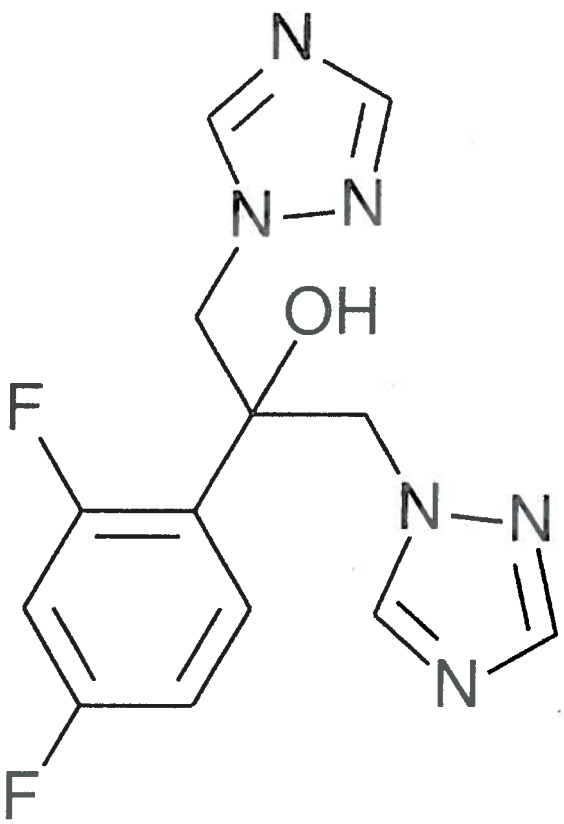
Stability Report

Fluconazole



$C_{13}H_{12}F_2N_6O$

Materials

Flavors		Lot#	Expiration
Bubblegum		W158177	7/2019
OrangeCream		W292126	11/2019
Banana		W237067	9/2019
Apple		R0927	9/2019
FLAVORx, INC			
9475 Gerwig Lane, Columbia, MD 21046			
Standards	**Part #**	**Lot #**	
Fluconazole	F4682	2597499	
LKT Laboratories, Inc.			
545 Phalen Blvd.St. Paul, MN 55130			
Reagents	**Part #**	**Lot #**	
Acetonitrile	A955-4	126501	
Formic Acid	A117-50	116758	
Fisher Scientific			
Water	9152-2.5	2207714	
Ricca Chemical Company			
Pharmaceutical	**NDC #**	**Lot #**	**Expiration**
Fluconazole for Oral Suspension(40mg/mL)	16714-696-01	UF4012003-A	3/2014
Manufactured For:			
Northstar Rx LLC			
Memphis, TN 38141			
1-800-206-7821			
Manufactured By:			
Aurobindo Pharma Limited			
Hyderabad-500-072, India			

Results

Table 1: Average % Potency Relative to Bottle Value Sample

Sample	Average % Potency Relative to Bottle Value (40mg/mL) vs. Time after FLAVORx Flavor Addition (±95%)		
	Day 0	Day 7	Day 14
Control	100.42 (4.98)	110.97 (0.88)	113.78 (3.23)
Apple	101.01 (1.51)	101.43 (1.69)	106.84 (0.55)
Bubblegum	109.86 (1.03)	96.37 (1.52)	110.02 (4.99)
OrangeCream	107.57 (2.37)	105.40 (2.31)	111.94 (2.50)

Table 2: Average % Potency Relative to Control Sample

Sample	Average % Potency Relative to Control vs. Time after FLAVORx Flavor Addition (±95%)		
	Day 0	Day 7	Day 14
Control	-	-	-
Apple	100.80 (3.94)	91.40 (0.99)	93.97 (2.46)
Bubblegum	109.67 (4.72)	86.84 (0.69)	96.89(7.68)
OrangeCream	107.54 (7.67)	94.98 (1.94)	98.52 (4.86)

Table 3: Sample pH over 14 day period

Sample	pH On Day of Testing		
	Day 0	Day 7	Day 14
Control	4.12	4.06	4.08
Apple	4.13	4.08	4.10
Bubblegum	4.16	4.09	4.11
OrangeCream	4.13	4.09	4.11

