subpart H <input type="checkbox"/> Approval based on animal studies       </p> <p>         REMS: <input type="checkbox"/> MedGuide  <input type="checkbox"/> Communication Plan  <input type="checkbox"/> ETASU  <input type="checkbox"/> MedGuide w/o REMS  <input type="checkbox"/> REMS not required       </p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> <li>Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>Press Office notified of action (by OEP)</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>Indicate what types (if any) of information dissemination are anticipated</li> </ul>	<input type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

<sup>3</sup> Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

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

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

Answer the following questions for **each** paragraph IV certification:

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

Yes     No

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

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

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

Yes     No

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

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

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

Yes     No

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

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

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

Yes     No

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

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

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p>
<b>CONTENTS OF ACTION PACKAGE</b>	
<p>❖ Copy of this Action Package Checklist<sup>4</sup></p>	<p>2/7/2013</p>
<b>Officer/Employee List</b>	
<p>❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)</p>	<p><input checked="" type="checkbox"/> Included</p>
<p>Documentation of consent/non-consent by officers/employees</p>	<p><input checked="" type="checkbox"/> Included</p>
<b>Action Letters</b>	
<p>❖ Copies of all action letters (<i>including approval letter with final labeling</i>)</p>	<p>Action(s) and date(s) 1/25/2013</p>
<b>Labeling</b>	
<p>❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)</p>	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	<p>1/15/2013, 1/22/2013</p>
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	

<sup>4</sup> Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> <li>❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)</li> </ul>	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	
<ul style="list-style-type: none"> <li>❖ Labels (<b>full color</b> carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most-recent draft labeling</li> </ul>	
<ul style="list-style-type: none"> <li>❖ Proprietary Name             <ul style="list-style-type: none"> <li>• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>• Review(s) (<i>indicate date(s)</i>)</li> <li>• Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name.</li> </ul> </li> </ul>	12/11/12 (Review)
<ul style="list-style-type: none"> <li>❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)</li> </ul>	<input type="checkbox"/> RPM <input type="checkbox"/> DMEPA 11/13/12 <input type="checkbox"/> DMPP/PLT (DRISK) <input type="checkbox"/> ODPD (DDMAC) <input type="checkbox"/> SEALD <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews DNRD, 11/27/12
<ul style="list-style-type: none"> <li>❖ Administrative Reviews (<i>e.g., RPM Filing Review<sup>5</sup>/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)</li> </ul>	5/31/12
<ul style="list-style-type: none"> <li>❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte</li> <li>❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)</li> </ul>	<input type="checkbox"/> Not a (b)(2) <input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> <li>❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)</li> </ul>	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> <li>❖ Application Integrity Policy (AIP) Status and Related Documents  <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a> </li> </ul>	
<ul style="list-style-type: none"> <li>• Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>• This application is on the AIP             <ul style="list-style-type: none"> <li>○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> <li>❖ Pediatrics (<i>approvals only</i>)             <ul style="list-style-type: none"> <li>• Date reviewed by PeRC _____ If PeRC review not necessary, explain: _____</li> <li>• Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Included

<sup>5</sup> Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent <i>(include certification)</i>	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications <i>(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)</i>	Included
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• EOP2 meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i>	EOP2-10/13/2009
❖ Advisory Committee Meeting(s)	<input type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	11/9/2012
• 48-hour alert or minutes, if available <i>(do not include transcript)</i>	
<b>Decisional and Summary Memos</b>	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Division Director Summary Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 12/21/12; 1/2/2013
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 12/5/2012
PMR/PMC Development Templates <i>(indicate total number)</i>	<input type="checkbox"/> None 1 (2010-1)
<b>Clinical Information<sup>6</sup></b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	12/5/2012
• Clinical review(s) <i>(indicate date for each review)</i>	11/19/2012
• Social scientist review(s) (if OTC drug) <i>(indicate date for each review)</i>	<input type="checkbox"/> None 11/15/2012
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not <i>(indicate date of review/memo)</i>	11/19/12
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
• REMS Documents and Supporting Statement <i>(indicate date(s) of submission(s))</i>	
• REMS Memo(s) and letter(s) <i>(indicate date(s))</i>	
• Risk management review(s) and recommendations (including those by OSE and CSS) <i>(indicate date of each review and indicate location/date if incorporated into another review)</i>	<input checked="" type="checkbox"/> None

<sup>6</sup> Filing reviews should be filed with the discipline reviews.

❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)	<input type="checkbox"/> None requested 11/2/2012
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input type="checkbox"/> None
<b>Biostatistics</b> <input checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None
<b>Clinical Pharmacology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	<input type="checkbox"/> None
<b>Nonclinical</b> <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 11/9/2012
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	<input type="checkbox"/> None requested
<b>Product Quality</b> <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)	<input type="checkbox"/> None 12/21/12, 11/16/2012
❖ Microbiology Reviews	<input checked="" type="checkbox"/> Not needed
<input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (indicate date of each review)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion ( <i>indicate review date</i> )( <i>all original applications and all efficacy supplements that could increase the patient population</i> )	11/16/12
<input type="checkbox"/> Review & FONSI ( <i>indicate date of review</i> )	
<input type="checkbox"/> Review & Environmental Impact Statement ( <i>indicate date of each review</i> )	
❖ Facilities Review/Inspection	
<input type="checkbox"/> NDAs: Facilities inspections (include EER printout) ( <i>date completed must be within 2 years of action date</i> ) ( <i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites<sup>7</sup></i> )	Date completed: 12/21/12 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER ( <i>date of most recent TB-EER must be within 30 days of action date</i> ) ( <i>original and supplemental BLAs</i> )	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation ( <i>check box only, do not include documents</i> )	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

<sup>7</sup> I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

## Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

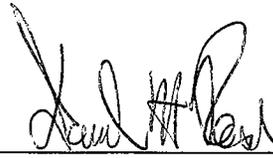
If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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/s/  
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DANIEL H REED  
02/08/2013

Post Marketing Requirements are identified in the NDA Approval Letter Dated 1/25/2013.



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Daniel H. Reed, MPH  
Regulatory Health Project Manager



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Date

**From:** Do, Phong  
**To:** ["Pierro, Nancy"](#)  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Wednesday, October 24, 2012 8:22:00 AM

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Dear Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We have the following request for information:

For Study 92062 (Label Comprehension Study of Enhanced Pregnancy Warning), we need clarification for the following two issues:

- For the general population (GP), we can reproduce the number of the subjects who "Demonstrate Comprehension" for Question 4 by counting all subjects who were in one of the three categories for the Q4NET variable: "CC" (correct/correct), "CD" (correct/partial comprehension and understanding of risk), or "CE" (correct/partial comprehension insufficient understanding of risk). For the low literate (LL) population, however, we can reproduce the number of the subjects who "Demonstrate Comprehension" by counting all subjects who were in one of the two categories for the Q4NET variable: "CC" (210 subjects) or "CD" (0 subject). Please clarify why the subjects with "CE" for variable Q4NET were treated differently in your analysis: eight (8) subjects in GP who had "CE" were considered as "Demonstrate Comprehension" while thirteen (13) subjects in the LL population who had "CE" were considered as "Did Not Demonstrate Comprehension".
- For the LL population, among 210 subjects who "Demonstrate Comprehension", you reported that 205 of them as "Demonstrate Complete Comprehension" and 5 of them "Demonstrate Partial Comprehension and Understanding of Risk". However, we cannot identify the variable that distinguishes subjects who "Demonstrate Complete Comprehension" from those who "Demonstrate Partial Comprehension and Understanding of Risk". Please identify the five (5) subjects in the LL population who "Demonstrate Partial Comprehension and Understanding of Risk" and explain the rationale.

Confirm receipt of this email and respond to this information request by COB Friday, October 26, 2012 .

Thank you,

Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager  
FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

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/s/  
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PHONG DO  
10/24/2012



FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

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**MEMORANDUM OF TELECONFERENCE MINUTES**

**Teleconference Date and Time:** Friday, July 20, 2012; 9:00 am EST  
**Application Number:** NDA 202211  
**Product Name:** Oxytrol for Women (oxybutynin) patch, 3.9 mg.  
**Sponsor/Applicant Name:** Merck Consumer Health Care, Inc. (MCC)  
**Teleconference Access:** Dial: 1-888-877-0620  
Participant Passcode: (b) (4)

**FDA ATTENDEES**

Eric Duffy, Ph.D., Division of New Drug Quality Assessment III Director  
Ali, Al Hakim, Ph.D., Branch VII Chief  
Terrance Ocheltree, Ph.D., Division of New Drug Quality Assessment II Director  
Sheldon B. Markofsky, Ph.D., Product Quality Reviewer  
Caroline Strasinger, Ph.D., Product Quality Reviewer  
Luz E Rivera, ONDQA Project Manager, DNCE

**SPONSOR ATTENDEES**

**Merck Consumer Care Attendees:**

Sangeeta Patel, Sr. Manager RA, CMC  
Steve Walker, Director of Global CMC  
Anna Kalika, Sr. Manager UR Franchise  
Stephenie Barba, VP Head of Global RA  
Fowler Kevin, Formulator, Memphis R&D  
Wiggins David, Director, Analytical, Memphis R &D  
Pierro Nancy, Director, Rx to OTC Switch

**Watson Laboratories Inc Attendees: Manufacturer of Oxytrol Patches**

Eric Nelson, Director Lab Operations  
Burke Byrne, Manager, RA CMC  
James Greenbaum, Manager, Quality Engineering  
Tate Edwards, Manager, Pharmaceutical Technology

## 1.0 BACKGROUND

The purpose of meeting was to discuss the (b) (4) observations of the drug product samples that were sent to FDA on June 11th, 2012 and further discuss the proposed quantitative and qualitative (appearance) method for (b) (4) for NDA 202 211, Oxytrol for Women (oxybutynin) patch, 3.9 mg.

On June 15, 2012, Merck Consumer Care provided samples of the drug product, Oxytrol for Women transdermal systems requested by the Chemistry Manufacturing and Control reviewer.

On June 22<sup>nd</sup>, 2012 an Information Request letter was sent to Merck Consumer Care regarding the drug product release specification and stability testing, with a response requested to be provided by July 20, 2012.

Merck Consumer Care requested an extension to provide a response to the IR letter which was granted. The CMC review team offered to discuss in a Telephone conference meeting the (b) (4) associated with the Oxytrol product, as well as the requested method and acceptance criterion for (b) (4) prior to the submission of the response.

## 2. DISCUSSION

**Topic 1:** Discussion of the (b) (4) observations from the samples that were sent to the FDA on June 11<sup>th</sup>

### Issue presented by FDA:

1. Applicant sent to the agency samples from batch 282995 with expiry date of (b) (4). The samples provided indicate that the Oxytrol Transdermal System experiences severe (b) (4).  
(b) (4) (b) (4) (b) (4)
2. FDA encourages the applicant to investigate using samples with a similar expiry date as samples sent to the FDA.
3. FDA is concerned with the (b) (4) issue presented in the samples at the (b) (4) time point in stability. Samples at the (b) (4) time point show evidence (b) (4).  
(b) (4)

### Applicant indicated:

1. Having some knowledge of the (b) (4) issue.
2. Studies have shown that even with the (b) (4) issue the patch can be removed from the package.
3. The Applicant expects the same degree of (b) (4) with the OTC product presentation as that seen with the current prescription drug product.

**Post meeting comment:**

In the response dated July 26, 2012, you indicated that acceptance criteria and test methods for (b) (4) adhesion will be provided by August 31, 2012.

**Action Items:**

<b>Action Item</b>	<b>Owner</b>	<b>Due Date</b>
Develop a quantitative and qualitative specification and acceptance criteria for (b) (4)	Merck Consumer Care	August 31, 2012
Define what is the criteria to define “product damage”	Merck Consumer Care	August 31, 2012
Modify the stability protocol to incorporate the test for (b) (4)	Merck Consumer Care	August 31, 2012

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/s/  
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LUZ E RIVERA  
10/21/2012

**From:** Do, Phong  
**To:** ["Pierro, Nancy"](#)  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Tuesday, September 25, 2012 11:14:00 AM

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Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We have the following request for information:

Of all subjects reporting new or worsening symptoms at the weeks 3, 7 and 12 interviews, please provide a table/line listing that includes those who checked "other," i.e., those who reported symptoms not included in the questionnaires' lists, and all the AEs they reported over the duration of the CONTROL trial. Please provide this as a simple table and as a SAS file, if possible. If there is a separate dataset that simply includes description of the "other" symptoms, please provide it as well.

Confirm receipt of this email and respond to this information request by COB Friday, September 28, 2012 .

