



Scientific Study

B4518, HRT Cream Base
(Estradiol Study)

Not appropriate for regulatory submission.
Please visit www.SpectrumRx.com or
contact Tech Services for the most up-to-
date information contained in this
information package.

Spectrum Pharmacy Products

777 Jersey Avenue
New Brunswick, NJ 08901
Phone 732.214.1300

Estriol 1.0 % w/w

0.50g Estriol raw drug powder from Tecoland Chemical (bulk API, Lot # 20120524) was added to 49.50g Spectrum Chemical Mfg. Corp. HRT Botanical Cream and levigated with an electronic mortar and pestle, resulting in a final concentration of 1.0% w/w. The sample was then stored at room temperature in the same 50/70 mL Unguator container.

Analytical samples were prepared within 14 days of the scheduled pull by accurately weighing a 5.00 g of the Estriol 1% sample and transferring it to a 50.0 ml volumetric flask. The contents of the flask were diluted to volume with matrix matched mobile phase for HPLC determination.

The prepared samples were analyzed within 14 days of the scheduled pull. The specification for each pull point was no less than 90% and no more than 110% of the theoretical concentration of initial prepared sample. In this case no less than 0.90% w/w and no more than 1.10% w/w. Copies of chromatograms are attached showing no detectable co-elution, baseline interference, or degradation products.

Results were compared and samples were analyzed at various pull points as follows:

Estriol 1% w/w		Actual days	HRT Botanical Cream
Sample preparation	7/20/2012	0	N/A
Initial	8/1/2012	12	1.00%
120 day pull	11/21/2012	124	1.05%
150 day pull	12/14/2012	147	0.82%
180 day pull	1/16/2013	180	Not Tested

Summary:

Estriol 1.0% w/w in Spectrum Chemical Mfg. Corp. HRT Botanical Cream is within specifications at 120 days, but is out of specifications at 150 day pull. The 180 day pull was not tested.

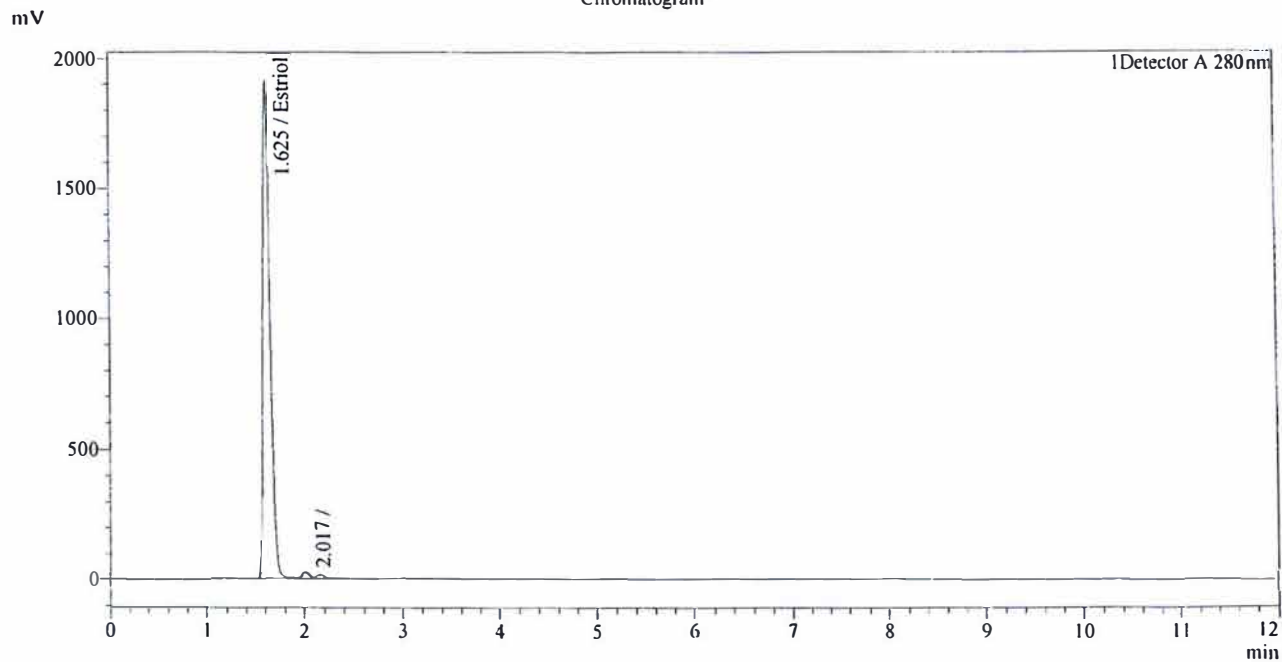
Attachments:

Copies of chromatographs of Estriol 1% in Spectrum Chemical Mfg. Corp. HRT Botanical Cream; Initial Standard, Initial Sample, 120-Day Standard, 120-Day Sample, 150-Day Standard, and 150-Day Sample.