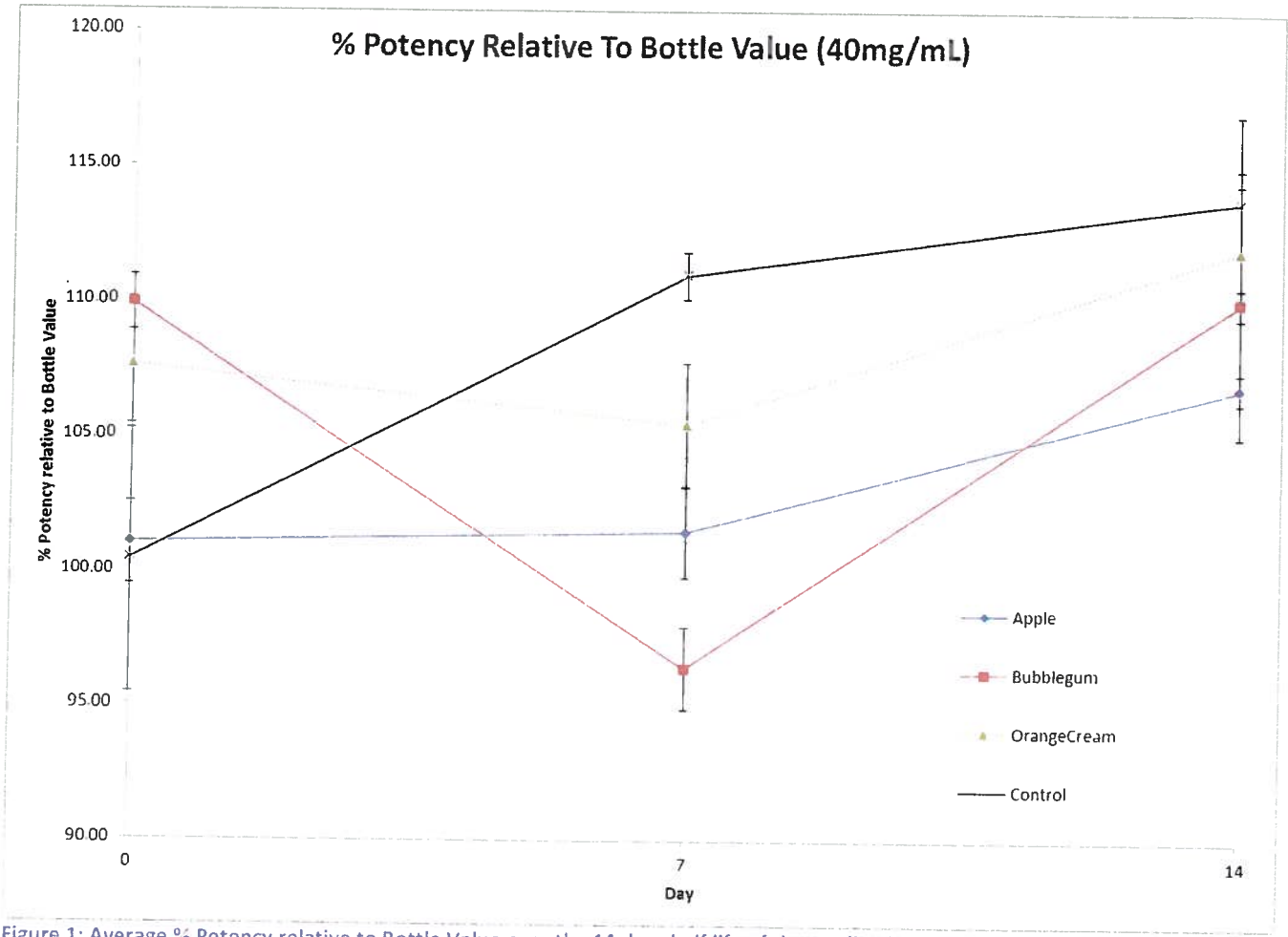


Figure 1: Average % Potency relative to Bottle Value over the 14 day shelf life of the medication. Lines do not represent a fit to an algorithm, they are presented for data clarity. Error bars represent ±95% confidence interval.