Thank you,

Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager  
FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

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/s/  
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PHONG DO  
09/26/2012



NDA 202211

**INFORMATION REQUEST**

MSD Consumer Care, Inc.  
Attention: Nancy Pierro  
Associated Director, Regulatory Affairs  
556 Morris Avenue Summit, NJ 07901

Dear Ms. Pierro:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg on March 26, 2012.

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

1. Regarding the (b) (4) method submitted on 30-AUG-2012, the Agency has the following consideration to communicate:

- (b) (4)

2. Regarding the proposed shelf life of (b) (4), the Agency has the following to communicate:

- Given the difficulties with removal of the product from the pouch and the degree of (b)(4) observed with the prescription (Rx) Oxytrol, particularly of older samples, a shelf-life of (b)(4) is not supported for the Over-the Counter (OTC) Oxytrol product without further justification. The Agency recognizes the historical Rx data provided in the amendment 30-AUG-2012, however, until the proposed method can be validated to properly assess the degree of (b)(4), greater experience with the proposed (b)(4) method can be provided, and the potential impact on usability of the product in the OTC patient population can be assessed, a shelf-life of (b)(4) cannot be granted. Based on stability data of the OTC product and samples provided to the Agency during the current review cycle, a shelf-life of 12 months is acceptable for the OTC Oxytrol product. Extensions of the 12 month shelf-life can be requested through annual reports with supportive data. The Applicant should also provide quarterly complaints to the Agency of the OTC Oxytrol product once marketed to support its use in the OTC patient population.

If you have any questions, call LCDR Luz E Rivera, Regulatory Project Manager, at (301) 796 4013.

Sincerely,

*{See appended electronic signature page}*

Terrance Ocheltree, RPh, PhD  
Director Division of New Drug Quality Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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/s/  
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TERRANCE W OCHELTRIE  
09/14/2012

## MEMORANDUM OF TELECON

DATE: September 13, 2012  
APPLICATION NUMBER: NDA 202211

BETWEEN:

Nancy Pierro - Regulatory  
Stephenie Barba - Head of Regulatory  
Dr. Ed Hemwall - R+D OTC Switch Franchise lead  
Amy Replogle - R+D program lead

(b) (4)

Dr. Raj Mishra - Head of Medical Affairs  
Dr. Alankar Gupta - Medical

Representing: MSD Consumer Care 888-877-0620

AND

Name: Lesley Furlong, Ryan Raffaelli, Phong Do, Melissa Furness  
Division of Nonprescription Clinical Evaluation, HFD-560

SUBJECT: NDA 202211 Case Report Forms clarification

The teleconference was held at FDA's request to help FDA reviewers understand how misuse was identified and mitigated in the applicant's actual use study (the "CONTROL" study). FDA stated that the call was made to review examples of case report forms. FDA was interested in subjects over 65 yo who were considered to misuse the patch by simultaneous use. FDA acknowledged the applicant's table listing case report forms that met those criteria. The table included columns showing if subjects' misuse was mitigated for simultaneous use and whether misuse was also mitigated for the secondary endpoint 5, combined misuse by simultaneous use or prolonged duration of use. FDA requested clarification on misuse for two examples (subjects #10-0008 and #22-0011).

The applicant stated that the way subjects were determined to have misused by simultaneous use was identification of overlapping dates on their diary cards. For example, subject #10-0008 applied the first patch on June 10, 2010 and removed on June 14, 2010. Subject then applied second patch on June 14, 2010. This was acceptable because a subject may remove and attach a patch on the same day. However on diary card #2, subject took off last patch on July 19, 2010 and on card #3 applied patch on July 17, 2010. Therefore, subject had overlap of 2-3 days. That is why subject#10-0008 was considered to have misused by simultaneous use. This subject was not considered to have mitigating factors because the subject was not asked pertinent End-of-Study questions #13/13a. These questions address multiple patch use. The applicant reported that eight subjects who had simultaneous use were not asked those questions, and therefore could not be mitigated.

Subject #22-0011 was determined to have a mitigating factor because subject's diary card #2 showed application of first patch on June 30, 2010 and removal on September 4, 2010. Subject's second patch was applied on July 5, 2010 and removed July 9, 2010. The

applicant's clinical reviewers performing mitigation review felt that was an obvious diary card error. The applicant's reviewers thought it highly unlikely that the subject wore the patch for more than two months.

FDA thanked the applicant for the clarifying information and informed the applicant to expect a request from the review team for several additional case report forms.

Phong Do, Regulatory Project Manager

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/s/  
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PHONG DO  
09/13/2012

**From:** Do, Phong  
**To:** ["Pierro, Nancy"](#)  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Thursday, September 13, 2012 12:45:00 PM

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Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We have the following requests for information:

Please provide the case report forms for the following subjects in the CONTROL trial:

12-0121

11-0085

23-0061

15-0050

21-0050

Confirm receipt of this email and respond to this information request by  
COB Monday, September 17, 2012.

Thank you,

Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager  
FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

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/s/  
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PHONG DO  
09/13/2012

**From:** Do, Phong  
**To:** "[Pierro, Nancy](#)"  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Tuesday, September 04, 2012 2:20:00 PM

---

Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We also refer to your August 28 and September 4, 2012 amendments responding to our August 20 and 30, 2012 requests for information.

We have the following requests for information:

We fully understand the objectives of Cohort 3 and how it was recruited. We also understand that this is not a self selection study but rather a label comp study. Our questions pertain to Cohort 1.

You have stated in your response that respondents who ended up in Cohort 1 and 2 were not asked about any self reported diabetes risk factors. However, the pre-recruit screener that was submitted with the NDA is confusing relative to this point, because 1) there is no "hard stop" after Q. 6 when respondents were determined to qualify for C1/C2 and 2) the "Cohort Score Sheet" (on page 27 of 42) implies that Q 7C and 8D could have been asked of Cohorts 1 and 2.

Since you have stated in your response that "if they did have OAB symptoms, they continued to be screened for Cohorts 1 and 2", please provide all of these questions that were asked of Cohorts 1 and 2 after Q 6 (OAB symptoms), as well as the page citation of where these can be found in the protocol.

Confirm receipt of this email and respond to this information request by COB Thursday , September 6 , 2012.

Thank you,

Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager  
FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

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PHONG DO  
09/05/2012

**From:** Do, Phong  
**To:** "[Pierro, Nancy](#)"  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Thursday, August 30, 2012 11:47:00 AM

---

Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We also refer to your August 28, 2012 amendment responding to our August 20, 2012 request for information.

We have the following requests for information:

- 1) Your response states that there was an overlap of the low literacy individuals between Cohorts 1 and 2 – in other words, that these were not two unique cohorts.
  - o Please clarify whether there was also any overlap of the low literacy individuals (of those with OAB symptoms) between Cohort 3 and Cohorts 1 and/or 2.
- 2) We understand that the subjects in Cohort 1 were not **screened** (ie, as in being administered the diabetes risk assessment calculator) for diabetes risk and that the risk assessment calculator screening per se only occurred in Cohort 3. We are distinguishing here between **“screening”** and **“asking about”**. (For example, subjects may be asked about income for demographic analysis purposes in standard consumer research studies, but it would incorrect to say that they are being screened for this)

So, to restate our August 20<sup>th</sup> question - It appears that Cohort 3 potential respondents were **asked** about self reported diabetes risk factors – and – from the protocol as well as your response to Q 3 – it appears that some of them ended up being placed into Cohort 1 (or 2) simply because those cohorts had not been filled yet.

- o Can you confirm, then, whether or not any of the respondents who ended up in Cohort 1 had been **asked** about any self reported diabetes risk factors. If so, please provide us with the relevant unique subject ids of these individuals, as well as their responses regarding the self reported diabetes risk factors.
- 3) Send the Oxytrol for Women 14-count carton labeling. Indicate if the 14-count carton labeling is representative and specifically, what it represents. We remind you that representative labeling should only be submitted when the only difference is the package count size or container volume (e.g., ml or oz).

Confirm receipt of this email and respond to this information request by COB Wednesday, September 5, 2012.

Thank you,

Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager

FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

APPEARS THIS WAY ON ORIGINAL



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PHONG DO  
08/30/2012

**From:** Do, Phong  
**To:** ["Pierro, Nancy"](#)  
**Bcc:** [Raffaelli, Ryan](#); [Furlong, Lesley-Anne](#)  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Wednesday, August 22, 2012 9:16:00 AM

---

Dear Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We have the following requests for information:

Submit to the Agency all quality-related reports or complaints (including those with or without adverse events) and any reports related to medication errors with the Oxytrol (oxybutynin) transdermal system for the duration of the CONTROL trial. We are specifically interested in those reports, errors, and adverse events pertaining to difficulty removing the system from the container closure (pouch), excessive (b) (4), and adhesion problems (excessive adhesion to skin, partial or complete adhesion failures, tight release). In addition, note any lot trends observed.

Confirm receipt of this email and respond to this information request by COB August 27, 2012.

Thank you,  
Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager  
FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

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PHONG DO  
08/22/2012

**From:** Do, Phong  
**To:** ["Pierro, Nancy"](#)  
**Bcc:** [Cohen, Barbara R \(CDER\)](#); [Furlong, Lesley-Anne](#)  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Monday, August 20, 2012 5:26:00 PM

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Dear Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We have the following requests for information:

1. Please provide us with the following analysis: for Questions 3 and 6 for Cohort 1 of the pivotal study, an analysis comparing responses between those who were at self reported risk for diabetes and those who were not. (It appears from your recruiting protocols that those ages 44+ were all asked to some degree about self reported diabetes risk, regardless of whether they ended up in Cohort 1 or 3.)
- 2) In the report on LCS 92099, targeted LCS on diabetic warnings among the general population of women, it states that (p.20):
  - a. If any LCS questionnaires were incomplete or unusable due to interviewer error in administration, they were not entered into the dataset" Please provide us with information on how many questionnaires - and at what sites - this occurred at.
    - b. The report goes on to state "if corrections were necessary, they were entered in the following manner: the wrong entry was crossed out and the correct entry was placed next to it. Corrections were initialed and dated". Please provide documentation on how often this occurred, and note if (and where) the protocol explicitly stated that respondents were not allowed to go back and change their answers.
- 3) In the report on 10054, self selection in pregnant women:
  - a. The discussion on data quality assurance (p. 21) states. "If any self selection questionnaires were incomplete and unusable due to interviewer error during the administration of this study, they were not entered into the data set." Please provide information on how many questionnaires – and at what sites – this occurred at.
    - b. The report goes on to state "if corrections were necessary, they were entered in the following manner: the wrong entry was crossed out and the correct entry was placed next to it. Corrections were initialed and dated". Please provide information on how often this occurred, and if the protocol explicitly stated that respondents were not allowed to go back and change their answers.

Confirm receipt of this email and respond to this information request by COB August 27, 2012.

Thank you,  
Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager  
FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

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PHONG DO  
08/21/2012

**From:** Do, Phong  
**To:** ["Pierro, Nancy"](#)  
**Bcc:** [Raffaelli, Ryan](#); [Furlong, Lesley-Anne](#)  
**Subject:** NDA 202211; Oxytrol for Women; Information Request  
**Date:** Friday, August 17, 2012 3:58:00 PM

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Ms. Pierro,

Please refer to your March 26, 2012 New Drug Application, NDA 202211, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We have the following requests for information:

- Please provide summary tables similar to Tables 14-14-35-1 through 14-14-35-3 (Proportion of Subjects who misused the patch, by race, age and literacy) for secondary endpoint 5. Please create separate tables for the proportion of users who misused based on increased duration of use (> 4 days) and those who misused based on simultaneous use.
- Provide the Subject IDs, or a collection of the Case Report Forms, for the subjects  $\geq$  65 years of age who are included in the above tables indicating misuse by simultaneous use.

Confirm receipt of this email and respond to this information request by COB Wednesday, August 22, 2012.

Thank you,

Phong Do, PharmD  
LCDR - USPHS  
Regulatory Project Manager  
FDA/CDER/ODEIV/DNCE  
Phone 301-796-4795

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PHONG DO  
08/17/2012



NDA 202211

**INFORMATION REQUEST**

MSD Consumer Care, Inc.  
Attention: Nancy Pierro  
Associated Director, Regulatory Affairs  
556 Morris Avenue  
Summit, NJ 07901

Dear Ms. Pierro:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg on March 26, 2012.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response by July 20, 2012 in order to continue our evaluation of your NDA.

