LABORATORY
NOTEBOOK

№ 1041

NOTEBOOK NO. R 1044
ISSUED TO John D'Arcuti
ON August 5 20 05
DEPARTMENT Product + Pcan Development
RETURNED November 29 20 07

LABORATORY NOTEBOOK ERROR CODES

CE CALCULATION ERROR
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INSTRUCTIONS

1. **The primary purpose of this notebook is to protect your and the Company's Patent-Rights by keeping records of all original work in a form acceptable as evidence if any legal conflict arises.**

2. • When starting a page, enter the title, project number, and book number.
   • Use ink for permanence -- avoid pencil.
   • Record your work as you progress, including any spur-of-the-moment ideas which may be developed later.
   • Avoid making notes on loose paper to be recopied.
   • Record your work in such a manner that a co-worker can continue from where you stop. You might be ill and to protect your priority it could be urgent that the work continue while you are absent.

3. • Give a complete account of your experiments and the results, both positive and negative, including your observations.
   • Record all diagrams, layouts, plans, procedures, new ideas, or anything pertinent to your work including the details of any discussions with suppliers, or other people outside the Company.
   • Do not try to erase any incorrect entries; draw lines deleting them, note the corrections, sign and date the changes. This extra care is worthwhile because of the necessity of original data to prove priority of new discoveries.

4. • After entering your data, sign and date the entries.
   • Explain your work to at least two witnesses who are not co-inventors, and have them sign and date the pages in the place provided.
   • Record the names of operators and witnesses present during any demonstration and have at least two witnesses sign the page. If no witnesses are present during an experiment of importance, repeat it in the presence of two witnesses.

5. Since computer programs can be patented these instructions apply to the development of computer software. In this case a description of the structure and operation of the program should be recorded in the notebook, together with a basic flow diagram which illustrates the essential features of the program. In the course of developing the code, the number of lines of code written each day should be recorded in the notebook, together with a statement of the portion of the flow diagram to which the section of code is directed.

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Form 590

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Project No. ——

Book No. ——

TITLE Ny-Tannic™ Tablets 03/20/06

NDC # 15686-100-01 / LOT # CRT011 / EXP. 10/07

From Page No. 82

Received Ny-Tannic™ tablets from B. Johns, same 100 count bottle as was logged in on 01/24/06, and was asked to retain 50 tablets in an HDPE bottle and return the bottle.

There was a total of 76 tablets in the bottle at this time ∴ B. Johns received the Ny-Tannic™ commercial bottle back from me with only 26 tablets.

The 50 tablet sample was placed with our other tablet retains in Rm. 134 and labeled accordingly.

26 tablets given to Janet for Sending Outside as per Alex.

3/20/06.

N/A

To Page No. N/A

Recorded by: [signature] Date 03/20/06

Verified by: [signature] Date 3/20/06

Project No. ——

Book No. ——

TITLE Astelin + Steroid

95

03/20/06

From Page No. N/A

Using a commercial 17mL bottle and Valois VP3 pump, we attempted to pass commercial Fluticasone Propionate nasal spray (Lot # C184889) through the Astelin packaging.

Tare = 10.98g (17mL bottle + VP3 pump, cap, & neck lock)
Gross = 25.55g (pump assembly + bottle + suspension)
Net = 14.57g

Four to Six priming sprays were attempted by K. Kale, after which a uniform plume was observed.

N/A

To Page No. N/A

Recorded by: [signature] Date 03/20/06

Verified by: Ed Balwani Date 10/25/07

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Project No. ___

Book No. ___

TITLE Physical Testing: Soma SR #1048-12 & 82 03/21/06
INITIAL vs. 3+ MONTH 40/75.

From Page No. N/A

Physical Testing: Soma 700mg SR Tablets #1048-12 & 82

Upper Comp. (kN)	Target Wt. (mg)	Tablet #	Weight (g)	Hardness (SCU)	Friability
1048-12	1000	1	1.0324	23.1	Initial Wt (g) =
@		2	0.9993	17.5	10.0660
20kN		3	0.9809	15.8	Final Wt (g) =
(initial)		4	0.9899	17.2	10.0250
		5	0.9932	17.8	%Friable =
	1000	average	[illegible]	[illegible]	0.41
		SD	[illegible]	[illegible]	
		%RSD	[illegible]	[illegible]	
1048-12	1000	1	1.0052	21.6	Initial Wt (g) =
@		2	1.0027	20.3	9.9338
20kN		3	0.9893	20.5	Final Wt (g) =
(40°C/75%RH)		4	1.0022	20.6	9.8774
		5	0.9949	20.2	%Friable =
	1000	average	[illegible]	[illegible]	[illegible]
		SD	[illegible]	[illegible]	
		%RSD	[illegible]	[illegible]	
1048-82	1000	1	1.0102	28.3	Initial Wt (g) =
@		2	1.0018	25.7	10.1100
20kN		3	1.0121	27.6	Final Wt (g) =
(initial)		4	1.0163	29.4	10.0917
		5	1.0102	28.8	%Friable =
	1000	average	[illegible]	[illegible]	0.18
		SD	[illegible]	[illegible]	
		%RSD	[illegible]	[illegible]	
1048-82	1000	1	1.0075	28.5	Initial Wt (g) =
@		2	1.0079	29.5	10.0430
20kN		3	1.0140	29.5	Final Wt (g) =
(40°C/75%RH)		4	1.0048	28.1	10.0236
		5	0.9994	25.4	%Friable =
	1000	average	[illegible]	[illegible]	[illegible]
		SD	[illegible]	[illegible]	
		%RSD	[illegible]	[illegible]	

**Hardness readings in bold = tablets that capped during testing

John S. D'Acosta 03/21/06

John S. D'Acosta 03/21/06

0.0000 g
SOMA SR 700mg
1.0052 g
1.0027 g
0.9893 g
1.0022 g
0.9949 g
9.9338 g
9.8774 g

1048-12 WITH DESICCANT

1.0075 g
1.0079 g
1.0140 g
1.0048 g
0.9994 g
10.0430 g
10.0236 g

1048-82

John S. D'Acosta 03/21/06

```
NR       5
XM     20.6 SC
SREL    2.8 %
SD      0.6 SC
XMIN   20.2 SC
XMAX   21.6 SC

 5     20.2 SC
 4     20.6 SC
ZERO
 3     20.5 SC
ZERO
 2     20.3 SC
 1     21.6 SC
```

1048-12

```
NR       5
XM     28.2 SC
SREL    6.0 %
SD      1.8 SC
XMIN   25.4 SC
XMAX   29.5 SC

 5     25.4 SC
 4     28.1 SC
 3     29.5 SC
 2     29.5 SC
 1     28.5 SC
0000000000000000000000
```

1048-82

N/A

To Page No. N/A

Recorded by: John S. D'Acosta	Date 03/21/06	Verified by: AA	Date 24 Oct 07

TITLE Physical Testing: Soma SR #1038-19, 20, 21, 22

Project No. ___

Book No. ___ 03/21/06

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From Page No. N/A

John S. D'Acosta

Physical Testing: Soma 700mg SR Tablets #1038-19, 20, 21, & 22

Batch #	Target Wt. (mg)	Tablet #	Weight (g)	Thickness (mm)	Hardness (SCU)	Friability
1038-19	1000	1	0.9971	6.58	23.7	Initial Wt (g) =
		2	0.9947	6.60	26.2	9.9650
		3	1.0048	6.65	25.3	Final Wt (g) =
		4	0.9940	6.60	25.0	9.9410
		5	0.9951	6.58	23.8	
		6	0.9990	6.60	25.7	
		7	0.9989	6.58	26.7	
		8	0.9931	6.60	24.0	
		9	0.9912	6.57	25.3	
		10	0.9912	6.59	22.6	%Friable =
[illegible]	[illegible]	[illegible]	[illegible]	6.60	24.8	0.24
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	1.2737	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	5.1297	
1038-20	900	1	0.9926	6.60	27.0	Initial Wt (g) =
		2	0.9977	6.61	24.5	9.9850
		3	0.9996	6.62	28.8	Final Wt (g) =
		4	0.9985	6.63	26.4	9.9500
		5	1.0015	6.62	28.8	
		6	0.9839	6.57	25.0	
		7	1.0011	6.65	27.0	
		8	1.0001	6.65	27.5	
		9	0.9901	6.60	26.9	
		10	1.0090	6.65	31.0	%Friable =
[illegible]	[illegible]	[illegible]	[illegible]	6.62	27.3	0.35
[illegible]	[illegible]	[illegible]	[illegible]	0.0262	1.9006	
[illegible]	[illegible]	[illegible]	[illegible]	0.3955	6.9843	
1038-21	900	1	1.0070	6.65	**27.9**	Initial Wt (g) =
		2	0.9983	6.58	24.3	9.9780
		3	1.0018	6.63	26.9	Final Wt (g) =
		4	0.9997	6.60	24.8	9.9370
		5	0.9914	6.57	24.0	
		6	0.9980	6.60	24.3	
		7	1.0082	6.64	29.7	
		8	0.9875	6.53	25.6	
		9	0.9990	6.59	27.8	
		10	0.9918	6.56	22.8	%Friable =
[illegible]	[illegible]	[illegible]	[illegible]	6.60	25.6	0.41
[illegible]	[illegible]	[illegible]	[illegible]	0.0378	2.1759	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	8.4363	
1038-22	900	1	1.0068	6.55	20.0	Initial Wt (g) =
		2	1.0108	6.52	25.4	10.0720
		3	1.0063	6.52	21.5	Final Wt (g) =
		4	0.9963	6.53	19.6	10.0320
		5	1.0021	6.57	24.0	
		6	1.0107	6.52	22.6	
		7	1.0028	6.52	23.2	
		8	1.0041	6.52	24.7	
		9	1.0134	6.51	31.3	
		10	1.0085	6.52	27.5	%Friable =
[illegible]	[illegible]	[illegible]	[illegible]	6.53	24.0	0.40
[illegible]	[illegible]	[illegible]	[illegible]	0.0187	3.5308	
[illegible]	[illegible]	[illegible]	[illegible]	0.2778	14.7237	