Sample Information

Acquired by : System Administrator
 Sample Name :
 Sample ID : Estriol Std
 Tray# : 1
 Vial# : 1
 Injection Volume : 5
 Data File : August 1-12 Estriol 101.lcd
 Method File : Estriol.lcm
 Batch File : 8-1-12 Estriol.lcb
 Report Format File : DEFAULT.lsr
 Date Acquired : 8/1/2012 3:58:02 PM
 Date Processed : 8/1/2012 6:08:42 PM
 Sample Amount : 1
 Dilution Factor : 1

Chromatogram



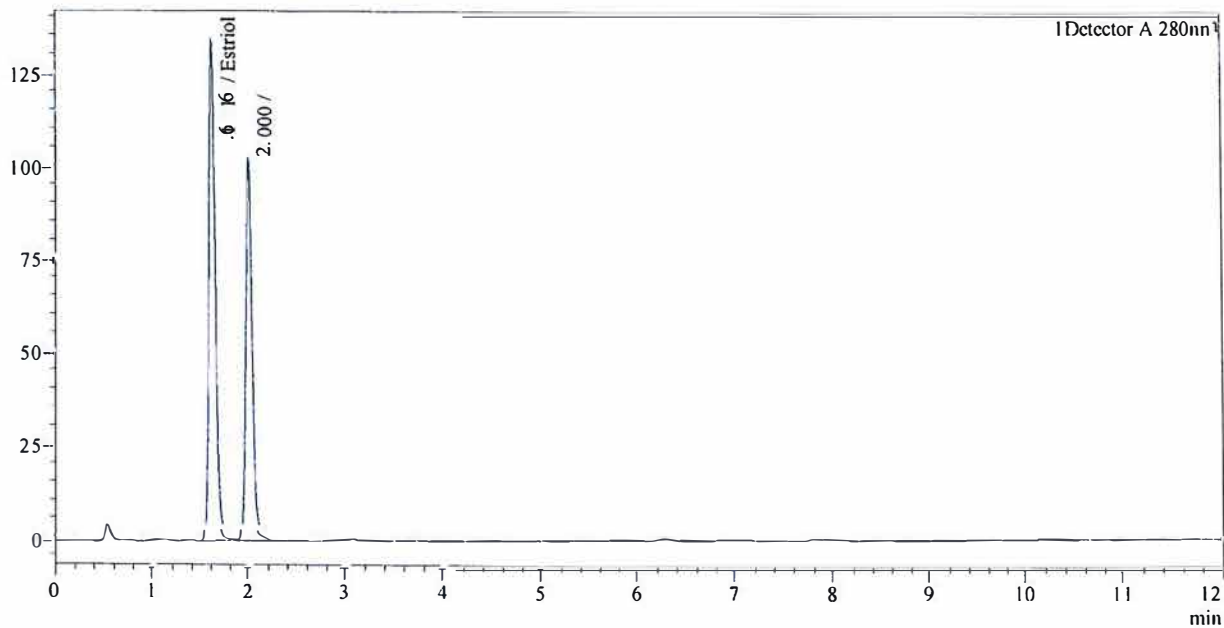
Detector A		QuantitativeResult					
ID#	Name	Ret. Time	Area	Tailing Factor	Conc.	Unit	
1	Estriol	1.625	9606967	1.239	8.172	mg/mL	
Total			9606967				

Sample Information

Acquired by System Administrator
 Sample Name 1% Estriol in HRT
 Sample ID Botanical Cream
 Tray# 1
 Vial# 3
 Injection Volume 5
 Data File August 1-12 Estriol 107.lcd
 Method File Estriol.lcm
 Batch File 8-1-12 Estriol.lcb
 Report Format File DEFAULT.lsr
 Date Acquired 8/1/2012 5:27:13 PM
 Date Processed 8/1/2012 6:08:52 PM 5.0855
 Sample Amount 10
 Dilution Factor

