NDA	202-211 (000)	
Applicant:	MSD Consumer Care, Inc.	
Trademark:	Oxytrol for Women	
Stamp Date	te March 26, 2012	
Established Name:	e: Oxybutynin Transdermal System	
Dosage Form:	Transdermal; 3.9 mg/day	
Route of Administration:	Topical	
Indication:	Relief of symptoms of over-active bladder	
	in adult women	
Reviewer Tapash Ghosh, Ph.D.		

ONDQA (Biopharmaceutics) Review

OVERALL ASSESSMENT:

As there is no change in formulation and the Applicant has appropriately bridged the batches manufactured by slightly modified equipments, the Applicant's proposal to use the approved *in-vitro* drug release acceptance criteria using the previously approved and validated analytical methodologies is acceptable.

RECOMMENDATION

From the Biopharmaceutics view point NDA 202- 211 (000) for Oxytrol for Women (Oxybutynin transdermal system 3.9 mg/day) is recommended for approval.

Tapash K. Ghosh, Ph. D. Primary Biopharmaceutics Reviewer Office of New Drug Quality Assessment

Angelica Dorantes, Ph. D. Biopharmaceutics Team Leader Office of New Drug Quality Assessment

BIOPHARMACEUTICS ASSESSMENT

Summary:

This is an e-CTD NDA application for oxybutynin transdermal system (oxybutynin 36 mg patch delivers 3.9 mg/day). The CMC and Biopharmaceutics information of this NDA is based on prescription Oxytrol NDA 21-351 commercialized by Watson Pharmaceuticals Inc. The manufacturing operations are the same for both NDAs regarding manufacturing site (Watson Laboratories Inc.), batch size, raw materials, manufacturing process and equipments with the exception of an additional ^{(b) (4)} and a child resistant pouch stock. Due to the similarity

in the CMC information for the proposed non prescription Oxytrol to the original prescription Oxytrol under NDA 21-351, the submission cross refers or duplicate most of the CMC information from the approved NDA 21-351.

This Biopharmaceutics review evaluates only the proposed *in-vitro* drug release method and acceptance criteria. The *in vitro* drug release profile comparison and f2 data demonstrate that the changes in the manufacturing equipments have no impact on the bioavailability of the drug product.

Proposed In-vitro Drug Release Method and Acceptance Criteria:

The *in-vitro* drug release methodology and acceptance criteria proposed for nonprescription Oxytrol for Women remain the same as those approved for the original prescription Oxytrol under NDA 21-351 as shown below:

Drug Release Method :

Equipment: USP Paddle Over Disk – USP Apparatus 5

3.1	Dissolution System Operating Conditions		
	PADDLE POSITION:	25 ± 2 mm above the TDS surface	
	VESSEL TEMPERATURE:	32 ± 0.5°C	
	PADDLE SPEED:	50 ± 1 rpm	
	DISSOLUTION SOLUTION:	900 mL	

Analytical Method:

3.2.P.5.2.8.5.3	IPLC Analysis Method
HPLC Conditions	
COLUMN:	Agilent Xorbax Bonus-RP (3.5 μm, 4.6 mm x 75 mm) with MacMod Column Saver pre-column filter
COLUMN TEMPERATURE:	30°C
MOBILE PHASE:	ACN: 10mM phosphate buffer pH 8.0 isocratic (60: 40,
	v/v)
MOBILE PHASE FLOW RATE	E: 1.4 mL/min
SAMPLE INJECTION VOLUM	IE: 50 microliters
DETECTOR WAVELENGTH:	240 nanometers
RUN TIME:	Adequate runtime is approximately 4 minutes

Proposed Drug Release Criteria:

Level	Number Tested	Criteria	
L1	6	No individual values lie outside the stated range	
L2	6	The average value of the 12 units (L1+L2) lies within the stated range. No individual value is outside stated range by more than 10% of the average of the stated range.	
L3	12	The average value of the 24 units (L1+L2+L3) lies within the stated range. Not more than 2 of the 24 units are outside the stated range by more than 10% of the average for the stated range; and none of the units is outside the stated range by more than 20% of the average of the stated range.	

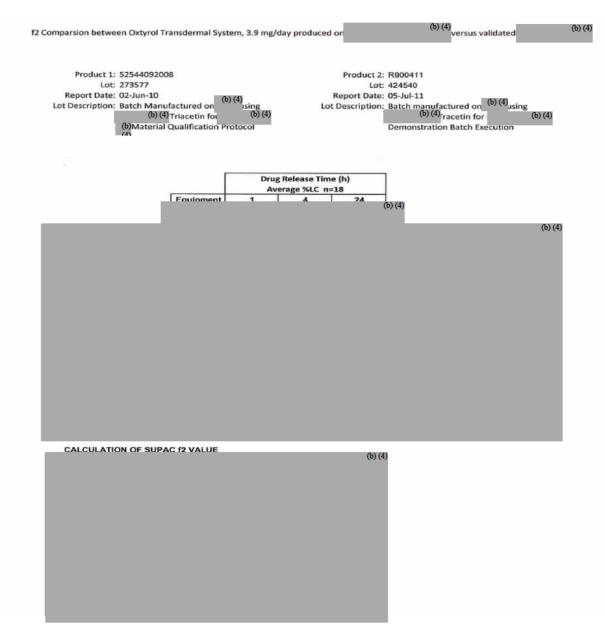
Test Method	TM-	TM-1006		
Test	Release Specification	Shelf-Life Specification		
Drug Release 1 Hours	Conforms to USP <724>	Conforms to USP <724>		
4 Hours 24 Hours	Label Claim _abel Claim	Label Claim (ه) ⁽⁴⁾ Label Claim		

Reviewer's Comment:

The Applicant's proposal to use the approved in-vitro drug release acceptance criteria using the previously approved and validated analytical methodologies is acceptable.

In-Vitro Dissolution Comparison to support Manufacturing Equipment Change

In order to demonstrate that the change in manufacturing equipment will have no impact on the bioavailability of the drug product, an *in-vitro* drug release profile comparison study was performed. The drug release of a batch produced using currently approved (b) (4) was compared to a batch produced using An f2 value between 50 and 100 demonstrates that two dissolution profiles are similar. The *in vitro* dissolution profile comparison yielded an f2 value of 74.8. Therefore, the drug release profiles are considered similar (see below).



Reviewer's Comment:

The dissolution profile comparison and f2 data support the approval of the proposed manufacturing equipment changes.

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/s/

TAPASH K GHOSH 11/16/2012

ANGELICA DORANTES 11/16/2012