**Hardness readings in bold = tablets that capped during testing

TESTING PERFORMED BY A. FAVARA WEEK OF 03/13/06

1038-22 03/21/06

```
NR      10
XM     24.0 SC
SREL   14.7 %
SD      3.5 SC
XMIN   19.6 SC
XMAX   31.3 SC

10     27.5 SC
 9     31.3 SC
 8     24.7 SC
 7     23.2 SC
 6     22.6 SC
 5     24.0 SC
 4     19.6 SC
 3     21.5 SC
 2     25.4 SC
 1     20.0 SC
```

[redacted]

N/A

To Page No. N/A

Recorded by: John S. D'Acosta	Date 03/21/06	Verified by: AA	Date 24 Oct 07

PTX0142-00008

MEDA_APTX03470955

Project No. ——

Book No. ——

TITLE Physical Testing: Soma SR # 1038-24,25,26 03/21/06

From Page No. N/A

John S Wilcox 03/21/06

Physical Testing: Soma 700mg SR Tablets #1038-24, 25, & 26

Batch #	Target Wt. (mg)	Tablet #	Weight (g)	Thickness (mm)	Hardness (SCU)	Friability
1038-24	1000	1	1.0067	6.52	27.3	Initial Wt (g) =
		2	1.0081	6.55	24.7	10.0910
		3	1.0073	6.53	26.7	Final Wt (g) =
		4	1.0097	6.56	26.3	10.0500
		5	1.0098	6.55	23.2	
		6	1.0046	6.54	25.9	
		7	1.0047	6.53	27.6	
		8	1.0051	6.53	24.8	
		9	0.9978	6.52	25.6	
		10	1.0206	6.55	27.5	%Friable =
1038-25	1000	1	1.0076	6.71	26.7	Initial Wt (g) =
		2	1.0032	6.67	28.1	10.0490
		3	0.9992	6.68	28.3	Final Wt (g) =
		4	0.9990	6.67	26.6	10.0180
		5	0.9954	6.67	28.3	
		6	1.0051	6.68	29.2	
		7	1.0036	6.68	22.4	
		8	1.0043	6.66	26.6	
		9	1.0061	6.70	27.9	
		10	1.0300	6.68	27.6	%Friable =
1038-26	1000	1	1.0061	6.53	27.3	Initial Wt (g) =
		2	1.0016	6.50	27.2	10.0480
		3	0.9998	6.50	29.2	Final Wt (g) =
		4	1.0003	6.50	26.3	9.9980
		5	1.0061	6.52	28.2	
		6	1.0020	6.50	26.6	
		7	1.0074	6.51	29.1	
		8	0.9926	6.47	25.6	
		9	0.9964	6.48	26.0	
		10	1.0036	6.52	25.1	%Friable =

**Hardness readings in bold = tablets that capped during testing

```
NR      10
XM    27.0 SC
SREL   5.2 %
SD     1.5 SC
XMIN  25.1 SC
XMAX  29.2 SC

 10   25.1 SC
  9   26.0 SC
  8   25.6 SC
  7   29.1 SC
ZERO
  6   26.6 SC
ZERO
  5   28.2 SC
ZERO
  4   26.3 SC
ZERO
  3   29.2 SC
ZERO
  2   27.2 SC
  1   27.3 SC
```

[redacted]

N/A

To Page No. N/A

Recorded by: John S Wilcox 03/21/06 | Date 03/21/06 | Verified by: QA | Date 24 Oct 07

Project No. ——

Book No. ——

TITLE Astelin 03-33 Registration Batches

99

03/21/06

From Page No. N/A

Astelin Registration Batches – Decatur 03/2006

Batch # 03-33-03c
DOM: 03/13/06
Batch Size: 3300L

No problems occurred during the making of this batch. This batch was made in the 940 gallon processing tank, samples were taken according to E-Req 1112 sampling record (see below), the batch was filtered through a Millipore 0.45 micron PVDF 20" filter (code # CVHL-72P-P3), and transferred into the 940 gallon holding tank.

JS 03/21/06

E-Requisition 1112

SAMPLING RECORD

03-33-05s
03-33-04s
Batch Number: 03-33-03c

Bulk Solution

ACTIVITY	SAMPLE LOCATION	AMOUNT REQUIRED	PURPOSE	COLLECTED BY/DATE
PROCESSING Following Step 11	Top of Compounding Tank	2 x 300 mL	Azelastine and BAC Assay	
	Bottom of Compounding Tank	2 x 300 mL	Azelastine and BAC Assay	
PROCESSING Following Step 18	Top of Holding Tank	2 x 300 mL	Azelastine and BAC Assay	
	Bottom of Holding Tank	2 x 300 mL	Azelastine and BAC Assay	N/A
PROCESSING Final Bulk Solution Prior to Packaging	Top of Holding Tank	1 x 300 mL	Specific Gravity	
		1 x 500 mL	Spray Pattern Test Solution	
		approx. 220 mL	Microbial Limits	
		2 x 500 mL	Bulk Release Testing	
		2 x 500 mL (glass bottles)	Bulk Retain	

The only point of note is that during the filtration process it became clear that the filtration rate slowed considerably after approximately the 1-hour mark. At this time, I began charting the filtration rate (see pg. 101), and will continue to do so for the three remaining batches, for comparison.

N/A

John S Wilcox 03/21/06

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Recorded by: John S Wilcox 03/21/06 | Date 03/21/06 | Verified by: QA | Date 24 Oct 07

From Page No. 99

Batch # 03-33-04s
DOM: 03/14/06
Batch Size: 330L

During the compounding of this batch, specifically steps # 8 through 11, it was observed that the 250 gallon processing tank began to shake (as it is equipped with shock-absorbing technology to counteract the force of the moving liquid inside) at a speed that caused the batch to "roll" or slosh around the inside of the tank, thus causing a loss of any true vortex. Without baffles to aid in the breaking up of the active and excipients, it was determined that the mixing speeds should be adjusted upwards until a suitable vortex could be obtained again.

Once this was done, no further problems arose in the manufacturing of the batch.

Samples were taken according to E-Req 1112 sampling record. The batch was filtered through a Millipore 0.45 micron PVDF 20" filter (code # CVHL-72P-P3), and transferred into a 375 gallon holding tank.

These new (greater) mixing speeds will be used for the two remaining 330L batches as well.

Batch # 03-33-05s
DOM: 03/15/06

No problems occurred during the making of this batch. This batch was made in the 250 gallon processing tank, samples were taken according to E-Req 1112 sampling record, the batch was filtered through a Millipore 0.45 micron PVDF 20" filter (code # CVHL-72P-P3), and transferred into a 375 gallon holding tank.

Batch # 03-33p-03s
DOM: 03/16/06

No problems occurred during the making of this batch. This batch was made in the 250 gallon processing tank, samples were taken according to E-Req 1113 sampling record (see below), the batch was filtered through a Millipore 0.45 micron PVDF 20" filter (code # CVHL-72P-P3), and transferred into a smaller holding tank.