**Regarding the Drug Product Release Specification and Stability Testing:**

1. Establish a package integrity or burst test and acceptance criteria.
2. Include in the appearance criterion an observation for the absence of (b) (4) and/or visible particulates. Provide justification if microscopic methods are not to be routinely employed.
3. Establish a tests and acceptance criteria for the following, to be used at release and on stability. Include upper and lower limits where appropriate.
  - (b) (4)
  - (b) (4)
  - (b) (4) adhesion

**General Comments:**

4. Submit to the Agency all quality-related reports or complaints (including those with or without adverse events) and any reports related to medication errors with the Oxytrol (oxybutynin) transdermal system for the past 9 years. We are specifically interested in those reports, errors, and adverse events pertaining to difficulty removing the system from the container closure (pouch), excessive (b) (4), and adhesion problems (excessive adhesion to skin, partial or complete adhesion failures, tight release). In addition, note any lot trends observed.

5. Please note that the final action for NDA 202-211 is dependent upon approval of pending Supplement-6 of the referenced NDA 21-351.

If you have any questions, call LT Luz E Rivera, Regulatory Project Manager, at (301) 796 4013.

Sincerely,

*{See appended electronic signature page}*

Terrance Ocheltree, PhD  
Division Director  
Division of New Drug Quality Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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/s/  
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TERRANCE W OCHELTRIE  
06/22/2012



NDA 202211

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

MSD Consumer Care, Inc.  
556 Morris Avenue  
Summit, NJ 07901

Attention: Nancy Pierro  
Associate Director, Regulatory Affairs

Dear Ms. Pierro:

Please refer to your New Drug Application (NDA) dated and received March 26, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Oxybutynin Transdermal System, 3.9 mg per day.

We also refer to your correspondence dated March 26, 2012, and received March 27, 2012, requesting review of your proposed proprietary name Oxytrol for Women. We have completed our review of the proposed proprietary name and have concluded that it is conditionally acceptable.

The proposed proprietary name, Oxytrol for Women, 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 dated March 26, 2012, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Ermias Zerislassie, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0097. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Phong Do at (301) 796-4795.

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  
06/22/2012



NDA 202211

**FILING COMMUNICATION**

MSD Consumer Care, Inc.  
Attention: Nancy Pierro  
Associate Director, Regulatory Affairs  
556 Morris Avenue  
Summit, NJ 07901

Dear Ms. Pierro:

Please refer to your New Drug Application (NDA) dated March 26, 2012, received March 26, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

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 January 26, 2013.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, 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 December 17, 2012.

During our filing review of your application, we identified the following potential review issues and request that you submit the following information:

1. Please provide the following literature references for our review (Module 2.7.5):  
References 3, 26, 76, 122-136, 174, and 216.
2. For the following subjects with mitigation profiles created (Subject IDs: CL2008-13-10-0133, CL2008-13-12-0086, CL2008-13-11-0019, CL2008-13-17-0124, CL2008-13-26-0152, CL2008-13-30-0084, CL2008-13-16-0019, CL2008-13-32-0058), please provide

their case report forms (CRFs) so that we can more fully evaluate examples of the mitigation assessment.

3. Table 14-14-45 lists those subjects who were considered misusers, based on the Secondary Endpoint 3, and who were assessed for mitigation. Please provide the CRFs for the following subjects (Subject number: CL2008-13-10-0021, CL2008-13-10-0025, CL2008-13-11-0098, CL2008-13-19-0007, CL2008-13-25-0028, CL2008-13-23-0067) so that we can more fully evaluate examples of the mitigation assessment.
4. Section 11.1.7 of the final study report for Protocol CL2008-13 describes patch misuse based on Secondary Endpoint 5. Such misuse was assessed for mitigation. If a table similar to Table 14-14-45 (“Secondary Endpoint 3: Listing of Misusers and Mitigation Assessment with Reasons for Mitigation by Subject Number”) exists for Secondary Endpoint 5, please identify its location. If no such table exists, please provide a similar table for subjects who misused the drug by multiple simultaneous patch use.
5. A drug product applied to the skin with the potential to be used chronically is typically supported by chronic toxicity and carcinogenicity data by this route. Please address if you are aware of any chronic dermal toxicity studies or dermal carcinogenicity studies conducted with the oxybutynin product.
6. You submitted a prescription consumer information leaflet in your package. Please clarify if you plan to market the over-the-counter product with an OTC consumer information leaflet. If so, submit an OTC consumer information leaflet.
7. Clarify if the 2-count carton is a retail-size or a sample-size.

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.

### **REQUIRED PEDIATRIC ASSESSMENTS**

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

Because none of these criteria apply to your application, you are exempt from this requirement.

If you have any questions, call Phong Do, Regulatory Project Manager, at (301) 796-4795.

Sincerely,

*{See appended electronic signature page}*

Joel Schiffenbauer, M.D.  
Deputy Director  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

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/s/  
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JOEL SCHIFFENBAUER  
06/04/2012

**From:** [Pierro, Nancy](#)  
**To:** [Rivera, Luz E \(CDER\)](#)  
**Cc:** [Do, Phong](#); [Patel, Sangeeta](#)  
**Subject:** RE: Request for NDA 202211  
**Date:** Friday, June 01, 2012 2:28:02 PM

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Dear Dr. Rivera,

I'm writing to acknowledge receipt of your request.

My colleague, Sangeeta Patel, will be responding, and may be contacting you if she has any questions.

Best regards,

**Nancy Pierro**  
**Regulatory Affairs**  
**Merck Consumer Care**  
556 Morris Avenue  
Summit, NJ 07901  
(908) 473-5709 phone  
(908) 473-3814 fax

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**From:** Rivera, Luz E (CDER) [mailto:Luz.E.Rivera@fda.hhs.gov]  
**Sent:** Friday, June 01, 2012 1:47 PM  
**To:** Pierro, Nancy  
**Cc:** Do, Phong  
**Subject:** Request for NDA 202211

Good afternoon Ms. Pierro,

We are reviewing the Chemistry Manufacturing and Control section of your NDA 202211. We need some additional information from you in order to continue our evaluation.

To aid in review of the NDA, provide 10 samples of each of the following by June 15, 2012:

- The transdermal system in the currently marketed (prescription packaging) near the beginning of shelf-life (b) (4)
- The transdermal system in the currently marketed (prescription packaging) nearing the end of shelf-life (b) (4)
- The transdermal system in the proposed OTC packaging near the beginning of shelf life (b) (4)
- The transdermal system in the proposed OTC packaging at the latest time point available in the on-going stability studies.

Include the batch numbers associated with the provided drug products. The transdermal systems may be sent to the Attention of:

FDA – White Oak  
Luz Rivera - CDER/OPS/ONDQA  
Bldg. 21, Rm 2605  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

Please contact me if you have any questions,

Luz.E. Rivera, Psy.D.  
LT, USPHS  
Regulatory Health Project Manager  
FDA/CDER/OPS/ ONDQA  
Division of New Drug Quality Assessment III  
Phone (301) 796-4013  
luz.e.rivera@fda.hhs.gov

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PHONG DO  
06/04/2012

## Promotional Review Template

<b>NDA/Supplement Number:</b> 202211	<b>Receipt Date of Consult:</b> 4-3-2012	<b>Due Date: of Consult:</b> 6-3-2012
<b>Regulatory References:</b> <ul style="list-style-type: none"><li>• <u>FDCA §502(a); 21 USC 352(a)</u>: A drug [whether prescription or OTC] is misbranded if its <u>labeling</u> is false or misleading in any particular.</li><li>• <u>FDCA §201(n); 21 USC 321(n)</u>: When a drug [prescription or OTC] is alleged to be misbranded because its <u>labeling</u> (or advertising) is misleading, the determination of whether the <u>labeling</u> (or advertising) is misleading should take into account not only representations made or suggested, but also the extent to which the <u>labeling</u> (or advertising) fails to reveal material facts.</li><li>• <u>21 CFR 201.10(c)(3)</u>: The drug [prescription or OTC] may be misleading by reason (among other reasons of): the employment of a fanciful proprietary name for a drug or ingredient in such a manner as to imply that the drug or ingredient has some unique effectiveness or composition when, in fact the drug or ingredient is a common substance, the limitations of which are readily recognized when the drug or ingredient is listed by its established name.</li></ul>		
<b>Proposed Tradename: Oxytrol for Women</b>		
<b><u>Promotional Review Considerations</u></b>		
Does the proposed OTC Tradename:		
Overstate the efficacy of the drug product?	YES	<b>NO</b>
Minimize the risk of the drug product?	YES	<b>NO</b>
Broaden the indication of the drug product?	YES	<b>NO</b>
Suggest superiority of the drug product without substantiation?	YES	<b>NO</b>
Implies unique effectiveness or composition because it is of a fanciful nature?	YES	<b>NO</b>
If the answer is "YES" to any of the above questions, provide an explanation of the conclusion and the appropriate regulatory citation to substantiate the conclusion:		

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/s/  
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BARBARA R COHEN  
05/31/2012

LESLEYANNE FURLONG  
05/31/2012

**From:** [Pierro, Nancy](#)  
**To:** [Do, Phong](#)  
**Subject:** RE: NDA 202211; Oxytrol for Women; Information Request  
**Date:** Thursday, April 26, 2012 4:08:28 PM

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Dear Phong,

Thanks for your email. I am writing to acknowledge receipt.

Best regards,

**Nancy Pierro**  
**Regulatory Affairs**  
**Merck Consumer Care**  
*556 Morris Avenue*  
*Summit, NJ 07901*  
*(908) 473-5709 phone*  
*(908) 473-3814 fax*

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**From:** Do, Phong [mailto:Phong.Do@fda.hhs.gov]  
**Sent:** Thursday, April 26, 2012 4:05 PM  
**To:** Pierro, Nancy  
**Subject:** NDA 202211; Oxytrol for Women; Information Request

Dear Ms. Pierro:

Please refer to your New Drug Application (NDA) submitted on March 26, 2012 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxytrol for Women (oxybutynin) patch, 3.9 mg.

We are reviewing the biostatistics section of your submission and have the following comments and information requests. We request a response by May 24, 2012 in order to continue our evaluation of your NDA.

1. Please resubmit the primary efficacy dataset ADEP1 with the following 24 flag variables (12 for pre-mitigation and 12 for post-mitigation) included:
  - One flag for “condition worsens” and one flag indicating whether the user stops use or not when the condition worsens
  - One flag for” new symptoms appear” and one flag indicating whether the user stops use or not when new symptoms appear
  - One flag for “condition does not improve after 2 weeks of use” and one flag indicating whether the user stops use or not when the condition worsens
  - One flag for “having an allergic reaction to the product” and one flag indicating whether the user stops use or not when having an allergic reaction to the product
  - One flag for “having severe redness, itchiness, or blistering at the site of application” and one flag indicating whether the user stops use or not when having severe redness, itchiness, or blistering at the site of application
  - One flag for “having abdominal and/or pelvic pain” and one flag indicating

whether the user stops use or not when having abdominal and/or pelvic pain

Please use the following format: 1 for Yes, 2 for No, and 99 for Missing for these variables. Please also submit the program codes used to derive these variables. We expect that these program codes will help us understand how the primary and key secondary endpoints are derived, and the derived variables will enable us to reproduce your results presented in Table 13, 14, 16, 18, and 20 of the study report and perform supportive analyses if needed during our review.

2. Please submit the program codes used to produce the primary efficacy results for all the label comprehension and self-selection studies.

Please confirm receipt of this email.

Thank you,

Phong Do, PharmD

Lieutenant - USPHS

Regulatory Project Manager

FDA/CDER/ODEIV/DNCE

Phone 301-796-4795

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/s/  
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PHONG DO  
04/26/2012



NDA 202211

**NDA ACKNOWLEDGMENT**

MSD Consumer Care, Inc.  
Attention: Nancy Pierro  
Associate Director, Regulatory Affairs  
556 Morris Avenue  
Summit, NJ 07901

Dear Ms. Pierro:

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: Oxytrol for Women (oxybutynin) patch, 3.9 mg

Date of Application: March 26, 2012

Date of Receipt: March 26, 2012

Our Reference Number: NDA 202211

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 May 25, 2012, in accordance with 21 CFR 314.101(a).

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.

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<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

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If you have any questions, call me at (301) 796-4795.

Sincerely,

*{See appended electronic signature page}*

Phong Do, Pharm.D.  
Regulatory 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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PHONG DO  
04/06/2012



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

IND 074288

**MEETING MINUTES**

MSD Consumer Care, Inc.  
Attention: Nancy Pierro  
Associate Director, Regulatory Affairs  
556 Morris Avenue  
Summit, NJ 07901

Dear Ms. Pierro:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Oxytrol (oxybutynin) patch, 3.9 mg.