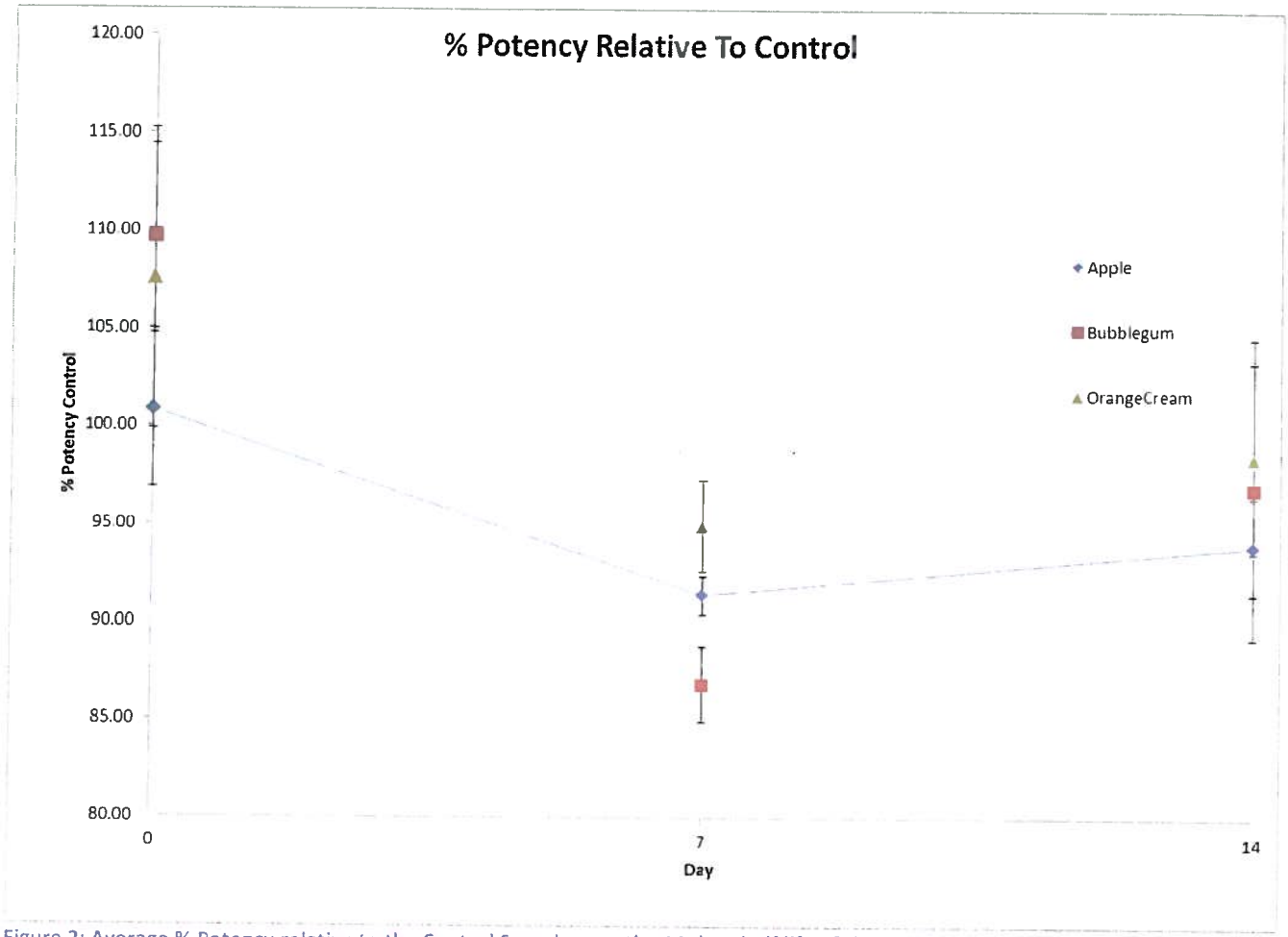


Figure 2: Average % Potency relative to the Control Sample over the 14 day shelf life of the medication. Lines do not represent a fit to an algorithm, they are presented for data clarity. Error bars represent ±95% confidence interval.