JSW 03/21/06 John S. Wilcox 03/21/06

ATTACHMENT D
SAMPLING RECORD

Batch Number: 03-33p-03s

Bulk Solution

ACTIVITY	SAMPLE LOCATION	AMOUNT REQUIRED	PURPOSE	COLLECTED BY/DATE
PROCESSING Final Bulk Solution	Top of holding tank	approx. 220 mL	Microbial Limits	N/A
		2 x 500 mL	Release Testing	
		8 x 500 mL	Bulk Retain	

To Page No. 101

Recorded by: John S. Wilcox Date 03/21/06 Verified by: Ene Balwani Date 10/25/07

From Page No. 100

Astelin 03-33 Registration Batches

Batch # 03-33-03c
D of M: 3/13/2006

Time	Batch Weight (kg)	Δ weight (kg)	
14:18	3350	n/a	after qs
15:20	214	3136	
15:21	200	14	
15:22	186	14	
15:23	174	12	
15:24	162	12	
15:25	150	12	
15:26	138	12	
15:27	126	12	
15:28	116	10	
15:29	104	12	
15:30	94	10	
15:31	84	10	
15:32	74	10	
15:33	64	10	
15:34	56	8	
15:35	48	8	
15:36	40	8	
15:37	30	10	
15:38	24	6	
15:39	14	10	
15:40	6	8	
15:41	4	2	
15:42	4	0	

Batch # 03-33-04s
D of M: 3/14/2006

Time	Batch Weight (kg)	Δ weight (kg)	
13:10:00	335	n/a	after qs
13:10:30	323	12	filter purge
13:11:00	313	10	
13:11:30	308	5	
13:12:00	302	6	
13:12:30	287	15	
13:13:00	265	22	
13:13:30	240	25	
13:14:00	213	27	
13:14:30	186	27	
13:15:00	159	27	
13:15:30	131	28	
13:16:00	103	28	
13:16:30	75	28	
13:17:00	47	28	
13:17:30	18	29	
13:18:00	0	18	

Batch # 03-33-05s
D of M: 3/15/2006

Time	Batch Weight (kg)	Δ weight (kg)	
	335	n/a	after qs
12:35:00	328	7	after sampling
12:35:30	308	20	after filter purge
12:36:00	270	38	
12:36:30	224	46	
12:37:00	178	46	
12:37:30	133	45	
12:38:00	88	45	
12:38:30	43	45	
12:39:00	2	41	
12:39:30	2	0	
12:40:00	0	2	

Batch # 03-33p-03s
D of M: 3/16/2006

Time	Batch Weight (kg)	Δ weight (kg)	
	335	n/a	after qs
12:42:00	306	29	after filter purge
12:42:30	292	14	
12:43:00	248	44	
12:43:30	203	45	
12:44:00	158	45	
12:44:30	114	44	
12:45:00	71	43	
12:45:30	37	34	
12:49:00*	34	3	
12:49:30	3	31	
12:50:00	3	0	

* FILTRATION WAS PAUSED AS THE HOLDING TANK WAS NEARING CAPACITY. WE ESTIMATED THAT THERE WAS ENOUGH ROOM & RESUMED FILTRATION.

John S. Wilcox 03/21/06

N/A

03/24/06 JSW

To Page No. 104

Recorded by: John S. Wilcox Date 03/21/06 Verified by: Ene Balwani Date 10/25/07

From Page No. N/A

Product: TUSSI-ORGANIDIN NR LIQUID **Form. #:** 1044-102P

Re: Codeine placebo of Tussi-Organidin NR for analytical testing.

BATCH SIZE: 2.000 L theoretical SG = 1.125

#	Ingredient	Code #	Lot #	mg per 5mL	theor. grams per batch (g)	actual grams per batch (g)
1	Guaifenesin USP	4055	0000002356	100.0	40.00	40.014
2	[illegible]	[illegible]	[illegible]	0.0	0.00	
3	Sodium Benzoate NF	0168	2L 2508	5.0	2.00	2.007
4	Saccharin Sodium USP	7260	0000001994	2.0	0.80	0.806
5	Citric Acid Anhydrous USP	1134	0000001292	4.6	1.84	1.848
6	Propylene Glycol USP	6257	0D0508	500.0	200.00	200.2
7	Glycerin USP	5100	0000002135	2160.0	863.50	863.5
8	Sorbitol Solution 70% USP	8135	0000001230	1000.0	400.00	400.0
9	Dye: FD&C Red #40	3073	0000002602	1.0	0.40	0.402
10	Flavor: Raspberry	3425	0000002416	18.7	7.48	7.487
11	Water, purified	8542	Q.S. (to make 2249.4g)			
			TOTAL:		**2249.4**	**g**

Theoretical specific gravity is 1.125 based on Processing Batch Record

Batch produced in Room #133

Manufacturing Procedure:

1. In a stainless steel beaker (FINAL CONTAINER 724.8 g tare), add approximately 600g of Purified water.
2. With mixing, add the Red #40 (✓) to the beaker and mix until uniform.
3. Lower the mixing speed and slowly add the Propylene Glycol (✓) and mix until uniform.
4. Raise the mixing speed again to obtain a sufficient vortex and add the Guaifenesin (✓), mixing until the solution is complete. Mixing Time: 5 min.
5. Lower the mixing speed and add the Glycerin (✓) and Sorbitol Solution (✓). Mix until uniform. Mixing Time: 5 min.
6. Raise the mixing speed and slowly add the following, mixing after each until the solution is complete:
   - Sodium Benzoate (✓)
   - Saccharin Sodium (✓)
   - Citric Acid (✓)
   - Raspberry Flavor (✓)
7. Adjust the batch weight to 2249.4g with Purified water.

Before adjustment:		After Adjustment:	
Gross:	3097.6	Gross:	N/A
Tare:	724.8	Tare:	
Net:	2372.8	Net:	

Amount of water needed _____ g to bring final net weight to 2249.4g

8. Mix for 10 minutes or until uniform.

Mixing Time: _____, Final pH: _____ (date_____), Final Viscosity: _____ (date_____)
Viscosity Testing – spindle #__, 60 RPM for 1 minute @ 25°C)

JSD 04/04/06

*BATCH HAS BEEN OVER-DILUTED WITH RINSE WATER DURING MANUFACTURING. WILL BE REPEATED

John S. O'Connor 04/04/06

To Page No. N/A

Recorded by: John S. O'Connor 04/04/06 | Verified by: Ekl Balwani 10/25/07

From Page No. N/A

Product: TUSSI-ORGANIDIN NR LIQUID **Form. #:** 1044-103P

Re: Codeine placebo of Tussi-Organidin NR for analytical testing.

BATCH SIZE: 2.000 L theoretical SG = 1.125

#	Ingredient	Code #	Lot #	mg per 5mL	theor. grams per batch (g)	actual grams per batch (g)
1	Guaifenesin, USP	4055	0000002356	100.0	40.00	40.009
2	[illegible]	[illegible]	[illegible]	0.0	0.00	
3	Sodium Benzoate, NF	0168	2L 2508	5.0	2.00	2.007
4	Saccharin Sodium, USP	7260	0000001994	2.0	0.80	0.802
5	Citric Acid, USP, Anhydrous	1134	0000001292	4.6	1.84	1.842
6	Propylene Glycol, USP	6257	0D0508	500.0	200.00	200.0
7	Glycerin, USP	5100	0000002135	2160.0	863.50	863.5
8	Sorbitol Solution, USP, 70%	8135	0000001230	1000.0	400.00	400.0
9	Dye: FD&C Red #40	3073	0000002602	1.0	0.40	0.405
10	Flavor: Raspberry	3425	0000002416	18.7	7.48	7.484
11	Water, purified	8542	Q.S. (to make 2249.4g)			
			TOTAL:		**2249.4**	**g**

Theoretical specific gravity is 1.125 based on Processing Batch Record

Batch produced in Room #133

Manufacturing Procedure:

1. In a stainless steel beaker (FINAL CONTAINER 598.5 g tare), add approximately 600g of Purified water.
2. With mixing, add the Red #40 (✓) to the beaker and mix until uniform.
3. Lower the mixing speed and slowly add the Propylene Glycol (✓) and mix until uniform.
4. Raise the mixing speed again to obtain a sufficient vortex and add the Guaifenesin (✓), mixing until the solution is complete. Mixing Time: 5 min.
5. Lower the mixing speed and add the Glycerin (✓) and Sorbitol Solution (✓). Mix until uniform. Mixing Time: 10 min.
6. Raise the mixing speed and slowly add the following, mixing after each until the solution is complete:
   - Sodium Benzoate (✓)
   - Saccharin Sodium (✓)
   - Citric Acid (✓)
   - Raspberry Flavor (✓)
7. Adjust the batch weight to 2249.4g with Purified water.