We also refer to the meeting between representatives of your firm and the FDA on September 12, 2011. The purpose of the meeting was to discuss the content and format requirements of a planned New Drug Application for Oxytrol (oxybutynin) patch, 3.9 mg.

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

If you have any questions, call Phong Do, Regulatory Project Manager, at (301) 796-4795.

Sincerely,

*{See appended electronic signature page}*

Andrea Leonard-Segal, M.D., M.S.  
Director  
Division of Nonprescription Clinical Evaluation  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

ENCLOSURE:  
Meeting Minutes



**FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH**

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** Type B

**Meeting Category:** Pre-NDA

**Meeting Date and Time:** September 12, 2011  
10:30 A.M. -11:30 A.M. EST

**Meeting Location:** FDA/White Oak  
10903 New Hampshire Avenue  
Building 22, Room 1419  
Silver Spring, MD 20903

**Application Number:** IND 074288

**Product Name:** Oxytrol (oxybutynin) patch, 3.9 mg

**Indication:** Treatment of overactive bladder

**Sponsor/Applicant Name:** MSD Consumer Care, Inc.

**Meeting Chair:** Andrea Leonard-Segal, M.D., M.S.  
Division Director  
Division of Nonprescription Clinical Evaluation

**Meeting Recorder:** Phong Do, Pharm.D.  
Regulatory Project Manager  
Division of Nonprescription Clinical Evaluation

**FDA ATTENDEES**

Office of Drug Evaluation IV  
Charles Ganley, M.D., Director

Division of Nonprescription Clinical Evaluation  
Andrea Leonard-Segal, M.D., M.S., Director  
Joel Schiffenbauer, M.D., Deputy Director  
Lesley-Anne Furlong, M.D., M.S., Medical Team Leader  
Linda Hu, M.D., Medical Officer  
Wafa Harrouk, Ph.D., Pharmacologist/Toxicologist  
Barbara Cohen, M.P.A., Social Science Analyst  
Melissa Hancock Furness, Chief, Project Management Staff  
Phong Do, PharmD, Regulatory Project Manager

IND 074288  
Meeting Minutes  
Type B Meeting

Office of Drug Evaluation IV  
Division of Nonprescription Clinical Evaluation

Division of Nonprescription Regulation Development

Colleen K. Rogers, Ph.D., Interdisciplinary Scientist Team Leader  
Maria E. Ysern, MSc., Interdisciplinary Scientist Reviewer

Division of Reproductive and Urologic Products

George Benson, M.D., Deputy Director  
Suresh Kaul, M.D., Medical Team Leader  
Christine Nguyen, M.D., Medical Officer

Division of New Drug Quality Assessment III

Sheldon Markofsky, Ph.D., Chemistry Reviewer

Division of Biometrics IV

Yunfan Deng, Ph.D., Mathematical Statistician

Division of Medication Error Prevention and Analysis

Zachary Oleszczuk, PharmD, Team Leader  
Cathy Miller, Safety Evaluator

Office of Scientific Evaluations

Sharon Gershon, Pharm.D., OSI Reviewer

**SPONSOR ATTENDEES**

MSD Consumer Care, Inc.

Stephenie Barba  
Alankar Gupta, M.D.  
Edwin Hemwall, Ph.D.  
Kristie Licata  
Nancy Miller-Rich  
Stephen Neumann  
Amy Repligole  
John O'Mullane, Ph.D.  
Nancy Pierro

Watson Pharmaceuticals, Inc.

Kevin Barber, Ph.D., RAC, PMP

## 1.0 BACKGROUND

MSD Consumer Care, Inc. (MCC) submitted a request to the FDA on March 30, 2011 for a meeting to discuss the content and format requirements of a planned New Drug Application for Oxytrol (oxybutynin) patch, 3.9 mg.

The Agency's preliminary responses to the questions contained in MCC's July 27, 2011 meeting background package were provided to MCC via e-mail on September 9, 2011. These preliminary responses appear in italics below. Following introductions the meeting agenda consisted of a discussion regarding questions 1, 2d, 5, and 'Additional Comments from Office of Scientific Investigations.'

For questions where no additional discussion is indicated, neither MCC nor FDA raised any additional issues pertaining to these questions.

## 2.0 DISCUSSION

### Questions:

#### 1. Does the Agency agree with MCC's planned analysis strategies for the data collected in the CONTROL actual use study?

##### FDA Preliminary Response:

*We do not have objections to mitigation. However, we do not have a clear understanding of what criteria will be applied in performing these analyses. You will have to submit sufficient information to allow us to perform an audit of your mitigations. Whether we agree with the results of the mitigation will be a review issue.*

*We would also like to be sure that you:*

- Calculate the proportion of subjects who did not stop use when they developed new symptoms referred to anywhere in the labeling, when their condition worsened, or when their OAB symptoms did not improve after 2 weeks of use. We would like to see the total numbers of subjects who stopped use correctly according to the label and who (same subject) talked to a doctor.*
- Analyze and present results for appropriate self-selection. Provide the total number of subjects who called to express interest in enrolling in the study and were excluded if they were male or if they were excluded for age or pregnancy. Also, report and analyze the number of subjects who declined to participate after reading the label or who were not allowed to enroll in the use phase of the study for medical reasons, although they had expressed interest in doing so after reading the label. Of the subjects who were enrolled in the use phase and received study drug, report the numbers and percentages of subjects who appropriately and inappropriately self-selected to use based on the information in the history obtained at enrollment. For subjects who selected inappropriately, provide an explanation for why the subject should not have used the drug.*

- *Provide an analysis of results of the urinalyses obtained to see if subjects may have had conditions for which the drug should not be used.*
- *Provide an analysis of individuals who had medical follow-up (medical diagnosis and outcome).*
- *Provide an analysis of the proportion of subjects who misused the patch (e.g., used more than 1 patch at a time or had a temporal overlap in patch use).*
- *Perform subanalyses in subjects > 65 years old for the above listed requests and for adverse events.*
- *Provide outcome data (for mother and child) for anyone who may have become pregnant during the trial.*
- *Your discussion of safety topics of special concern related to Oxytrol should include falls, disorientation, and confusion.*
- *Mitigated entries in tables should be hyperlinked to patient profiles referenced so reviewers can evaluate the mitigation assessment.*
- *Please provide all of the original verbatim open-ended responses as well as the schematics for classifying and coding.*

*As we recommended previously, the primary endpoint should be a composite of the proportion of subjects who did not stop use when they developed new symptoms, when their condition worsened, or when their OAB symptoms did not improve after 2 weeks. We recommend you submit an updated statistical analysis plan (SAP) for us to review, and document the date that the SAP was finalized. The SAP should provide details on exactly how each primary or secondary endpoint will be derived from the questionnaire responses (i.e., which questionnaire answers will be used and what derivations will be used). The SAP should also include details on the mitigation analysis strategies you proposed in the briefing meeting package.*

**Discussion:**

MCC agreed to submit their mitigation analysis criteria to the Agency. MCC plans to analyze self-selection using the purchase decisions of study subjects. MCC will provide an analysis of why subjects inappropriately self-selected and will also explore why subjects used the product if they inappropriately chose to use it. MCC agreed to analyze the results of urinalyses. In addition, MCC agreed to provide an analysis of the proportion of subjects who misused the patch both by using it for more than four days or by simultaneously using more than one patch. MCC stated that their plan was to analyze both types of misuse together but agreed to also analyze them separately.

MCC agreed to perform subanalyses of subjects greater than 65 years of age and of subjects greater than 75 years of age. MCC stated they will hyperlink tables that include mitigation to the patient profiles and will include the verbatim open-ended responses in the SDTM dataset. MCC stated they will provide all guidelines for coding and classifying the data. MCC agreed to include falls, disorientation, and confusion in their discussion of safety topics of special concern

related to Oxytrol. MCC agreed to provide an analysis of individuals who had medical follow-up.

MCC agreed to calculate the proportion (and number) of subjects who did not stop using Oxytrol when they developed new symptoms referred to anywhere in the labeling, when their condition worsened, or when their OAB symptoms did not improve after 2 weeks of use. MCC agreed to also calculate the total number of subjects who, if they developed new symptoms referred to anywhere in the label, or their condition worsened, or their OAB symptoms did not improve after 2 weeks of use, stopped use correctly and who (same subject) asked/spoke to a doctor about it. The Agency clarified that MCC will not be required to verify if study subjects contacted their doctor.

MCC stated, however, that they will keep their primary endpoint as defined in the protocol. In MCC's opinion their primary endpoint addresses the key safety issues of new conditions emerging and of symptoms getting worse while taking the product. MCC stated that a full analysis will be provided of all subjects that did not stop treatment when symptoms did not improve after two weeks. MCC reminded the Agency this is a secondary endpoint already predefined in the protocol. MCC stated that an ad hoc analysis can be performed containing a composite of the proportion of subjects who did not stop use when they developed new symptoms, when their condition worsened, or when their OAB symptoms did not improve after 2 weeks. That analysis will be part of the revised SAP that MCC will send in after the meeting.

## 2. Integrated Summaries of Efficacy and Safety

### a. Does the Agency agree with MCC's proposed content of the Integrated Summary of Efficacy and Consumer Behavior?

*FDA Preliminary Response:  
See above comments.*

### b. Does the Agency agree with MCC's proposed content of the Integrated Summary of Safety?

*FDA Preliminary Response:  
The ISS should also contain an integrated summary of post marketing reports.*

*The ISS should include foreign marketing history. Provide foreign marketing information on where the product is approved, what formulation, whether prescription or nonprescription, and whether the product has been withdrawn or restricted for safety reasons. Note where there are safety data provided on the foreign label(s) that are not on the U.S. label and indicate and explain any differences.*

*Provide any foreign labels with translations for nonprescription transdermal oxybutynin products. Note if any safety information is in the foreign labels that is not in the proposed Drug Facts label.*

*Summarize and analyze literature for all forms of oxybutynin for the past 15 years.*

- c. Does the Agency agree with MCC's proposal regarding the content and time period covered for the review of post-marketing data?**

*FDA Preliminary Response:*

*It is acceptable to provide post-marketing data covering the timeframe of the prescription NDA approval in February 2003 through approximately 6 months prior to the anticipated filing of the NDA.*

*You should also provide post-marketing data from your internal databases in addition to post-marketing data from the AERS and WHO databases.*

*AEs need to also be tabulated according to PT as well as SOC. Serious and nonserious reports should be tabulated separately. Provide Medwatch reports and narrative summaries for serious reports, deaths, and discontinuations.*

- d. Does the Agency agree with MCC's proposal that the review of the post-marketing data be specific to the transdermal system form of oxybutynin?**

*FDA Preliminary Response:*

*Provide a rationale for only presenting post-marketing data specific to transdermal forms of oxybutynin.*

**Discussion:**

In general, FDA acknowledges that there may be a good rationale for submitting postmarketing data related only to the transdermal system form of oxybutynin. MCC stated that a detailed rationale for only presenting post-marketing data specific to the transdermal forms of oxybutynin will be provided in the NDA submission. MCC asked if this is acceptable. FDA responded that the proposal to send in a detailed rationale is acceptable. FDA will review the rationale.

- 3. Does the Agency agree with the proposed content of this NDA?**

**{In Section 5.3.5.4 Other Study Reports and Related Information, the label comprehension and self-selection studies are listed in chronological order, as opposed to grouping by study type (label comprehension, self-selection). This chronological order follows the progression of the development program, and is the order in which these studies will be discussed in Section 5.3.5.3 Integrated Summary of Efficacy and Consumer Behavior.}**

FDA Preliminary Response:

*The proposal to list the study reports in chronologic order is acceptable. See other comments in Q1 and Q2.*

*In reference to Module 4 (nonclinical study reports), your current plan is to cross reference the nonclinical information to the Rx Oxytrol (oxybutynin transdermal system) NDA 21-351. It is not clear to us whether you plan to submit a nonclinical overview in the proposed OTC NDA; we would prefer that such an overview be provided. If it is not possible for you to submit a nonclinical overview, you should provide the specific volumes and page numbers where the relevant nonclinical sections are located in the original Rx NDA submission.*

- 4. In the period before MCC has full eCTD capabilities, will MCC's proposed format of paper CTD submission with an electronic review aid meet DNCE's needs?**

FDA Preliminary Response:

*While we prefer an eCTD submission, we will accept a paper CTD submission with an electronic review aid. Your CTD should follow the folder structure that is outlined in the eCTD guidance, under item III. ORGANIZING THE MAIN SUBMISSION FOLDER. The guidance is located at:*

*<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidance/UCM072349.pdf>*

*If you have any questions, you should contact [ESUB@fda.hhs.gov](mailto:ESUB@fda.hhs.gov).*

**5. Data for Statistical Analysis**

- a. Does the Agency agree with the proposed format of the data for statistical analysis from CONTROL?**

FDA Preliminary Response:

*We recommend the dataset include one flag variable for each of the following conditions stated in the label (total five flag variables):*

- Condition worsens*
- New symptoms appear*
- Condition does not improve after 2 weeks of use*
- Having an allergic reaction to the product*
- Having severe redness, itchiness or blistering at the site of application*

*We also recommend you submit the program codes used to derive variables and the key summary tables in the study report.*

- b. Does the Agency want MCC to submit data for statistical analysis for the other consumer research studies that will be filed in the NDA?**

FDA Preliminary Response:

*Yes*

**Discussion:**

MCC stated that the data for the statistical analysis will be provided in SDTM format. MCC also stated statistical review aids will be provided which will contain the ADaM data sets. MCC asked the FDA if the flag variables recommended by the Agency can be provided in the ADaM data sets. FDA responded that this was acceptable.