Physical Appearance/Observations

When reconstituted, the medication had a white, viscous appearance. When diluted in the sample preparation step prior to analysis each sample was cloudy. The smell and appearance of each sample was consistent over the two week trial.

Standards Preparation

The initial standard solution was prepared to approximately 1.0 $mg \cdot mL^{-1}$. The remaining standard solutions were prepared by serial dilution from this standard. Each solution was thoroughly mixed and visually inspected to ensure no standard remained un-dissolved. The concentration range included 1.0 $mg \cdot mL^{-1}$, 0.8 $mg \cdot mL^{-1}$, 0.6 $mg \cdot mL^{-1}$, 0.4 $mg \cdot mL^{-1}$ and 0.1 $mg \cdot mL^{-1}$. An aliquot of each standard was transferred to a 2mL glass sample vial to be used with the HPLC.

Sample Preparation

The Fluconazole for Oral Suspension was reconstituted as directed on the bottle. The reconstitution directions instruct that the medication be reconstituted with 24mL of water. The medication was then shaken to ensure proper mixing. From the medication bottle, 4 equal aliquots of medication were removed and placed into 4 separate containers. Three of the containers will contain the three flavor formulations to be tested. The fourth will contain no flavor and act as the control. The flavors were prepared according to the FLAVORx formulation, adjusted for the decreased sample size. To prepare the Apple flavor, 0.100mL of Apple was added to one container. To prepare the Bubblegum flavor, 0.100mL of Bubblegum, 0.050mL of Banana were added to the second container. To prepare the Orange Cream flavor, 0.100mL of Orange Cream was added to the third container. The final concentration of each solution was approximately 40 $mg \cdot mL^{-1}$ fluconazole.

To prepare the samples for analysis by HPLC each sample needed to be diluted. To prepare these dilutions, 0.300 mL of each sample was quantitatively transferred into a 25mL volumetric flask. The flask was then brought to volume using water. The final concentration was approximately .48 $mg \cdot mL^{-1}$. At this concentration fluconazole is completely soluble in water. After vigorous mixing the solutions still remained cloudy as a result of other excipients in the pharmaceutical formulation. A portion of the solution was removed and placed in a 2mL centrifuge tube. The tubes were centrifuged for 3 minutes at 12,400 rpm. The supernatant of each sample was transferred to a 2mL glass sample vial to be used with the HPLC.

The samples were stored at room temperature. On each day of testing the samples were thoroughly mixed followed by a pH measurement.

Blank Preparation

A blank sample was prepared with the water used in the dilutions.

Mobile Phase Composition:

The mobile phase consisted of water and acetonitrile each containing 0.1% formic acid.

Column:

Phenomenex Gemini-NX 5µm C18, 250x4.60mm
Part #: 00G-4454-E0
S/N: 612008-10

Guard Column:

Phenomenex SecurityGuard Cartridge System
Part #: KJO-4282
Cartridge: Gemini-NX C18 4x3.0mm
Part #: AJO-8368

Conclusion

The results of this testing showed no significant variation in potency or physical appearance between the control sample and the flavored samples. USP does not have a monograph for Fluconazole for Oral Suspension. However, other oral suspension monographs state that the formulation must contain between 90% and either 110%, 115% or 120% of the stated amount. The results above show that the formulation test with flavors stayed between 90% and 115% of the stated value over the course of the trial. Also, the physical appearance and pH of the flavored and control samples were consistent over the entire trial. Based on this analysis, Fluconazole for Oral Suspension from any manufacture that has the same formulation and concentration as the medication tested is appropriate to use with the flavors tested.

Tested By: _____ Date 2/19/2014
Greg Winter

Reviewed By: _____ Date 2/4/2014
William R. LaCourse, Ph.D.