Before adjustment:		After Adjustment:	
Gross:	2720.5	Gross:	2847.9
Tare:	598.5	Tare:	598.5
Net:	2122.0	Net:	2249.4

Amount of water needed 127.4 g to bring final net weight to 2249.4g

8. Mix for 10 minutes or until uniform.

Mixing Time: 20 min., Final pH: 4.25 (date 04/05/06), Final Viscosity: 18.0 cps (date 04/05/06)
Viscosity Testing – spindle # 2, 60 RPM for 1 minute @ 25°C)

John S. O'Connor 04/05/06

To Page No. N/A

Recorded by: John S. O'Connor 04/05/06 | Verified by: Ekl Balwani 10/25/07

From Page No. 104

Astelin 03-33 Registration Batches

Batch # **03-33-03c**
DOM: 3/13/2006

Time	Batch Weight (kg)	Amount Filtered (kg)	Δ weight (kg)	Rate (kg/min)
14:18	3350	n/a	n/a	n/a
15:20	214	3136	3136	50.6
15:21	200	3150	14	14.0
15:22	186	3164	14	14.0
15:23	174	3176	12	12.0
15:24	162	3188	12	12.0
15:25	150	3200	12	12.0
15:26	138	3212	12	12.0
15:27	126	3224	12	12.0
15:28	118	3234	10	10.0
15:29	104	3246	12	12.0
15:30	94	3256	10	10.0
15:31	84	3266	10	10.0
15:32	74	3276	10	10.0
15:33	64	3286	10	10.0
15:34	56	3294	8	8.0
15:35	48	3302	8	8.0
15:36	40	3310	8	8.0
15:37	30	3320	10	10.0
15:38	24	3326	6	6.0
15:39	14	3336	10	10.0
15:40	6	3344	8	8.0
15:41	4	3346	2	2.0
15:42	4	3346	0	0.0

Batch # **03-33-04s**
DOM: 3/14/2006

Time	Batch Weight (kg)	Amount Filtered (kg)	Δ weight (kg)	Rate (kg/min)
13:10:00	335	n/a	n/a	n/a
13:10:30	323	12	12	n/a
13:11:00	313	22	10	22.0
13:11:30	308	27	5	15.0
13:12:00	302	33	6	11.0
13:12:30	287	48	15	21.0
13:13:00	265	70	22	37.0
13:13:30	240	95	25	47.0
13:14:00	213	122	27	52.0
13:14:30	186	149	27	54.0
13:15:00	159	176	27	54.0
13:15:30	131	204	28	55.0
13:16:00	103	232	28	56.0
13:16:30	75	260	28	56.0
13:17:00	47	288	28	56.0
13:17:30	18	317	29	57.0
13:18:00	0	335	18	47.0

N/A

To Page No. 105

Recorded by: [signature] Date 03/24/06 Verified by: Eric Balwani Date 10/25/07

From Page No. 104

Batch # **03-33-05s**
DOM: 3/15/2006

Time	Batch Weight (kg)	Amount Filtered (kg)	Δ weight (kg)	Rate (kg/min)
	335	n/a	n/a	n/a
12:35:00	328	n/a	7	n/a
12:35:30	308	n/a	20	n/a
12:36:00	270	65	38	58.0
12:36:30	224	111	46	84.0
12:37:00	178	157	46	92.0
12:37:30	133	202	45	91.0
12:38:00	88	247	45	90.0
12:38:30	43	292	45	90.0
12:39:00	2	333	41	86.0
12:39:30	2	333	0	41.0
12:40:00	0	335	2	2.0

Batch # **03-33p-03s**
DOM: 3/16/2006

Time	Batch Weight (kg)	Amount Filtered (kg)	Δ weight (kg)	Rate (kg/min)
	335	n/a	n/a	n/a
12:42:00	306	n/a	29	n/a
12:42:30	292	43	14	43.0
12:43:00	248	87	44	58.0
12:43:30	203	132	45	89.0
12:44:00	158	177	45	90.0
12:44:30	114	221	44	89.0
12:45:00	71	264	43	87.0
12:45:30	37	298	34	77.0
12:49:00	34	301	3	37.0
12:49:30	3	332	31	34.0
12:50:00	3	332	0	31.0

N/A

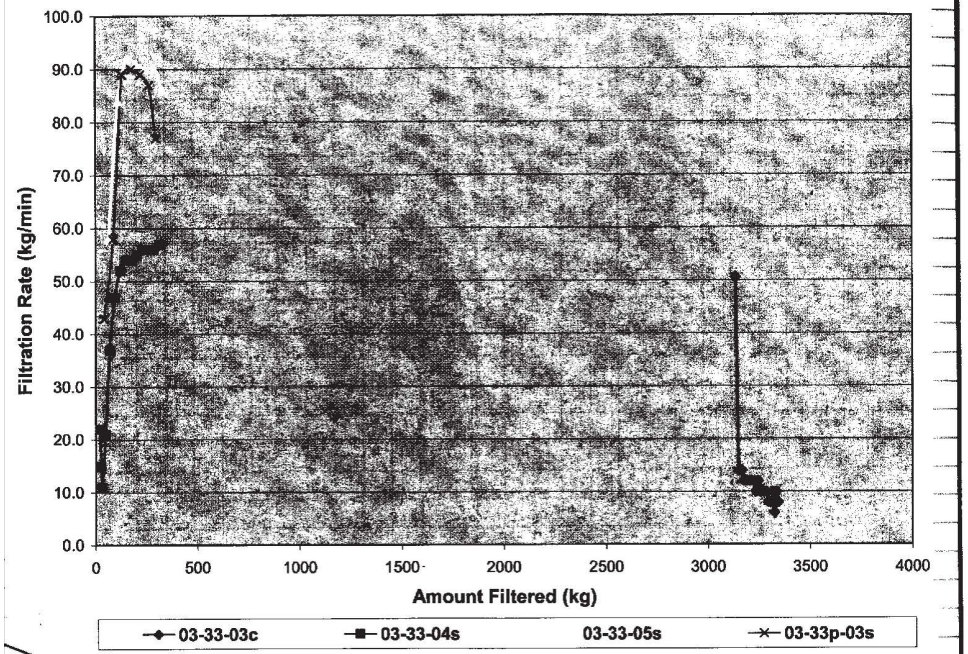
To Page No. 106

Recorded by: [signature] Date 03/24/06 Verified by: Eric Balwani Date 10/25/07

Project No. ——
Book No. ——
TITLE Astelin 03-33 Reg. Batches 03/24/06

From Page No. 105

Filtration Study: Astelin Registration Batches
(Decatur - March 2006)



N/A

To Page No. N/A

Recorded by: John S. McCord Date 03/24/06 Verified by: Kal Babani Date 10/25/07

Project No. ——
Book No. ——
TITLE Astelin #102717 Freeze/Thaw 03/27/06 107

From Page No. N/A

At the request of C. Yavac, 20 bottles of Astelin Reformulates #1027-17 were placed on Freeze/Thaw stability.

Ten bottles were numbered & placed upright
Ten bottles were numbered & placed in the prone position.

They were placed in the freezer in Room #129 and will undergo freeze/thaw with extreme differences (from freezer to 40°C oven).

Wed. 03/29/06 : (20) samples moved from freezer in Room #129 to 40°C/Ambient oven in stability chamber room = Thaw #1.

Fri. 03/31/06 : (20) samples, which have thawed, are removed from the 40°C oven and returned to the freezer in Room #129. No changes to the outside of the containers observed.

Mon. 04/03/06 : (20) samples are moved from the freezer in Rm. #129, back to the 40°C/Ambient oven in the stability chamber room for ~~To~~ Thaw #2. JSD 04/05/06

Wed. 04/05/06 : (20) samples are moved from 40°C/Ambient oven, to the freezer in Room #129 for Freeze #3.
No changes to the outside of the containers was observed.

Fri. 04/07/06 : (20) samples removed from freezer & placed in 40°C/Ambient.
No changes observed upon Freeze #3.

Mon. 04/10/06 : (20) samples removed from 40°C/Ambient after Thaw #3
No changes observed to the outside of the container.

Bottles will be placed in stability lab for retain/possible future testing. JSD 04/11/06

To Page No. N/A

Recorded by: John S. McCord Date 03/27/06 Verified by: Kal Babani Date 10/25/07

PTX0142-00013

HIGHLY CONFIDENTIAL
-SUBJECT TO STIPULATED PROTECTIVE ORDER

MEDA_APTX03470960

CIPLA LTD. EXHIBIT 2039 PAGE 13

From Page No. 4A POST DECATUR TRIP SUMMARY By K. KALE.

E1112: Post Manufacturing Observations Report.

Authors: John D'Aconti & Kalidas Kale

Date: March 24, 2006

3300L Batch

In the week of March 13th four batches of Astelin Improved taste were manufactured. One full scale, 3300 liter size registration batch (Batch Number 03-33-03C), two 330 liter size batches (batch numbers 03-33-04S and 03-33-05S) and one 330 liter size placebo batch (batch number 03-33P-03S) were manufactured.

The 3300 liter size batch was prepared in the 940 gallon capacity processing tank. During the filtration of this batch after one hour, the filtration rate was considerably decreased. At this point 3136 kg of material was filtered. From this time onward filtration rate as a function of time was measured. The filtration rate at this point was only 14 liters per minute; it decreased to 8 liters per minute at the end of the filtration, when all liquid was filtered. The total batch was filtered within one hour and twenty four minutes.