In regards to the non-drug consumer research studies, MCC requested clarification if the verbatim data can be provided in Excel spreadsheets. MCC stated that the remaining data can be provided as SAS transport files. FDA responded that this was acceptable.

**6. Does the Agency agree with MCC's proposal to not provide paper printouts of Case Report Forms?**

**FDA Preliminary Response:**

*Yes, it is acceptable to not provide paper printouts of the Case Report Forms, but we request that you submit a CD-ROM with the case report forms in PDF format. See response to Q4.*

**Additional Comments from Office of Scientific Investigations:**

*The Office of Scientific Investigations (OSI) has enclosed guidance for you (see Enclosure: OSI Request) regarding items to be included in your NDA submission to facilitate development of clinical investigator and sponsor/monitor/CRO inspection assignments and related background packages.*

**Discussion:**

MCC asked for clarification regarding the format for submitting site specific datasets for use in the site selection tool. Specifically, MCC asked if there is a concern that the data for their actual use study might be in a format not usable by the tool. FDA agreed to provide a post-meeting addendum to address MCC's question on how to proceed.

**Additional Administrative Comments:**

*Comments shared with you today are based upon the contents of the meeting package, which is considered to be an informational aid to facilitate the meeting discussion. The comments are not meant to be viewed as commitments from the Agency. Review of the information submitted to the IND might identify additional comments or information requests.*

*For applications submitted after February 2, 1999, applicants are required either to certify to the absence of certain financial interests of clinical investigators or disclose those financial interests. For additional information, please refer to 21CFR 54 and 21CFR 314.50(k).*

*A request for proprietary name to be re-reviewed for Oxytrol for Women should be submitted once the NDA is submitted.*

### 3.0 SUMMARY OF KEY DISCUSSION POINTS

1. MCC agreed to provide the following:
  - Mitigation analysis criteria.
  - Analysis of self-selection based on purchase decision. The Sponsor will provide an analysis of how subjects inappropriately self-selected and will also explore how subjects used the product if they inappropriately chose to use.
  - Analysis of the results of urinalyses obtained.
  - Analysis of subjects greater than 65 and 75 years of age.
  - Analysis of the proportion of subjects who misused the patch by using for more than 4 days or had simultaneous use of more than one patch. The Sponsor will also analyze these criteria separately.
  - A discussion of falls, disorientation, and confusion under safety topics of special concern related to Oxytrol.
  - The proportion (and number) of subjects who did not stop use when they developed new symptoms referred to anywhere in the labeling, when their condition worsened, or when their OAB symptoms did not improve after 2 weeks of use.
  - A calculation of the number of subjects who, if they developed new symptoms referred to anywhere in the label, or their condition worsened, or their OAB symptoms did not improve after two weeks of use, stopped use correctly and who (same subject) asked/spoke to a doctor about it. The Agency clarified that MCC will not be required to verify if study subjects contacted their doctor.
  - Analysis of subjects who had medical follow up.
2. MCC will keep the primary endpoint as stated in the protocol but will amend the SAP to include analyses that the Agency is interested in.
3. MCC's rationale for presenting post-marketing data specific to the transdermal form of oxybutynin will be provided in the NDA.
4. MCC will include the five variables the Agency recommends in the statistical analysis as part of the ADaM data sets. MCC will provide SAS data sets for the consumer behavior studies but verbatim data will be in Excel spreadsheets.
5. The FDA will conduct further internal discussion to address MCC's question regarding guidelines provided by OSI. A post meeting addendum will be provided.
6. MCC suggested a post NDA submission meeting to enable MCC to assist the Agency with navigation and structure of the NDA. The FDA was receptive to such a meeting.

### 4.0 POST MEETING ADDENDUM

MCC asked for clarification regarding the format for submitting site specific datasets for use in the site selection tool. Specifically, MCC asked if there is a concern that the data for their actual use study might be in a format not usable by the tool.

OSI Response:

Prior to the September 12 meeting, OSI provided the sponsor a document describing the format in which to submit site specific datasets for use in the site selection tool. This document now appears in section 6.0 of these meeting minutes.

With respect to this actual use study, there is no reason to believe that the endpoint data cannot be run utilizing the site selection tool. If the sponsor has further questions concerning the documents or how to submit datasets, you should submit questions in writing to Sharon Gershon and OSI will address them.

Additional Post-Meeting Clarification:

Please note that it is acceptable to provide the verbatim data for the nonclinical consumer studies in Excel spreadsheets and the remaining data as SAS transport files assuming that both the SAS and Excel data files contain unique subject identifiers – the subject ID and the site ID – so that linkages between the two files can be easily facilitated.

**6.0 ATTACHMENTS AND HANDOUTS**

OSI Request

OSI Request

The Office of Scientific Investigations (OSI) requests that the following items be provided to facilitate development of clinical investigator and sponsor/monitor/CRO inspection assignments, and the background packages that are sent with those assignments to the FDA field investigators who conduct the inspections (Item I and II).

The dataset that is requested as per Item III below is for use in a clinical site selection model that is being piloted in CDER. Electronic submission of site level datasets will facilitate the timely selection of appropriate clinical sites for FDA inspection as part of the application and/or supplement review process.

This request also provides instructions for where OSI requested items should be placed within an eCTD submission (Attachment 2, Technical Instructions: Submitting Bioresearch Monitoring (BIMO) Clinical Data in eCTD Format).

**I. Request for general study related information and specific Clinical Investigator information (if items are provided elsewhere in submission, describe location or provide link to requested information).**

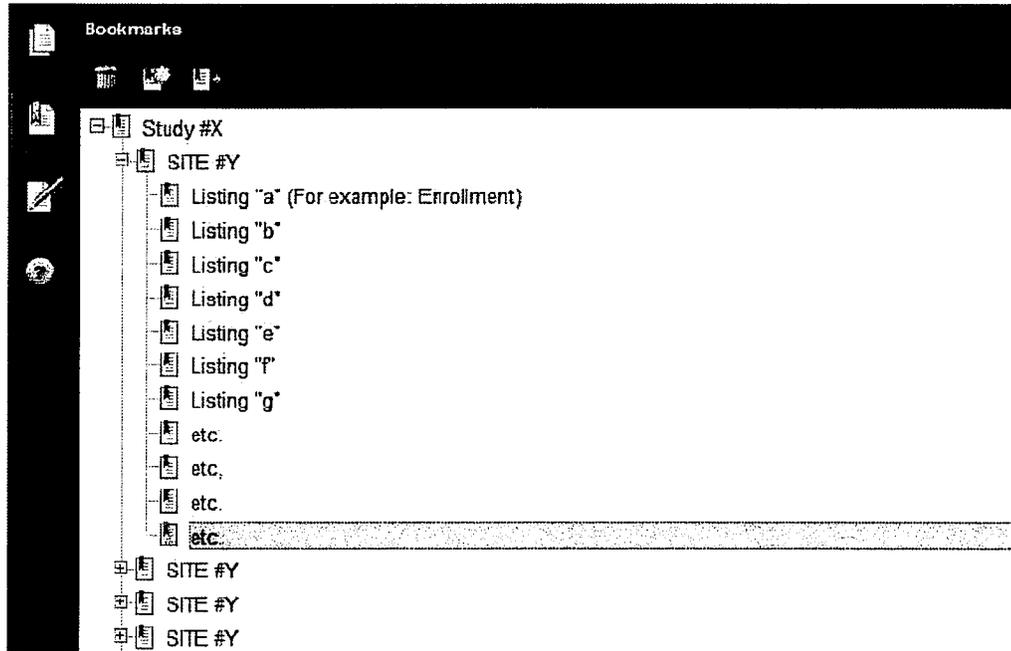
1. Please include the following information in a tabular format in the original NDA for each of the completed Phase 3 clinical trials:
  - a. Site number
  - b. Principal investigator
  - c. Site Location: Address (e.g. Street, City, State, Country) and contact information (i.e., phone, fax, email)
  - d. Current Location of Principal Investigator (if no longer at Site): Address (e.g. Street, City, State, Country) and contact information (i.e., phone, fax, email)
2. Please include the following information in a tabular format by site in the original NDA for each of the completed Phase 3 clinical trials:
  - a. Number of subjects screened for each site by site
  - b. Number of subjects randomized for each site by site
  - c. Number of subjects treated who prematurely discontinued for each site by site
3. Please include the following information in a tabular format in the NDA for each of the completed Phase 3 clinical trials:
  - a. Location of Trial Master File [actual physical site(s) where documents are maintained and would be available for inspection]
  - b. Name, address and contact information of all CROs used in the conduct of the clinical trials
  - c. The location (actual physical site where documents are maintained and would be available for inspection) for all source data generated by the CROs with respect to their roles and responsibilities in conduct of respective studies

- d. The location (actual physical site where documents are maintained and would be available for inspection) of sponsor/monitor files (e.g., monitoring master files, drug accountability files, SAE files, etc.)
4. For each pivotal trial provide a sample annotated Case Report Form (if items are provided elsewhere in submission please describe the location or provide a link to requested information).
5. For each pivotal trial provide original protocol and all amendments (if items are provided elsewhere in submission, please describe the location or provide a link to requested information).
6. Please provide a copy of the Data Management Plan that describes how the data was managed and reviewed throughout the conduct of the study.

## II. Request for Subject Level Data Listings by Site

For each pivotal trial: Site-specific individual subject data (“line”) listings. For each site provide line listings for:

- a. Listing for each subject/number screened and reason for subjects who did not meet eligibility requirements
  - b. Subject listing of drop-outs and subjects that discontinued with date and reason
  - c. Evaluable subjects/ non-evaluable subjects and reason not evaluable
  - d. By subject listing of eligibility determination (i.e., inclusion and exclusion criteria)
  - e. By subject listing, of AEs, SAEs, deaths and dates
  - f. By subject listing of protocol violations and/or deviations reported in the NDA, description of the deviation/violation
  - g. By subject listing of the primary and secondary endpoint efficacy parameters or events. For derived or calculated endpoints, provide the raw data listings used to generate the derived/calculated endpoint.
  - h. By subject listing of concomitant medications (as appropriate to the pivotal clinical trials)
  - i. By subject listing, of laboratory tests performed for safety monitoring
1. We request that one PDF file be created for each pivotal Phase 2 and Phase 3 study using the following format:



### III. Request for Site Level Dataset:

OSI is piloting a risk based model for site selection. Electronic submission of site level datasets will facilitate the timely selection of appropriate clinical sites for FDA inspection as part of the application and/or supplement review process. Please refer to Attachment 1, "Summary Level Clinical Site Data for Data Integrity Review and Inspection Planning in NDA and BLA Submissions" for further information. We request that you provide a dataset, as outlined, which includes requested data for each pivotal study submitted in your application.

## **Attachment 1**

### Summary Level Clinical Site Data for Data Integrity Review and Inspection Planning in NDA and BLA Submissions

#### **INTRODUCTION**

The purpose of this pilot for electronic submission of a single new clinical site dataset is to facilitate the timely selection of appropriate clinical sites for FDA inspection as part of the application and/or supplement review process in support of the evaluation of data integrity.

#### **DESCRIPTION OF THE SUMMARY LEVEL CLINICAL SITE DATASET**

The summary level clinical site data are intended (1) to clearly identify individual clinical investigator sites within an application or supplement, (2) to specifically reference the studies to which those clinical sites are associated, and (3) to present the characteristics and outcomes of the study at the site level.