Chromatogram

mV



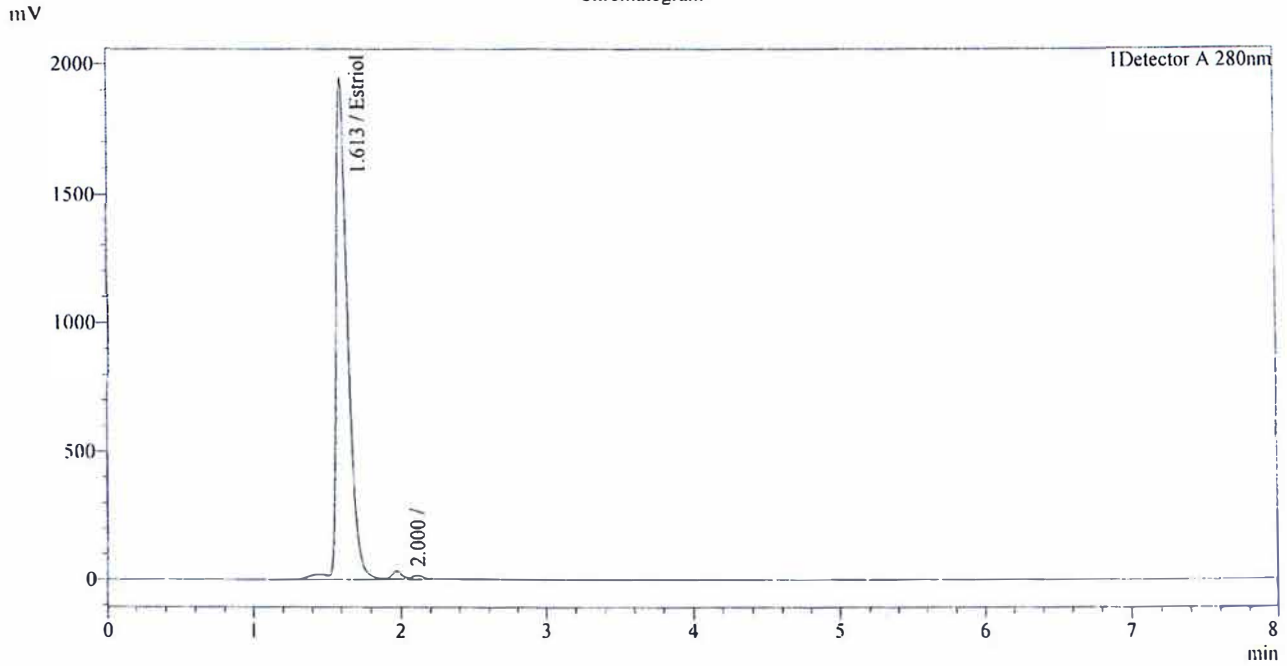
QuantitativeResult

Detector A ID#	Name	Ret. Time	Area	Tailing Factor	Conc.	Unit
1	Estriol	1.616	597707	1.188	0.999	mg/mL
Total			597707			

Sample Information

Acquired by : System Administrator
 Sample Name : Estriol Std
 Sample ID : 1
 Tray# : 1
 Vial# : 1
 Injection Volume : 5
 Data File : November 21-12 Estriol 101.lcd
 Method File : Estriol.lcm
 Batch File : 11-21-12 Estriol.lcb
 Report Format File : DEFAULT.lsr
 Date Acquired : 11/21/2012 9:31:22 AM
 Date Processed : 11/21/2012 10:58:17 AM
 Sample Amount : 1
 Dilution Factor : 1

Chromatogram



Detector A		QuantitativeResult				
ID#	Name	Ret. Time	Area	Tailing Factor	Conc.	Unit
1	Estriol	1.613	10541671	1.348	8.172	mg/mL
Total			10541671			