The filter used was Durapore Cartridge filter without prefilter 20 inch, 0.45 micron from Millipore Corporation. The filtration area of this filter was 1.38 m^2. To maintain the good filtration rate throughout the filtration step, there are two options, either use same size filter with a prefilter or use 30 inch cartridge with larger filtration area 2.07 m^2. These options will be evaluated during the next manufacture of 3300 liter size batches.

330 liter size batches

Batch# 03-33-04S
These batches were processed in the 250 gallon capacity processing tanks. It was observed that at the time of addition of Azelastine HCl (step 8) the liquid was sloshing around the processing tank at the stirrer speed of 120 (+-20) rpm. To create a vortex for proper mixing conditions, the stirrer speed was increased to 200 rpm. In step 9 the proper vortex was achieved at 175 rpm. In step 10 the stirrer speed was 175 rpm. In step 11 it was 125 rpm. Total batch was filtered without slowdown of the filtration rate.

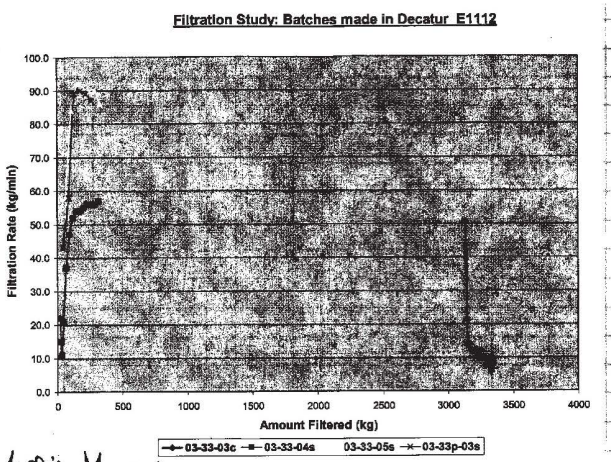
Batch# 03-33-05S and Batch # 03-33P-03S
The stirrer speed was maintained at the same rate as used in the manufacture of batch# 03-33-04S. These two batches were filtered without slowdown of the filtration rate.

03/27/06

To Page No. 109

Recorded by:	Date	Verified by:	Date
	03/27/06	Gul Balwani	10/25/07

From Page No. 108



03/27/06

N A

To Page No. A

Recorded by:	Date	Verified by:	Date
	03/27/06	Gul Balwani	10/25/07

PTX0142-00014

HIGHLY CONFIDENTIAL
-SUBJECT TO STIPULATED PROTECTIVE ORDER

MEDA_APTX03470961

Project No. ——
Book No. ——
TITLE ~~Fuss-Originating NR~~ Astelin Nasal Spray JSD 04/06/06 04/07/06
FORM: 03-33

From Page No. N/A

Product: Astelin® Nasal Spray pg. 1044-110

Re: Lab batch to match Investigational Formulation 03-33, for Analytical Testing.

Ingredient	Code #	Lot #	%w/v	Theo. grams per batch	Actual grams per batch
Azelastine HCl	1105	0000002047	0.100%	2.000	2.011
HPMC 2910, USP	3340	0000002822	0.100%	2.000	2.002
Sorbitol Solution, USP, 70%	8135	0000001230	6.446%	128.920	128.9
Sucralose, NF	7474	04073	0.150%	3.000	3.008
Edetate Disodium, USP	1349	0000002353	0.050%	0.500	0.502
Sodium Citrate, USP, Dihydrate	0734	2C1804	0.068%	1.360	1.368
Benzalkonium Chloride, NF, 50% Soln.	2202	1C1304	0.025%	0.500	0.502
Water, Purified or Deionized			QS to 100%	QS to 2030.0g	

Manufacturing Procedure

1. To a suitably sized container (tare weight 726.7 g), obtain 740g of deionized water. Begin mixing and heat to 80°C (175°F). Record the temperature. While mixing, *Slowly* add the HPMC (√) to the vortex of the mixing water.
   Mix for 20 minutes or until the mixture is lump-free. Record the mixing time. Do NOT let the mixture cool to below 60°C (140°F) while mixing. Temp: 80 °C Mixing Time: 20min.
2. Add approx. 1000g of deionized water. Cool to 32°C (90°F). Record the temperature.
   Temp: 28 °C
3. Add the Azelastine HCl (√), mixing until completely dissolved. Record the mixing time and temperature.
   Temp.: 28 °C Mixing Time: 10min.
4. Add the following ingredients, one at a time, to the mixture: sucralose (√), sorbitol solution (√), EDTA (√), sodium citrate (√). Mix after each until solution is clear and record the overall mixing time.
   Mixing Time: 20min.
5. Add the Benzalkonium Chloride (√) to the batch and mix for 10 minutes. Mixing Time: 10min.
6. Adjust batch weight to (2030.0g) with deionized water. Mix for 30 minutes or until uniform.

Before adjustment:		After adjustment:	
Gross:	2673.0 g	Gross:	2756.7 g
Tare:	726.7 g	Tare:	726.7 g
Net:	1946.3 g	Net:	2030.0 g

   Amount of Water dded: 83.7 g to bring final net weight to 2030.0g.
   Mixing Time: 30min. Temperature at end of mixing: 22 °C Description: CLEAR, VERY
7. Filter finished product through a 0.22µm Millipore Stainless Steel High Pressure Filter Holder. LITTLE FOAM
   Filter Info: DURAPORE 0.22µm GVMP14250 LOT# R0AN29130
   Discard the first 50mL to 100mL and retain the rest of the product for testing and packaging.
8. Measure the pH, viscosity, and specific gravity (viscosity testing – spindle #2, 60rpm for 1 minute at 25°C).
   Final pH: 6.36 (date 04/06/06). **Final viscosity:** 5.0 cps (date 04/10/06).
   ~~Specific Grav.:~~ ____ (date ____) [pyc.: ____ g / pyc+ water= ____ g / pyc+sample= ____ g] OMIT JSD 04/10/06

To Page No. N/A

Recorded by: [signature] Date 04/07/06 Verified by: Ekl Balwani Date 10/25/07

Project No. ——
Book No. ——
TITLE ~~Fuss~~ Astelin Nasal Spray JSD 04/06/06 04/07/06
FORM: 03-33p

From Page No. N/A

Product: Astelin® Nasal Spray pg. 1044-111

Re: Lab batch to match Investigational Placebo 03-33p, for Analytical Testing.

Ingredient	Code #	Lot #	%w/v	Theo. grams per batch	Actual grams per batch
~~Azelastine HCl~~	1105		0.000%	0.000	
HPMC 2910, USP	3340	0000002822	0.100%	2.000	2.006
Sorbitol Solution, USP, 70%	8135	0000001230	6.446%	128.920	128.9
Sucralose, NF	7474	04073	0.150%	3.000	3.009
Edetate Disodium, USP	1349	0000002353	0.050%	0.500	0.504
Sodium Citrate, USP, Dihydrate	0734	2C1804	0.068%	1.360	1.361
Benzalkonium Chloride, NF, 50% Soln.	2202	1C1304	0.025%	0.500	0.501
Water, Purified or Deionized			QS to 100%	QS to 2028.0g	

Manufacturing Procedure

1. To a suitably sized container (tare weight 724.9 g), obtain 740g of deionized water. Begin mixing and heat to 80°C (175°F). Record the temperature. While mixing, *Slowly* add the HPMC (√) to the vortex of the mixing water.
   Mix for 20 minutes or until the mixture is lump-free. Record the mixing time. Do NOT let the mixture cool to below 60°C (140°F) while mixing. Temp: 78 °C Mixing Time: 20min.
2. Add approx. 1000g of deionized water. Cool to 32°C (90°F). Record the temperature.
   Temp: 32 °C
3. ~~Add the Azelastine HCl ( ), mixing until completely dissolved. Record the mixing time and temperature.~~ JSD 04/07/06
   PLACEBO ~~Temp.: ____ °C Mixing Time: ____~~
4. Add the following ingredients, one at a time, to the mixture: sucralose (√), sorbitol solution (√), EDTA (√), sodium citrate (√). Mix after each until solution is clear and record the overall mixing time.
   Mixing Time: 20min.
5. Add the Benzalkonium Chloride (√) to the batch and mix for 10 minutes. Mixing Time: 15min.
6. Adjust batch weight to (2028.0g) with deionized water. Mix for 30 minutes or until uniform.