For each study used to support efficacy, data should be submitted by clinical site and treatment arm for the population used in the primary analysis to support efficacy. As a result, a single clinical site may contain multiple records depending on the number of studies and treatment arms supported by that clinical site.

The site-level efficacy results will be used to support site selection to facilitate the evaluation of the application. To this end, for each study used to support efficacy, the summary level clinical site dataset submission should include site-specific efficacy results by treatment arm and the submission of site-specific effect sizes.

The following paragraphs provide additional details on the format and structure of the efficacy related data elements.

#### **Site-Specific Efficacy Results**

For each study and investigator site, the variables associated with efficacy and their variable names are:

- Treatment Efficacy Result (TRTEFFR) – the efficacy result for each primary endpoint, by treatment arm (see below for a description of endpoint types and a discussion on how to report this result)
- Treatment Efficacy Result Standard Deviation (TRTEFFS) – the standard deviation of the efficacy result (treatEffR) for each primary endpoint, by treatment arm
- Site-specific Efficacy Effect Size (SITEEFFE) – the effect size should be the same representation as reported for the primary efficacy analysis

- Site-specific Efficacy Effect Size Standard Deviation (SITEEFFS) – the standard deviation of the site-specific efficacy effect size (SITEEFFE)
- Endpoint (endpoint) – a plain text label that describes the primary endpoint as described in the Define file data dictionary included with each application.
- Treatment Arm (ARM) – a plain text label for the treatment arm that is used in the Clinical Study Report.

In addition, for studies whose primary endpoint is a time-to-event endpoint, include the following data element:

- Censored Observations (CENSOR) –the number of censored observations for the given site and treatment.

If a study does not contain a time-to-event endpoint, record this data element as a missing value.

To accommodate the variety of endpoint types that can be used in analyses please reference the below endpoint type definitions when tabulating the site-specific efficacy result variable by treatment arm, “TRTEFFR.”

- Discrete Endpoints – endpoints consisting of efficacy observations that can take on a discrete number of values (e.g., binary, categorical). Summarize discrete endpoints by an event frequency (i.e., number of events), proportion of events, or similar method at the site for the given treatment.
- Continuous Endpoints – endpoints consisting of efficacy observations that can take on an infinite number of values. Summarize continuous endpoints by the mean of the observations at the site for the given treatment.
- Time-to-Event Endpoints – endpoints where the time to occurrence of an event is the primary efficacy measurement. Summarize time-to-event endpoints by two data elements: the number of events that occurred (TRTEFFR) and the number of censored observations (CENSOR).
- Other – if the primary efficacy endpoint cannot be summarized in terms of the previous guidelines, a single or multiple values with precisely defined variable interpretations should be submitted as part of the dataset.

In all cases, the endpoint description provided in the “endpoint” plain text label should be expressed clearly to interpret the value provided in the (TRTEFFR) variable.

The site efficacy effect size (SITEEFFE) should be summarized in terms of the primary efficacy analysis (e.g., difference of means, odds ratio) and should be defined identically for all records in the dataset regardless of treatment.

The Define file for the dataset is presented in Exhibit 1: *Table 1 Clinical Site Data Elements Summary Listing (DE)*. A sample data submission for the variables identified in Exhibit 1 is provided in Exhibit 2. The summary level clinical site data can be submitted in SAS transport file format (\*.xpt).

Exhibit 1: Table 1 Clinical Site Data Elements Summary Listing (DE)

Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
1	STUDY	Study Number	Char	String	Study or trial identification number.	ABC-123
2	STUDYTL	Study Title	Char	String	Title of the study as listed in the clinical study report (limit 200 characters)	Double blind, randomized placebo controlled clinical study on the influence of drug X on indication Y
3	DOMAIN	Domain Abbreviation	Char	String	Two-character identification for the domain most relevant to the observation. The Domain abbreviation is also used as a prefix for the variables to ensure uniqueness when datasets are merged.	DE
4	SPONNO	Sponsor Number	Num	Integer	Total number of sponsors throughout the study. If there was a change in the sponsor while the study was ongoing, enter an integer indicating the total number of sponsors. If there was no change in the sponsor while the study was ongoing, enter "1".	1
5	SPONNAME	Sponsor Name	Char	String	Full name of the sponsor organization conducting the study at the time of study completion, as defined in 21 CFR 312.3(a).	DrugCo, Inc.
6	IND	IND Number	Num	6 digit identifier	Investigational New Drug (IND) application number. If study not performed under IND, enter -1.	010010
7	UNDERIND	Under IND	Char	String	Value should equal "Y" if study at the site was conducted under an IND and "N" if study was not conducted under an IND (i.e., 21 CFR 312.120 studies).	Y
8	NDA	NDA Number	Num	6 digit identifier	FDA new drug application (NDA) number, if available/applicable. If not applicable, enter -1.	021212
9	BLA	BLA Number	Num	6 digit identifier	FDA identification number for biologics license application, if available/applicable. If not applicable, enter -1.	123456
10	SUPPNUM	Supplement Number	Num	Integer	Serial number for supplemental application, if applicable. If not applicable, enter -1.	4
11	SITEID	Site ID	Char	String	Investigator site identification number assigned by the sponsor.	50
12	ARM	Treatment Arm	Char	String	Plain text label for the treatment arm as referenced in the clinical study report (limit 200 characters).	Active (e.g., 25mg), Comparator drug product name (e.g., Drug x), or Placebo
13	ENROLL	Number of Subjects Enrolled	Num	Integer	Total number of subjects enrolled at a given site by treatment arm.	20
14	SCREEN	Number of Subjects Screened	Num	Integer	Total number of subjects screened at a given site.	100
15	DISCONT	Number of Subject Discontinuations	Num	Integer	Number of subjects discontinuing from the study after being enrolled at a site by treatment arm as defined in the clinical study report.	5

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Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
16	ENDPOINT	Endpoint	Char	String	Plain text label used to describe the primary endpoint as described in the Define file included with each application (limit 200 characters).	Average increase in blood pressure
17	ENDTYPE	Endpoint Type	Char	String	Variable type of the primary endpoint (i.e., continuous, discrete, time to event, or other).	Continuous
18	TRTEFFR	Treatment Efficacy Result	Num	Floating Point	Efficacy result for each primary endpoint by treatment arm at a given site.	0, 0.25, 1, 100
19	TRTEFFS	Treatment Efficacy Result Standard Deviation	Num	Floating Point	Standard deviation of the efficacy result (TRTEFFR) for each primary endpoint by treatment arm at a given site.	0.065
20	SITEEFFE	Site-Specific Efficacy Effect Size	Num	Floating Point	Site effect size with the same representation as reported for the primary efficacy analysis.	0, 0.25, 1, 100
21	SITEEFFS	Site-Specific Efficacy Effect Size Standard Deviation	Num	Floating Point	Standard deviation of the site-specific efficacy effect size (SITEEFFE).	0.065
22	CENSOR	Censored Observations	Num	Integer	Number of censored observations at a given site by treatment arm. If not applicable, enter -1.	5
23	NSAE	Number of Non-Serious Adverse Events	Num	Integer	Total number of non-serious adverse events at a given site by treatment arm. This value should include multiple events per subject and all event types (i.e., not limited to only those that are deemed related to study drug or treatment emergent events).	10
24	SAE	Number of Serious Adverse Events	Num	Integer	Total number of serious adverse events excluding deaths at a given site by treatment arm. This value should include multiple events per subject.	5
25	DEATH	Number of Deaths	Num	Integer	Total number of deaths at a given site by treatment arm.	1
26	PROTVIOL	Number of Protocol Violations	Num	Integer	Number of protocol violations at a given site by treatment arm as defined in the clinical study report. This value should include multiple violations per subject and all violation type (i.e., not limited to only significant deviations).	20
27	FINLMAX	Maximum Financial Disclosure Amount	Num	Floating Point	Maximum financial disclosure amount (\$USD) by any single investigator by site. Under the applicable regulations (21 CFR Parts 54, 312, 314, 320, 330, 601, 807, 812, 814, and 860), if unable to obtain the information required to the corresponding statements, enter -1.	20000.00
28	FINLDISC	Financial Disclosure Amount	Num	Floating Point	Total financial disclosure amount (\$USD) by site calculated as the sum of disclosures for the principal investigator and all sub-investigators to include all required parties. Under the applicable regulations (21 CFR Parts 54, 312, 314, 320, 330, 601, 807, 812, 814, and 860), if unable to obtain the information required to the corresponding statements, enter -1.	25000.00
29	LASTNAME	Investigator Last Name	Char	String	Last name of the investigator as it appears on the FDA 1572.	Doe

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Variable Index	Variable Name	Variable Label	Type	Controlled Terms or Format	Notes or Description	Sample Value
30	FRSTNAME	Investigator First Name	Char	String	First name of the investigator as it appears on the FDA 1572.	John
31	MINITIAL	Investigator Middle Initial	Char	String	Middle initial of the investigator, if any, as it appears on the FDA 1572.	M
32	PHONE	Investigator Phone Number	Char	String	Phone number of the primary investigator. Include country code for non-US numbers.	44-555-555-5555
33	FAX	Investigator Fax Number	Char	String	Fax number of the primary investigator. Include country code for non-US numbers.	44-555-555-5555
34	EMAIL	Investigator Email Address	Char	String	Email address of the primary investigator.	john.doe@mail.com
35	COUNTRY	Country	Char	ISO 3166-1-alpha-2	2 letter ISO 3166 country code in which the site is located.	US
36	STATE	State	Char	String	Unabbreviated state or province in which the site is located. If not applicable, enter NA.	Maryland
37	CITY	City	Char	String	Unabbreviated city, county, or village in which the site is located.	Silver Spring
38	POSTAL	Postal Code	Char	String	Postal code in which site is located. If not applicable, enter NA.	20850
39	STREET	Street Address	Char	String	Street address and office number at which the site is located.	1 Main St, Suite 100

The following is a fictional example of a data set for a placebo-controlled trial. Four international sites enrolled a total of 205 subjects who were randomized in a 1:1 ratio to active or placebo. The primary endpoint was the percent of responders. The site-specific efficacy effect size (SITEEFFE) is the difference between the active and the placebo treatment efficacy result. Note that since there were two treatment arms, each site contains 2 rows in the following example data set and a total of 8 rows for the entire data set.

Exhibit 2: Example for Clinical Site Data Elements Summary Listing (Table 1)

STUDY	STUDYTL	DOMAIN	SPONNO	SPONNAME	IND	UNDERIND	NDA	BLA	SUPPNUM	SITEID	ARM	ENROLL	SCREEN	DISCONT
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	001	Active	26	61	3
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	001	Placebo	25	61	4
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	002	Active	23	54	2
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	002	Placebo	25	54	4
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	003	Active	27	62	3
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	003	Placebo	26	62	5
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	004	Active	26	60	2
ABC-123	Double blind...	DE	1	DrugCo, Inc.	000001	Y	200001	-1	0	004	Placebo	27	60	1

ENDPOINT	ENDTYPE	TRTEFFR	TRTEFFS	SITEEFFE	SITEEFFS	CENSOR	NSAE	SAE	DEATH	PROTVIOL	FINLMAX	FINLDISC	LASTNAME	FRSTNAME
Percent Responders	Binary	0.48	0.0096	0.34	0.0198	-1	0	2	0	1	-1	-1	Doe	John
Percent Responders	Binary	0.14	0.0049	0.34	0.0198	-1	2	2	0	1	-1	-1	Doe	John
Percent Responders	Binary	0.48	0.0108	0.33	0.0204	-1	3	2	1	0	45000.00	45000.00	Washington	George
Percent Responders	Binary	0.14	0.0049	0.33	0.0204	-1	0	2	0	3	20000.00	45000.00	Washington	George
Percent Responders	Binary	0.54	0.0092	0.35	0.0210	-1	2	2	0	1	15000.00	25000.00	Jefferson	Thomas
Percent Responders	Binary	0.19	0.0059	0.35	0.0210	-1	3	6	0	0	22000.00	25000.00	Jefferson	Thomas
Percent Responders	Binary	0.46	0.0095	0.34	0.0161	-1	4	1	0	0	0.00	0.00	Lincoln	Abraham
Percent Responders	Binary	0.12	0.0038	0.34	0.0161	-1	1	2	0	1	0.00	0.00	Lincoln	Abraham

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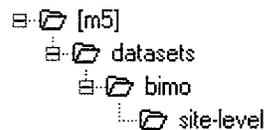
MINITIAL	PHONE	FAX	EMAIL	COUNTRY	STATE	CITY	POSTAL	STREET
M	555-123-4567	555-123-4560	John@mail.com	RU	Moscow	Moscow	103009	Kremlin Road 1
M	555-123-4567	555-123-4560	John@mail.com	RU	Moscow	Moscow	103009	Kremlin Road 1
	020-3456-7891	020-3456-7890	george@mail.com	GB	Westminster	London	SW1A 2	10 Downing St
	020-3456-7891	020-3456-7890	george@mail.com	GB	Westminster	London	SW1A 2	10 Downing St
	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FR	N/A	Paris	75002	1, Rue Road
	01-89-12-34-56	01-89-12-34-51	tom@mail.com	FR	N/A	Paris	75002	1, Rue Road
	555-987-6543	555-987-6540	abe@mail.com	US	Maryland	Rockville	20852	1 Rockville Pk.
	555-987-6543	555-987-6540	abe@mail.com	US	Maryland	Rockville	20852	1 Rockville Pk.