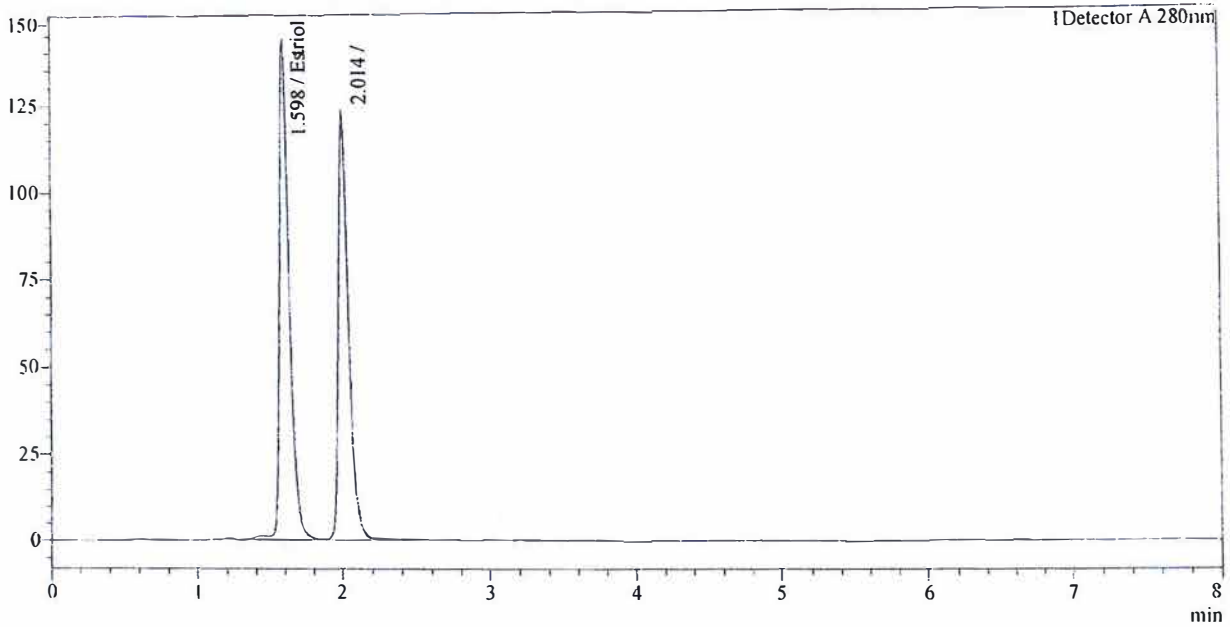
System Administrator

Sample Information

Acquired by : 1% Estriol in HRT
Sample Name : Botanical Cream
Sample ID :
Tray# : 1
Vial# : 3
Injection Volume : 5
Data File : November 21-12 Estriol 107.lcd
Method File : Estriol.lcm
Batch File : 11-21-12 Estriol.lcb
Report Format File : DEFAULT.lsr
Date Acquired : 11/21/2012 10:29:35 AM
Date Processed : 11/21/2012 10:58:26 AM
Sample Amount : 5.1207
Dilution Factor : 10

Chromatogram

mV



QuantitativeResult

Detector A

ID#

1 Estriol

Total

Name

Ret. Time

1.598

Area

693948

693948

Tailing Factor

1.398

Conc.