Before adjustment:		After adjustment:	
Gross:	2623.0 g	Gross:	2752.9 g
Tare:	724.9 g	Tare:	724.9 g
Net:	1898.1 g	Net:	2028.0 g

   Amount of Water dded: 129.9 g to bring final net weight to 2028.0g.
   Mixing Time: 30min. Temperature at end of mixing: 28 °C Description: CLEAR, SOME FOAM.
7. Filter finished product through a 0.22µm Millipore Stainless Steel High Pressure Filter Holder. 22 JSD 04/07/06 AS PER K. KALE
   Filter Info: MILLIPORE-DURAPORE 0.22µm GVWP14250
   Discard the first 50mL to 100mL and retain the rest of the product for testing and packaging. Lot # R0AN29130
8. Measure the pH, viscosity, and specific gravity (viscosity testing – spindle #2, 60rpm for 1 minute at 25°C).
   Final pH: 6.27 (date 04/10/06). **Final viscosity:** 5.0cps (date 04/10/06).
   ~~Specific Grav.:~~ ____ (date ____) [pyc.: ____ g / pyc+ water= ____ g / pyc+sample= ____ g] OMIT JSD 04/10/06

To Page No. N/A

Recorded by: [signature] Date 04/07/06 Verified by: Ekl Balwani Date 10/25/07

PTX0142-00015

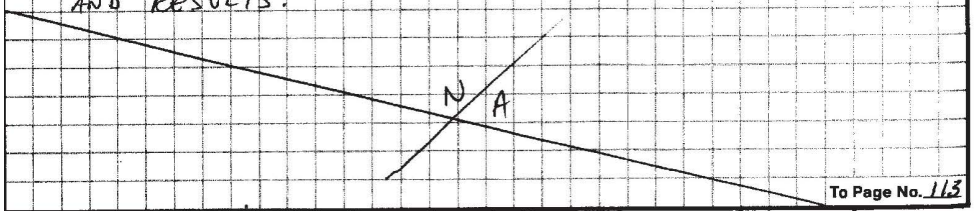
From Page No. 111

Optivar (Azelastine HCl Eye Drops 0.05%) Lot #02306A was received from Cardinal, from a 250 L batch manufactured on 04/04/06. It will undergo Osmolarity testing, an osmolarity adjustment using Sorbitol Solution, and repeat Osmolarity testing to observe any change.

The Osmette-A Automatic Osmometer (Model #5002, Ser #HH10073) was calibrated as follows:

- turn toggle to "operate"
- allow machine to warm up for ≈15 min.
- add coolant until full
- prepare multiple 500 mOsm/kg & 100 mOsm/kg std. samples.
- set range to 0-2
  operate to special
- place 500 std into machine, adjust reading with "I" knob.
- switch to operate and read a new, clean 500 std.
  Result = 504, repeat: Result = 501
- Repeat with 100 mOsm/kg std, adjusting with "II" knob.
  Result - 97, 101
- Test Optivar sample (Cardinal result ≈250 mOsm/kg)
  Result #1 = 242 mOsm/kg
  #2 = 241 mOsm/kg

Osmometer calibrated... see pg. 113 for directions for osmolarity adjustment of sample (Lot #02306A) and results.



To Page No. 113

Recorded by:	Date	Verified by:	Date
John Sullivan	04/14/06	Gul Balwani	10/25/07

From Page No. 112

Adjustment #1

Adjustment of Osmolarity of Sorbitol Solution
Azelastine Hydrochloride Eye Drops 0.05% Lot 02306A, 250 liter batch made at Cardinal. Date 04/04/2006

Amount of Sorbitol Solution Required for the batch	=	16666.5g
Amount of Sorbitol Solution Added in the batch	=	16000.5g
Difference	=	666.5g/250 liter
		666.5g/253.75 kg
	=	2.6266g/kg
	=	0.0026266g/g

To 10g of the product add 0.02627g of Sorbitol solution.
Measure Osmolarity.

John Sullivan 04/14/06

Lot # 02306A = 10.005g
Sorbitol Sol 70% = 0.0274g (Lot # 0000001230)

Osmolarity Results:

Test # 1a = 251 mOsm/kg
Test # 1b = 251 mOsm/kg

Adjustment #2

Weighed 5x Sorbitol Solution 70% & QS to 50g total. (Theo. Sorb. = 0.1313g)

Sorbitol Solution, 70% (Lot #0000001230) = 0.1390g (actual)
Optivar (Lot # 02306A) QS to 50g = 50.0048g (actual)

Retest 500 mOsm/kg std = 502
Retest 100 mOsm/kg std = 103
Adjusted Optivar #2a = 251
Adjusted Optivar #2b = 251 mOsm/kg

To Page No. N/A

Recorded by:	Date	Verified by:	Date
John Sullivan	04/14/06	Gul Balwani	10/25/07

From Page No. N/A

FLUTICASONE PROPIONATE NASAL SPRAY (LOT #C184889)

17mL AZELASTINE HCl NS COMMERCIAL BOTTLE + PUMP

= 10.9713 g

BOTTLE w/o PUMP

= 4.5717 g

COMMERCIAL BOTTLE + FLUTICASONE N.S.

= 19.1669 g

AMOUNT OF FLUTICASONE N.S. ADDED

= 14.5952 g

AMOUNT OF AZELASTINE HCl NEEDED FOR 0.1% w/v

= 0.0146 g

AMOUNT OF AZELASTINE HCl WEIGHED:

= 0.0158 g (0.0009 g LEFT ON WEIGHBOAT ∴ AMOUNT ADDED = 0.0149 g)

BOTTLE IS THEN SONICATED FOR 15 MINUTES, AND WILL BE OBSERVED.

FINAL SAMPLE APPEARS TO BE UNIFORM, WITH NO PRECIP

N/A

To Page No. 116

Recorded by: [signature] Date 04/24/06 Verified by: Kim Bahrami Date 10/25/07

N/A

Stability Testing: Soma 700mg SR Tablets #1048-10, 12, 14 @ 2 months (40°C/75%RH)

	Target Wt. (mg)	Tablet #	Weight (g)	Thickness (mm)	Hardness (SCU)	Friability
[redacted]	1000	1	0.9827	6.62	18.0	Initial Wt (g) =
[redacted]		2	1.0075	6.69	21.8	10.0080
[redacted]		3	1.0009	6.65	19.3	Final Wt (g) =
[redacted]		4	1.0056	6.67	21.2	9.9590
[redacted]		5	0.9999	6.67	21.6	%Friable =
[redacted]						
1048-12	1000	1	0.9964	6.60	19.1	Initial Wt (g) =
[redacted]		2	0.9855	6.77	17.2	9.9660
[redacted]		3	1.0117	6.85	22.9	Final Wt (g) =
[redacted]		4	0.9944	6.77	18.4	9.9160
[redacted]		5	0.9849	6.74	16.8	%Friable =
[redacted]						
1048-14	1000	1	0.9968	7.01	18.0	Initial Wt (g) =
[redacted]		2	0.9975	7.02	17.7	9.9870
[redacted]		3	1.0021	7.02	16.5	Final Wt (g) =
[redacted]		4	1.0006	6.99	18.1	9.9380
[redacted]		5	1.0072	7.06	17.8	%Friable =

Stability Testing: Soma 700mg SR Tablets #1048-66 & 82 @ 2 months (40°C/75%RH)

Lot #	Target Wt. (mg)	Tablet #	Weight (g)	Thickness (mm)	Hardness (SCU)	Friability
1048-66	950	1	0.9436	6.45	25.1	Initial Wt (g) =
with desiccant		2	0.9330	6.45	24.7	9.4710
		3	0.9489	6.45	23.8	Final Wt (g) =
		4	0.9484	6.45	29.7	9.4400
		5	0.9586	6.48	27.5	%Friable =
1048-66	950	1	0.9558	6.49	26.6	Initial Wt (g) =
without desiccant		2	0.9599	6.54	27.2	9.3760
		3	0.9482	6.48	24.8	Final Wt (g) =
		4	0.9421	6.45	25.0	9.3380
		5	0.9641	6.63	26.3	%Friable =
[redacted]	1000	1	0.9999	6.75	26.3	Initial Wt (g) =
[redacted]		2	0.9958	6.68	25.9	10.0050
[redacted]		3	1.0065	6.76	26.4	Final Wt (g) =
[redacted]		4	0.9985	6.73	*	9.9780
[redacted]		5	0.9987	6.71	*	%Friable =
1048-82	1000	1	1.0024	6.73	26.2	Initial Wt (g) =
without desiccant		2	0.9912	6.67	29.1	9.9390
		3	0.9901	6.67	26.7	Final Wt (g) =
		4	0.9913	6.67	27.3	9.9160
		5	0.9957	6.69	26.7	%Friable =

*not enough tablets remaining to perform hardness testing.

4/25/06

To Page No. N/A

Recorded by: [signature] Date 04/25/06 Verified by: AP Date 24 OCT 07

From Page No. 114

FLUTICASONE PROPIONATE NASAL SPRAY, 50 mcg
LOT # C184889 EXP. AUG. 2007

13.0834g = CENTRIFUGE TUBE TARE WT.
14.5465g = FLUTICASONE N.S.