**Attachment 2**  
**Technical Instructions:**  
**Submitting Bioresearch Monitoring (BIMO) Clinical Data in eCTD**  
**Format**

A. Data submitted for OSI review belongs in Module 5 of the eCTD. For items I and II in the chart below, the files should be linked into the Study Tagging File (STF) for each study. Leaf titles for this data should be named “BIMO [list study ID, followed by brief description of file being submitted].” In addition, a BIMO STF should be constructed and placed in Module 5.3.5.4, Other Study reports and related information. The study ID for this STF should be “bimo.” Files for items I, II and III below should be linked into this BIMO STF, using file tags indicated below. The item III site-level dataset filename should be “clinsite.xpt.”

<b>DSI Pre-NDA Request Item<sup>1</sup></b>	<b>STF File Tag</b>	<b>Used For</b>	<b>Allowable File Formats</b>
I	data-listing-dataset	Data listings, by study	.pdf
I	annotated-crf	Sample annotated case report form, by study	.pdf
II	data-listing-dataset	Data listings, by study  (Line listings, by site)	.pdf
III	data-listing-dataset	Site-level datasets, across studies	.xpt
III	data-listing-data-definition	Define file	.pdf

B. In addition, within the directory structure, the item III site-level dataset should be placed in the M5 folder as follows:



<sup>1</sup> Please see the OSI Pre-NDA Request document for a full description of requested data files

- C. It is recommended, but not required, that a Reviewer's Guide in PDF format be included. If this Guide is included, it should be included in the BIMO STF. The leaf title should be "BIMO Reviewer Guide." The guide should contain a description of the BIMO elements being submitted with hyperlinks to those elements in Module 5.

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References:

eCTD Backbone Specification for Study Tagging Files v. 2.6.1  
(<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM163560.pdf>)

FDA eCTD web page  
(<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm>)

For general help with eCTD submissions: [ESUB@fda.hhs.gov](mailto:ESUB@fda.hhs.gov)

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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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ANDREA LEONARD SEGAL  
10/06/2011



PIND 74,288

**MEETING MINUTES**

Schering-Plough Healthcare Products  
Attention: Nancy Pierro, Associate Director  
Regulatory Affairs  
56 Livingston Avenue  
Roseland, NJ 07068

Dear Ms. Pierro:

Please refer to your Pre-Investigational New Drug Application (PIND) file for Oxytrol (3.9 mg/day, oxybutynin transdermal system).

We also refer to the meeting between representatives of your firm and the FDA on October 13, 2009. The purpose of the meeting was to discuss the study designs and additional studies in order to switch Oxytrol to over-the-counter for use by women to treat overactive bladder (OAB).

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

If you have any questions, call Mary Lewis, Regulatory Project Manager at (301) 796-0941.

Sincerely,

*{See appended electronic signature page}*

Andrea Leonard Segal, M.D.  
Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

**MEMORANDUM OF MEETING MINUTES**

**MEETING DATE:** October 13, 2009

**TIME:** 2:30 – 3:30 p.m. EST

**LOCATION:** FDA  
10903 New Hampshire Avenue  
Silver Spring, MD 20903

**APPLICATION:** PIND 74,288

**DRUG NAME:** Oxytrol (3.9 mg/day, oxybutynin) transdermal system

**TYPE OF MEETING:** B

**MEETING CHAIR:** Andrea Leonard-Segal, M.D.  
Director, Division of Nonprescription Clinical Evaluation

**MEETING RECORDER:** Mary M. Lewis  
Regulatory Project Manager

**FDA ATTENDEES:**

**Division of Nonprescription Clinical Evaluation**

Andrea Leonard-Segal, M.D., Director  
Joel Schiffenbauer, M.D., Deputy Director  
Melissa Hancock Furness, Chief, Project Management Staff  
Lesley Furlong, M.D., Medical Team Leader  
Linda Hu, M.D., Medical Officer  
Murewa Oguntimein, M.H.S., C.H.E.S.  
Wafa Harrouk, Ph.D., Pharmacology-Toxicology Reviewer  
Mary M. Lewis, R.N., Regulatory Project Manager

**Division of Nonprescription Regulation Development:**

Colleen K. Rogers, Ph.D., Interdisciplinary Scientist Team Leader  
Maria Ysern, MSc., Interdisciplinary Scientist Reviewer

**Office of Reproductive and Urologic Products**

Suresh Kaul, M.D., MPH, Medical Team Leader  
Christine P. Nguyen, M.D., Medical Officer

**Pediatric and Maternal Health Staff**

Karen Feibus, M.D., Medical Team Leader  
Leyla Sahin, M.D., Medical Officer

**Division of Biostatistics III**

Xin Fang, Ph.D., Statistician

**Schering-Plough HealthCare Products**

Stephanie Barba, Vice President, Regulatory Affairs  
Kristie Egstrand, Director, New Ventures  
Nancy Miller-Rich, Group Vice President, New Ventures  
Stephen Neumann, Vice President, Marketing Services  
John O'Mullane, Ph.D., Group Vice President, R&D  
Nancy Pierro, Associate Director, Regulatory Affairs  
Paul Starkey, M.D., Head, Medical Affairs  
Gretchen Trout, Director, Regulatory Policy  
Roger Dmochowski, M.D., Professor, Department of Urology

**Watson Laboratories, Inc.**

Naomi V. Dahl, PharmD, Director, Clinical Affairs  
Gary Hoel, R.Ph, Ph.D., Executive Director, Clinical Research  
Kevin Barber, PhD., RAC, PMP, Executive Director, Proprietary Regulatory Affairs

**1.0 BACKGROUND:**

Schering-Plough HealthCare Products (SPHCP) submitted a meeting request to the FDA on July 7, 2009 to discuss the study designs and additional studies that will be needed to support a switch from prescription to over-the-counter (OTC) status for Oxytrol (oxybutynin) transdermal system, 3.9 mg/day, for use by women to treat overactive bladder (OAB).

Previously, SPHCP met with the FDA on April 16, 2007 requesting guidance on their proposed development plan to support this switch.

According to the February 2, 2007 submission, SPHCP is working collaboratively with Watson Pharmaceuticals, the current sponsor of the prescription NDA 21-351. Included in the submission from SPHCP was correspondence dated January 10, 2007, from Watson Pharmaceuticals granting full right of reference for their NDA 21-351 to SPHCP.

**2.0 MEETING OBJECTIVES:**

The purpose of the meeting is for SPHCP to receive feed back from the FDA on their proposed program to support an Rx-to-OTC switch for Oxytrol.

### **3.0 DISCUSSION:**

Preliminary responses to the questions enclosed in September 10, 2009 meeting package were sent to SPHCP via email transmittal on October 9, 2009.

Following introductions and a brief discussion of the purpose of the meeting, the meeting agenda consisted of further discussion based on the preliminary responses from the FDA. The questions from SPHCP appear below followed by the preliminary FDA responses in italics. A summary of the discussion during the meeting follows each question. For questions where no additional discussion is noted, neither SPHCP nor FDA raised any additional issues pertaining to these questions at the meeting.

### **3.1 QUESTIONS AND FDA PRELIMINARY RESPONSES:**

#### Preamble

*We recommend that you consider including a urine dipstick in the Oxytrol package that measures glucose, white blood cells, and blood in order to enable consumers who may have undiagnosed diabetes, urinary tract infections, and hematuria to obtain the information needed to correctly select not to use Oxytrol.*

*If you choose to co-package a urine dipstick, you should develop a package insert and revise the Drug Facts label to include instructions for when and how to use the dipstick. You should also conduct a study to demonstrate that consumers can follow all the steps required to use the dipstick and interpret the results correctly according to the label instructions, after which they can make a self-selection decision. An evaluation of self-selection could use sample dipsticks with positive and negative results to test whether the participants make the appropriate self-selection decision.*

*It is very likely that, after you submit the NDA, input from an advisory committee will be sought as this will be a new over-the-counter (OTC) indication and a first in-class switch.*

#### Additional Discussion

SPHCP brought up several concerns regarding the use of the urine dipstick test by consumers, such as the proper administration and interpretation of such a diagnostic test and the background “noise” of microscopic hematuria (common in women) that may prompt unnecessary physician evaluations such as workups for bladder cancer. The sponsor asked whether data could be provided to obviate the need for a dipstick. The Agency stated that use of a dipstick was a suggestion to try to help consumers with self-selection and not a requirement. SPHCP also asked whether a point of purchase strategy might be useful; the Agency stated that this approach might place restrictions on OTC use and thus would generate additional regulatory issues.

#### Question 1a:

**In relation to the pregnancy warning, does the Agency agree that no further testing should be required of the codified Drug Facts warning required by CFR 201.63?**

FDA Preliminary response:

*Yes, we agree that no further testing is required of the codified Drug Facts warning required by CFR 201.63.*

**Additional Discussion:**

SPHCP asked for clarification as to whether the Agency would like to see further testing of the pregnancy warning. The Agency is interested in seeing pregnant women with urinary frequency not use the drug. It is SPHCP's challenge to accomplish this.

**Question 1b:**

**In relation to undiagnosed pregnancy we believe the proposed warning is adequate and that no additional testing of the labeling is necessary. Does the Agency agree?**

FDA Preliminary response:

*No, we do not agree. The enhanced warning should be tested in a targeted label comprehension study to ensure that women of childbearing age comprehend the undiagnosed pregnancy warning in your proposed label. It was concerning that a majority of pregnant women chose to use Oxytrol without first talking with a health care provider in your study.*

**Question 2a:**

**In relation to diabetes, does the Agency agree that the proposed targeted label comprehension study will be sufficient to demonstrate that the labeling adequately addresses the Agency's concern regarding delayed diagnosis of potential new cases of diabetes?**

FDA Preliminary response:

*No, we do not agree. A self-selection study enriched with a cohort of women at risk for diabetes would be a more appropriate study to demonstrate that prospective users with undiagnosed diabetes would correctly select not to use this product based on the information in the label. This study may require a large sample size. If you choose to co-package a urine dipstick and test self-selection as described under the preamble, you will not need to test a cohort of undiagnosed diabetics.*

**Additional Discussion:**

SPHCP asked about a targeted self-selection study for women at risk for diabetes. The Agency stated that data are needed to show that an undiagnosed diabetic would not select to use the product. It would not be necessary to do a self-selection study targeted to diabetics if SPHCP decides to use the dipstick. Dr. Dmochowski stated that from a practicing urologist's perspective, he has not seen any undiagnosed diabetics referred to him for mistaken OAB in the past 8 years in his practice. Also, diabetics with polyuria and urgency are rarely seen in clinic. However, he admitted that the majority of his patients are referred by another physician, so his population may not accurately reflect the OTC consumer population of self-selectors. The sponsor commented that recruitment of women at risk for diabetes would be challenging.