1.047

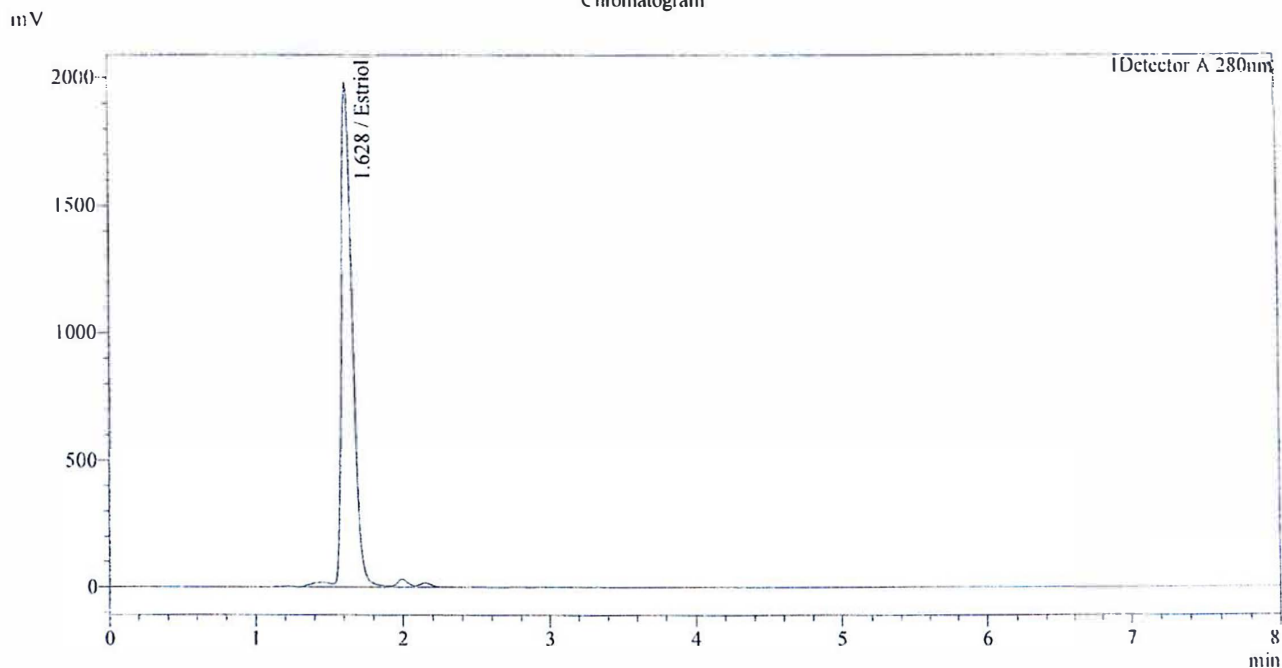
Unit

mg/mL

Sample Information

Acquired by : System Administrator
Sample Name : Estriol Std
Sample ID :
Tray# : 1
Vial# : 1
Injection Volume : 5
Data File : December 14-12 Estriol 101.lcd
Method File : Estriol.lcm
Batch File : 12-14-12 Estriol.lcb
Report Format File : DEFAULT.lsr
Date Acquired : 12/14/2012 8:46:34 AM
Date Processed : 12/14/2012 10:52:21 AM
Sample Amount : 1
Dilution Factor : 1

Chromatogram



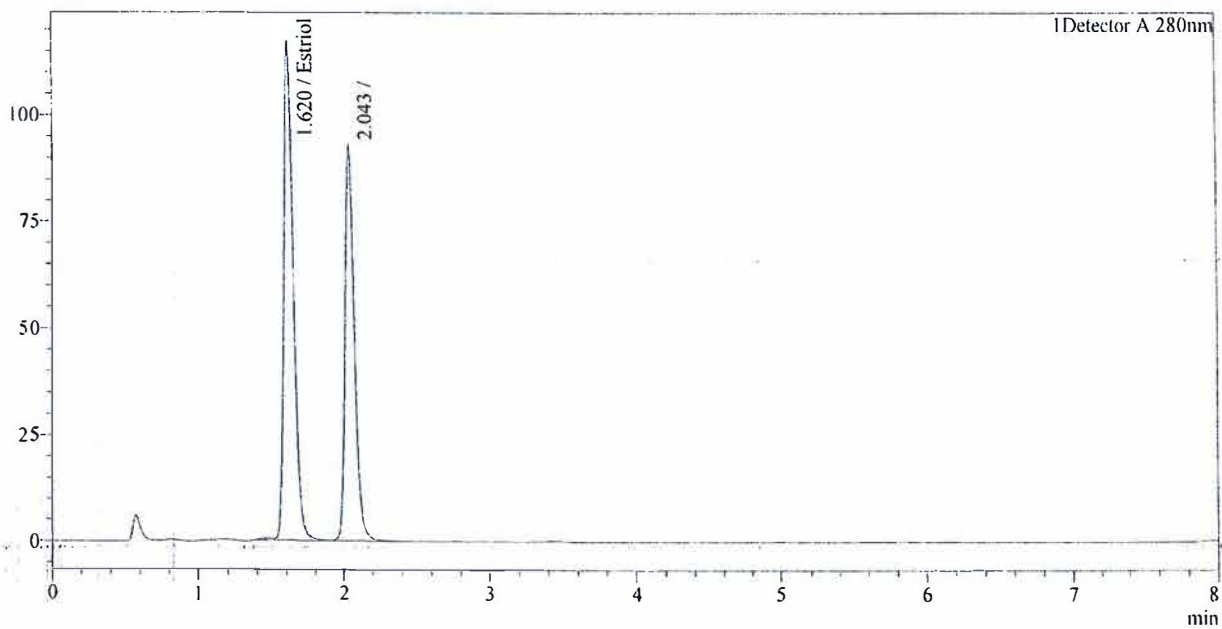
Detector A		QuantitativeResult				
ID#	Name	Ret. Time	Area	Tailing factor	Conc.	Unit
1	Estriol	1.628	10450333	1.274	8.172	mg/mL
Total			10450333			

Acquired by : System Administrator
Sample Name :
Sample ID : 1% Estriol in HRT Botanical
Tray# : Cream
Vial# : 1
Injection Volume : 3
Data File : 5
Method File : December 14-12 Estriol 107.lcd
Batch File : Estriol.lcm
Report Format File : 12-14-12 Estriol.lcb
Date Acquired : DEFAULT.Isr
Date Processed : 12/14/2012 10:25:43 AM
Sample Amount : 12/14/2012 10:52:31 AM 5.1999
Dilution Factor : 10

Sample Information

Chromatogram

mV



Detector A		QuantitativeResult				
ID#	Name	Ret. Time	Area	Tailing Factor	Conc.	Unit
1	Estriol	1.620	530198	1.208	0.820	mg/mL
Total			530198			