SAMPLE WAS PLACED IN CENTRIFUGE FOR 30 MIN. SUPERNATANT WAS STILL CLOUDY ∴ RETURNED TO CENTRIFUGE FOR AN ADDITIONAL 30 MINUTES.

THE SUPERNATANT WAS STILL CLOUDY. IT WAS POURED OFF INTO A SCINTILLATION VIAL. THE SAMPLE WAS OPAQUE WHITE.

A MICROSCOPY SLIDE WAS PREPARED WITH A DROP OF THE SAMPLE AND VIEWED @ 40 x MAGNIFICATION. THE SLIDE APPEARED TO BE FREE OF ANY SOLIDS, HOWEVER THE SAMPLE WAS PREPARED TO BE FILTERED.

USING A 10mL SYRINGE AND A 5µm STERILE ACRODISC, THE SAMPLE WAS FILTERED AND PLACED IN A NEW SCINTILLATION VIAL.

THE SAMPLE WAS NOT CLEAR (STILL OPAQUE AND WHITE) ∴ IT WAS PASSED THROUGH A 2µm STERILE ACRODISC. THE RESULTING SAMPLE WAS STILL OPAQUE ∴ IT WAS NEXT PASSED THROUGH A 1µm FILTER. THE RESULTING SAMPLE WAS STILL OPAQUE ∴ IT WAS DECIDED THAT IT WOULD NEXT BE PASSED THROUGH A 0.45µm STERILE ACRODISC.

ATTEMPTING TO PASS THE SAMPLE THROUGH THE 0.45µm FILTER WAS EXTREMELY DIFFICULT. AFTER ≈3 mL OF THE SAMPLE HAD PASSED THROUGH (AND WAS SEEMINGLY CLEAR NOW) THE PRESSURE NECESSARY TO FORCE THE SAMPLE THROUGH THE FILTER WAS MORE THAN THE FILTER COULD WITHSTAND. THE ACRODISC GAVE WAY ALONG ITS' CIRCUMFRENCE AND THE REMAINING SAMPLE WAS SPILLED AND LOST.
THIS PROCESS WILL BE ATTEMPTED AGAIN TOMORROW.

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Recorded by:	Date	Verified by:	Date
John S. McCord Jr.	04/25/06	Gul Babwani	10/25/07

From Page No. 116

15.3786g = SCINTILLATION VIAL + STIR ROD
23.5168g = VIAL + STIRRER + PRODUCT. *
8.1382g = PRODUCT (FLUTICASONE N.S. LOT # C184889)
∴ 0.0081g = AZELASTINE HCl (LOT #0000002047) TO BE ADDED = 0.1%
∴ 23.5249g = TARGET GROSS WT.
23.52492g = ACTUAL WT. (GROSS)

* THE SAMPLE WAS PREPARED IN A SIMILAR FASHION TO THE SAMPLE FROM 04/25. FLUTICASONE PROPIONATE NASAL SPRAY (LOT # C184889) SAMPLE WAS ~~ZERO~~ STD 04/26/06 SHAKE WELL, TO MIX AND SUSPEND THE SAMPLE PROPERLY. THE SPRAY ATTACHMENT WAS CUT OFF THE AMBER GLASS BOTTLE AND POURED INTO A 50mL CENTRIFUGE VIAL. THE SAMPLE WAS SPUN FOR ONE HOUR, THE SUPERNATANT POURED OFF, THE SOLIDS WERE DISCARDED.
THE SUPERNATANT SAMPLE WAS INTRODUCED INTO A 10mL SYRINGE AND PASSED THROUGH AN INTERCONNECTED SERIES OF 5µm, 2µm, AND 1µm STERILE ACRODISC (PVDF) FILTERS. THE RESULTING SAMPLE WAS THEN SLOWLY AND DIFFICULTLY PASSED THROUGH A 0.45µm ACRODISC.

THIS SAMPLE WAS TRANSFERRED INTO A PRE-WEIGHED SCINTILLATION VIAL CONTAINING A MAGNETIC STIR ROD, A 0.1% w/v ALLOQUOT OF AZELASTINE HCl WAS ADDED, USING AN ANALYTICAL BALANCE, AND THE SAMPLE WAS PLACED ON A STIRRER/HOTPLATE AND MIXED OVERNIGHT.

THE FOLLOWING MORNING THE SAMPLE WAS OBSERVED FOR CLARITY/SOLUBILITY AND IT WAS FOUND THAT THERE WAS STILL A MAJOR PORTION OF THE AZELASTINE HCl THAT HAD NOT GONE INTO SOLUTION.

THIS SAMPLE WAS COVERED (CAPPED) AND LABELED FOR POSSIBLE FURTHER EXPERIMENTATION.

To Page No. 118

Recorded by:	Date	Verified by:	Date
John S. McCord Jr.	04/26/06	Gul Babwani	10/25/07

Project No. —
Book No. 1044 TITLE ASTELIN + STEROID EXPERIMENT 04/27/06

From Page No. 117

THE REMAINING SAMPLE FROM YESTERDAY'S EXPERIMENT WAS PLACED ON A STIRRING/HOTPLATE. A THERMOMETER WAS PLACED IN THE SAMPLE

INITIAL TEMP. = 19°C
TARGET TEMP. = 60°C OR OBSERVED CLARITY OF THE SAMPLE.

SAMPLE WAS HEATED, WITH STIRRING, TO ≈60°C (TOP TEMP. = 64°C) AND HELD STEADY FOR 15 MIN. AFTER 15 MIN. THE STIRRING WAS STOPPED AND THE SAMPLE WAS REMOVED FROM THE HEAT.

THE SAMPLE REMAINED TRANSLUCENT AND IT IS ASSUMED THAT IF ALLOWED TO SIT LONG ENOUGH, THE UNDISSOLVED AZELASTINE WILL BECOME VISIBLE AGAIN.

=

AFTER 30+ MIN., NO SOLID WAS VISIBLE ∴ THE NOW WHITE OPAQUE SAMPLE WAS PLACED BACK ON THE STIRRER/HOTPLATE

INITIAL TEMP. = 21°C
TARGET TEMP. = 60°C FOR ≈ 15 MORE MIN., OR CLARITY OF SAMPLE.

AFTER ANOTHE 15 MINUTES OF HEAT/MIXING, THE SAMPLE DID NOT CHANGE. IT REMAINS WHITE AND OPAQUE. IT WILL BE ALLOWED TO SETTLE AND FULLY COOL & BE OBSERVED FOR PRECIP. OR JSD 04/27/06

=

THE FOLLOWING MORNING (04/28/06) IT IS OBSERVED THAT SOME OF THE SOLID HAS, IN FACT, PRECIPITATED OUT OF THE 1044-117 SAMPLE.

IT IS DEEMED NECESSARY TO SUBMIT 1044-117 TO ANALYTICAL FOR AZELASTINE HCl ASSAY, AFTER IT HAS BEEN FILTERED AGAIN THROUGH A 0.45 µm ACRODISC PVDF FILTER.

N/A

To Page No. 119

Recorded by: [signature] Date 04/28/06 Verified by: Ami Balwani Date 10/25/07

Project No. —
TITLE ASTELIN + STEROID EXPERIMENT Book No. 1044 04/28/06

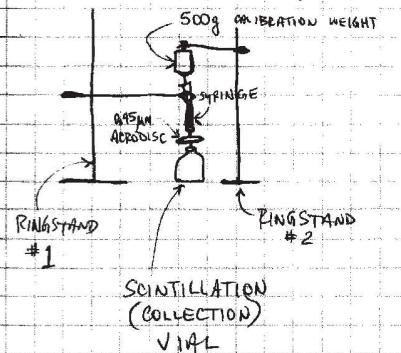
From Page No. 118

AS PER K. KALE, THE REMAINING SAMPLE FROM 1044-117 WILL BE PASSED THROUGH A 0.45 µm FILTER AND SUBMITTED FOR ANALYTICAL TESTING.

AT THE REQUEST OF ANALYTICAL, AN ADDITIONAL SAMPLE OF FLUTICASONE NASAL SPRAY SUPERNATANT (FILTERED THROUGH 0.45 µm ACRODISC) WILL BE PREPARED AND SUBMITTED FOR SIDE-BY-SIDE ANALYSIS/COMPARISON.

ONCE AGAIN A SAMPLE FROM LOT # C184889 OF FLUTICASONE PROPIONATE NASAL SPRAY, 50 mcg WAS OPENED. THE SAMPLE WAS SHAKEN TO SUSPEND THE MATERIAL, PLACED IN A CENTRIFUGE @ ≈ 3300 rpm FOR 1 HOUR, THE SOLIDS DISCARDED, AND THE SUPERNATANT POURED OFF.