**Question 2b:**

**Does the Agency agree with the proposed design of the targeted label comprehension study?**

*FDA Preliminary response:*

*No, we do not agree. Obese women and women with a family history of diabetes should not be the only participants included in the study. Because any woman who is interested in purchasing this product should understand this important communication element, a cohort of women of the general population should also be included. We recommend that you send a revised protocol for our review and comments before proceeding with the study.*

**Question 3a:**

**In relation to urinary tract infection does the Agency agree that the proposed targeted self-selection/self diagnosis study will be sufficient to demonstrate that the labeling adequately addresses the Agency's concern regarding delayed diagnosis of potential new UTI cases?**

*FDA Preliminary response:*

*No, we do not agree. We are concerned that some consumers, especially elderly women who are a likely target population of Oxytrol, may experience urinary tract infection with symptoms that may be limited to urinary frequency/urgency without pain or hematuria. We strongly recommend that you send the screening materials and the full protocol for our review and comment before proceeding with the study.*

**Question 3b:**

**Does the Agency agree with the proposed design of the targeted self-selection study among women suffering from urinary symptoms other than OAB (e.g. pain, burning, blood, back/side pain, cloudy or foul-smelling urine)?**

*FDA Preliminary response:*

*No, we do not agree. The threshold for success for the primary objective should be high enough to ensure that consumers are able to make the appropriate self-selection decision based on the label. Please note that individuals should be excluded who have participated in any market research study, product label study, or clinical trial in the past 12 months, not 3 months.*

*It is unclear how the investigator will make an independent decision on the subject's product selection. You will need to describe fully how this decision will be made. A medical history, urinalysis, and pregnancy test (if applicable) should be obtained at least from those participants who self-select to use the product.*

*Only the PDP and Drug Facts label of Oxytrol should be presented to the subject. Since AZO standard and Cystex are indicated to treat urinary tract infection (UTI), presenting these products to subjects may bias the study.*

*If you choose to co-package a urine dipstick and test self-selection as described under the preamble, this targeted self-selection study may not be necessary.*

*We strongly recommend that you send the screening materials and the full protocol for our review and comment before proceeding with the study.*

**Additional Discussion:**

SPHCP proposed a 90% target threshold for success for the primary objective. The Agency responded that they were not prepared to address specific target thresholds during this meeting.

The Agency clarified that the purpose of the pregnancy test is to verify that pregnant consumers accurately self-select.

The Agency also commented that woman in assisted living facilities would not be an appropriate target population.

**Question 4:**

**Does the Agency agree that the proposed labeling addresses the concern regarding consumers with bladder cancer using Oxytrol and delaying diagnosis of bladder cancer?**

**FDA Preliminary response:**

*This is a review issue as bladder cancer, particularly bladder carcinoma in situ, may only present with urgency, frequency, and microscopic hematuria. There are no data to indicate whether anticholinergic treatment would alleviate these symptoms, which may contribute to delay in diagnosis of bladder cancer. A co-packaged urine dipstick may help to detect microscopic hematuria.*

**Question 5a:**

**Does the Agency agree with the proposed design of the targeted self-selection study among males?**

**FDA Preliminary response:**

*No, we do not agree. Placing the Oxytrol package on the shelf with other feminine hygiene products biases the study because males in study will be clued into the fact that this product is for women based on its location on the feminine hygiene shelf. In addition, this does not simulate the OTC setting because the shelf placement of the product may vary from store to store. Therefore you should not incorporate a simulated store shelf placement scenario that may bias the results of the study.*

**Additional Discussion:**

The sponsor stated that the proposed shelf placement of Oxytrol with feminine hygiene products for the self-selection study was based on feedback from retailers. The Agency asked SPHCP to provide the retailer data for review the data and comment. The Agency commented that the sponsor could compare one study arm where the product is placed with other feminine products with an oxytrol only arm in their self-selection study to determine if product placement impacts correct self-selection.

**Question 5b:**

**Does the Agency agree that the proposed targeted self-selection study will be sufficient to demonstrate that men will not purchase Oxytrol for their own use?**

*FDA Preliminary response:*

*No. We do not agree.*

*You have only provided a brief protocol summary so we cannot say much about your intended study. We strongly recommend that you send the full protocol for our review and comment before proceeding with the study. Ultimately, what a study demonstrates can only be known after the data are collected and reviewed.*

**Question 6:**

**Does the Agency agree that SPHCP's proposed development plan, if supported by the study results, is sufficient to support the OTC switch application for Oxytrol?**

*FDA Preliminary response:*

*No, we do not agree. An actual use study is needed for your proposed OTC product, because its use and indication differ significantly from those of existing OTC products. We note that you referenced the MATRIX study as a predictor of actual use in the OTC setting. Some reasons why this study can not be used as an actual use study follow:*

- *The prescription label and not the proposed to-be-marketed OTC label was used in the study.*
- *Patient educational materials were used in the study. Proposed educational materials for the OTC product have not been submitted.*
- *The investigator applied the first patch on the participant.*
- *The participants were allowed to ask questions.*
- *A self-selection component was not included in the study.*
- *The exclusion criteria were too restrictive. For example,*
  - *Patients for whom Oxytrol is contraindicated (patients with or at risk for urinary retention or controlled narrow angle glaucoma).*
  - *Patients with demonstrated hypersensitivity to oxybutynin or other components of the product.*
  - *Patients with other treatable causes of urinary incontinence (UTI, prostatitis, bladder tumor, bladder stone, prostate cancer)*
  - *Patients judged by the investigator to be unsuitable for enrollment into the study. It is unclear what this exclusion means.*
- *Subjects on prior therapy but not currently being treated or subjects currently receiving treatment for OAB who were not satisfied with their current therapy or wish to try a different mode of therapy were all included in the study.*
- *Women of childbearing potential were required to use contraception and have a pregnancy test to rule out pregnancy prior to use of drug.*

*The following concerns need to be addressed:*

1. *The risk that a prospective user with only OAB-like symptoms may have undiagnosed urinary tract infection, diabetes, or pregnancy. Treating misclassified patients may delay important diagnoses or, in the best circumstance, unnecessarily expose users to significant risks of anticholinergic therapy, such as urinary retention and cognitive/CNS adverse effects.*
2. *Pregnant women seeking medical advice prior to using Oxytrol.*
3. *Ensuring that men would not use Oxytrol even if they understand that Oxytrol is for women only. In the self-selection/self-diagnosis study, 15% of men who incorrectly self-selected chose to use Oxytrol despite comprehending that Oxytrol is not for men.*
4. *Ensuring that the product is not used by consumers who have narrow-angle glaucoma.*
5. *Longitudinal safety information on users who do not adequately respond to drug therapy. Medical follow-up of patients diagnosed with conditions of exclusion, such as OAB, is important and is an integral component of safe patient care. Furthermore, the results from the label comprehension study on the "Stop and ask a doctor" section showed that a significant proportion of subjects did not understand that they should stop drug use and seek medical help should their condition fail to improve (lower bound of correct responses were in the 50% range) or worsen (lower bound of correct responses in the 70% range).*

**Additional Discussion:**

SPHCP clarified that only half the patients in the study received educational materials.

SPHCP clarified that there was a mistake in the briefing book in that the investigator did not apply the first patch.

The FDA stated that the MATRIX study would not suffice as an actual use study since it examined a restricted population; however, it could provide supportive safety data. An actual use study would provide an opportunity to obtain safety data in a simulated real world setting. The actual use study should include 'all comers' as well as enrich for populations of concern.

SPHCP asked how long a duration FDA recommends for an actual use study. The Agency was not prepared to answer that at the meeting and advised the sponsor to submit a proposal with rationale for review and comment.

**Question 7:**

**Does the Agency agree, based on the medical rationale provided, that improvements in irritative voiding symptoms are unlikely to mask serious underlying conditions?**

**FDA Preliminary Response:**

*We agree that pain, burning, and hematuria are not likely to be relieved with Oxytrol. Whether Oxytrol will mask serious underlying conditions will be a review issue. Symptoms of bladder cancer may be similar to that of overactive bladder with hematuria that might not be apparent to a consumer (for example, microscopic hematuria).*

**Question 8:**

**Does the Agency agree with the exclusion of a drug holiday in the Oxytrol labeling?**

FDA Preliminary response:

*Yes, we agree with the exclusion of a “drug holiday” in the Oxytrol labeling.*

**Question 9a:**

Does the Agency agree with SPHCP’s proposed carton labeling for the targeted label comprehension study and the two targeted self-selection studies?

FDA Preliminary response:

*At this time, we have the following comments on the Drug Facts label:*

*Under the “Use” heading:*

- *Change (b) (4) to “2 or more” of the following symptoms... in the second bulleted statement; “You may be suffering from overactive bladder if you have (b) (4) of the following symptoms....”*

*Under the “Warnings” heading: How do potential users have the insight that they may “have one of these conditions [pregnancy, diabetes, urinary tract infection, or a more serious condition]” prior to use?*

*Under the “Do not use” subheading:*

- *Narrow-angle glaucoma should be included.*

*Under the “Ask a doctor before use if you have” subheading:*

- *Include the phrase “Frequent urination with” to the first bulleted statement (that is, “frequent urination with excessive thirst, extreme hunger or increased tiredness”)*
- *Narrow-angle glaucoma should be moved to “Do not use” section.*

*Under the “Stop use and ask a doctor” subheading:*

- *Include text that describes urinary retention in consumer-friendly language.*

*The prescription label has the following information that needs to be addressed in the proposed OTC label:*

- *Put the patch on a clean, dry and smooth area of skin on your abdomen, hips or buttocks. The areas you choose should not be oily, damaged (cut, or scraped), irritated (rashes) or have any other skin problems. Do not put Oxytrol on areas that have been treated with oils, lotions or powders that could keep the patch from sticking well to your skin.*

*As stated in the May 15, 2007 meeting minutes, the prescription label has the following precautions that need to be addressed in the proposed OTC label:*

- *Common side effects include dizziness, dry mouth, and constipation.*

- *The proposed Drug Facts label should be in compliance with 21 CFR 201.66 (c) and (d).*

*If you choose to co-package a urine dipstick, you will also need to develop a package insert and to revise the Drug Facts label. The package insert could include information on how to use the dipstick and instructions on when and how to read the results. Additional information on the symptoms of pregnancy can also be included in the insert.*

*The above labeling recommendations are preliminary review of the Drug Facts content only for your targeted label comprehension study and your targeted self-selection studies. Further changes may be necessary based on our review.*

**Additional Discussion:**

SPHCP stated the anticholinergic side effects are low for this product. SPHCP proposed to add dizziness as a labeled adverse effect, but not to add dry mouth and constipation as these occur at a low rate. The Agency asked that SPHCP submit a justification for this proposal.

**Question 9b:**

**Does the Agency agree with SPHCP's draft pouch labeling?**

FDA Preliminary response:

*We recommend that you also include the highlighted section of the warnings on the pouch label. Final agreement on labeling is a review issue.*

**Question 10:**

**Does the Agency agree that it is appropriate for this product to receive a pediatric waiver?**

FDA Preliminary Response

*This product does not appear to trigger Pediatric Research Equity Act (PREA) (21 U.S.C. 355c) because you are not proposing a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. However, please note that this could change if you alter your drug development program to include a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration.*

**ADDITIONAL COMMENTS:**

Completed Self-Selection Study:

- *The Self-Selection question (Do you believe this product is appropriate for you to treat your symptoms of frequent urination, strong need to urinate right away or inability to control the urge to urinate? ) is a leading question that may potentially bias the study.*
- *It is unclear how the self-selection decisions for the subjects in Cohort 3 (referred to as Special Pop) were verified. There are two contradictory statements in the meeting background package; in the study summary section of the background package it states "Special pop subjects made a self-selection decision only, and did not undergo medical or pelvic examination or make a self-diagnosis decision," and in the description of the*

*self-selection decision section it states “For the remaining sub-population for Special Pop, those with glaucoma and those who were pregnant/nursing, the lower results were due to a difference in the physician’s selection decision (not recommended for use) based on their additional insight from the medical history, medication history, laboratory results and physical (including pelvic) exam results.”*

**Additional Discussion:**

SPHCP stated that there was 90% or greater adhesion based on visual patch adhesion data from clinical studies. SPHCP will submit these data for review.

**4.0 DECISIONS (AGREEMENTS) REACHED:**

- The sponsor proposes to add ‘dizziness’ to the common side effects on the label and will provide a rationale for not including other anticholinergic effects.
- An actual use study, enriched with groups of concern, is recommended.
- The urine dipstick advice is a suggestion as a path forward, not a requirement.
- Protocols should be submitted to FDA for review and comment prior to initiating the studies.

**5.0 UNRESOLVED ISSUES OR ISSUES REQUIRING FURTHER DISCUSSION:**

- Use of a dipstick packaged in a starter kit or in each unit of sale. How this issue is resolved has further implications as to what additional targeted self-selection studies may be needed.

**6.0 ACTION ITEMS:**

- SPHCP will submit data to support their proposed shelf placement proposal for the self-selection study among males in a naturalistic setting (placing the Oxytrol label with other feminine products).
- SPHCP will submit data to support not labeling for some anticholinergic symptoms.
- SPHCP will submit patch adhesion data.
- SPHCP will submit consumer study protocols for review and comment prior to initiating the studies.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
IND-74288	GI-1	SCHERING PLOUGH	OXYTROL(OXYBUTYNIN TRANSDERMAL SYSTEM 3.

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/s/

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ANDREA LEONARD SEGAL  
11/09/2009