THE SAMPLE WAS THEN POURED INTO A 10cc SYRINGE AND FILTERED THROUGH 5µm, 2µm, AND 1µm ACRODISC FILTERS (STACKED). THE REMAINING SAMPLE WAS POURED INTO A NEW 10cc SYRINGE AND PLACED INTO A HOME-MADE CONSTANT PRESSURE SYSTEM AND ALLOWED TO SLOWLY FILTER THROUGH A 0.45µm ACRODISC.



THE RESULTING SAMPLE WAS SUBMITTED TO ANALYTICAL (SYED) FOR TESTING, MARKED "#1044-119."

To Page No. N/A

Recorded by: [signature] Date 04/28/06 Verified by: Ami Balwani Date 10/25/07

From Page No. N/A

Physical Testing: Soma 700mg SR Tablets # 27-18-01c

Lot #	Target Wt. (mg)	Tablet #	Weight (g)	Thickness (mm)	Hardness (SCU)	Friability
27-18a-01c	1000	1	1.0144	6.57	28.6	Initial Wt (g) =
		2	1.0024	6.55	25.7	10.0540
		3	1.0080	6.56	22.8	Final Wt (g) =
		4	1.0087	6.53	27.8	10.0330
		5	1.0045	6.53	26.6	%Friable =
27-18b-01c	1000	1	1.0065	6.68	28.3	Initial Wt (g) =
		2	1.0063	6.70	25.6	10.0200
		3	1.0031	6.68	25.7	Final Wt (g) =
		4	1.0008	6.70	28.3	9.9990
		5	0.9881	6.64	26.6	%Friable =
27-18c-01c	1000	1	1.0049	6.80	28.2	Initial Wt (g) =
		2	0.9922	6.73	26.2	9.9440
		3	0.9977	6.75	23.5	Final Wt (g) =
		4	0.9915	6.75	27.2	9.9240
		5	0.9915	6.75	26.4	%Friable =

04/28/06

Physical Testing: Soma 700mg SR Tablets # 27-19-01c

Lot #	Target Wt. (mg)	Tablet #	Weight (g)	Thickness (mm)	Hardness (SCU)	Friability
27-19a-01c	1000	1	0.9916	6.43	25.7	Initial Wt (g) =
		2	0.9905	6.41	26.3	9.9470
		3	0.9913	6.43	23.4	Final Wt (g) =
		4	0.9925	6.43	27.0	9.9220
		5	0.9961	6.48	25.1	%Friable =
27-19b-01c	1000	1	1.0058	6.65	26.9	Initial Wt (g) =
		2	1.0095	6.68	28.1	10.0440
		3	1.0051	6.63	27.2	Final Wt (g) =
		4	1.0004	6.63	26.2	10.0260
		5	0.9995	6.62	27.2	%Friable =
27-19c-01c	1000	1	0.9745	6.55	23.2	Initial Wt (g) =
		2	0.9915	6.60	24.5	9.8170
		3	0.9845	6.58	23.1	Final Wt (g) =
		4	0.9842	6.59	22.1	9.7990
		5	0.9714	6.55	20.9	%Friable =

ACTUAL TESTING PERFORMED BY: A. FAVATA.
ELECTRONIC COPY SUBMITTED TO B. JOHNS.
TABLETS ARE (6) CLINICAL BATCHES, MANUFACTURED AT THE DECATUR FACILITY.

To Page No. N/A

Recorded by: [signature] Date 04/28/06 Verified by: GVT Date 29 OCT 07

From Page No. N/A

55.4500g = TARE WT. OF 1oz. FLINT GLASS JAR

58.6771g = JAR + STIR ROD

73.7000g = JAR + STIR ROD + ~15g PEG 400 (LOT # OP10-110)

0.0075g = AZELASTINE @ 0.05% ADDED, ALLOWED TO MIX 15 MIN. STILL UNDISSOLVED. MIX ANOTHER 15 min., UNDISSOLVED. MIXED ANOTHER 30 MIN., SOLUTION IS CLEAR.

0.0076g = AZELASTINE ADDED TO BRING TO 0.1% AFTER 1 HOUR, SOLUTION IS CLEAR.

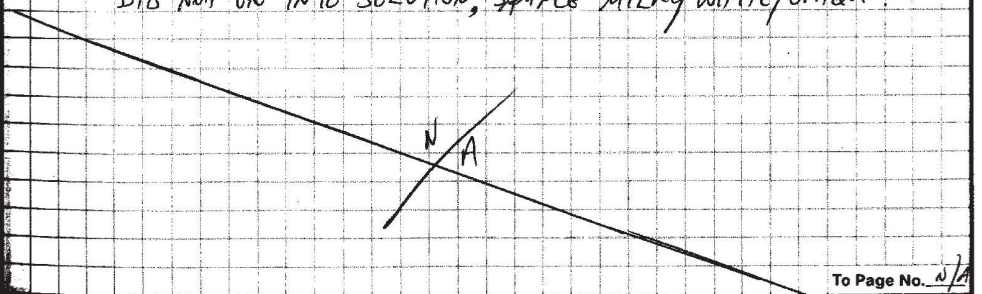
DECIDED TO RAISE AZELASTINE HCl TO 10 mg/mL, REFERENCING TABLE 5 OF THE NDA (pg. 03-63) WHICH STATES PEG 300 SOLUBILITY = 10.9mg/mL

0.1500g = TARGET AZL. HCl
- 0.0151g = ALREADY ADDED.
0.1349g = TO BE ADDED

0.1347g = AZELASTINE ADDED.

SAMPLE ALLOWED TO MIX OVERNIGHT.

DID NOT GO INTO SOLUTION, SAMPLE MILKY WHITE/OPAQUE.



To Page No. N/A

Recorded by: [signature] Date 05/1/06 Verified by: BM Balwani Date 10/25/07

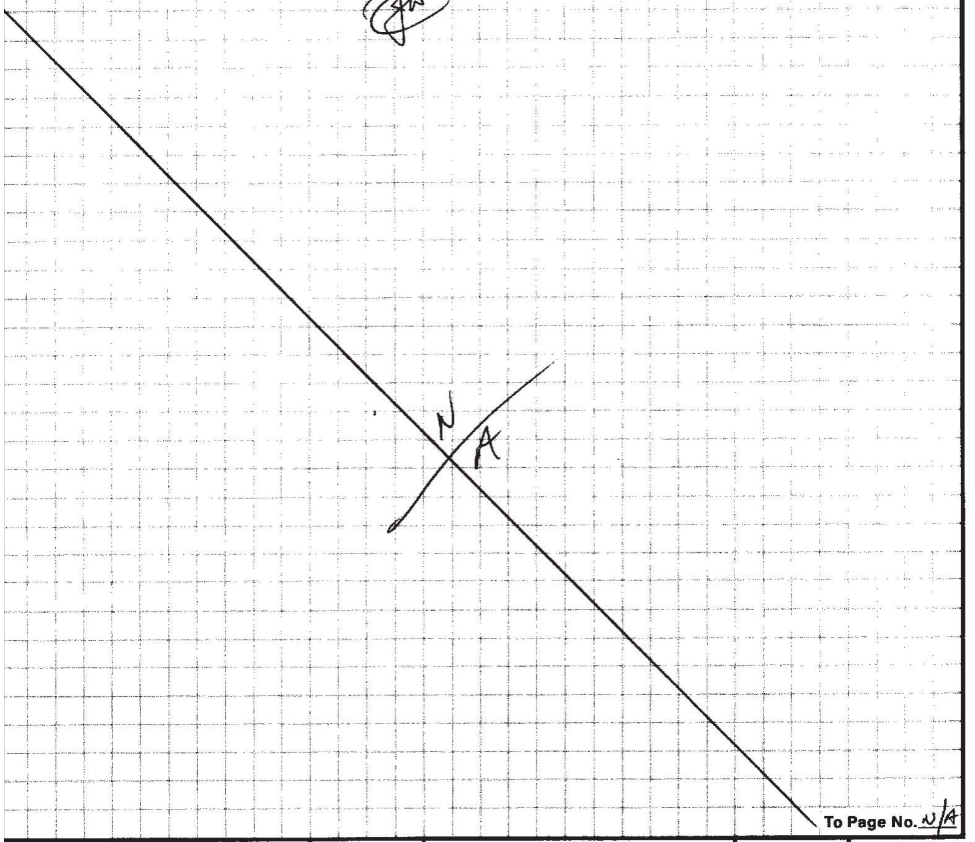
Project No. —

52 Book No. 1044 TITLE Methylene Blue Dye Test : Optivar 08/22/06

From Page No. 151

SPECTROPHOTOMETRY RESULTS:

12/05/06: FOLLOWING ABSENCE FROM WORK, SAMPLES WERE NOT TESTED IN AUGUST, AND ARE NOW PARTIALLY (AND SOME TOTALLY) EVAPORATED ∴ WILL NOT BE TESTED.



To Page No. N/A

Recorded by: [signature] Date 12/05/06 Verified by: Anil Balwani Date 10/25/07

Project No. —

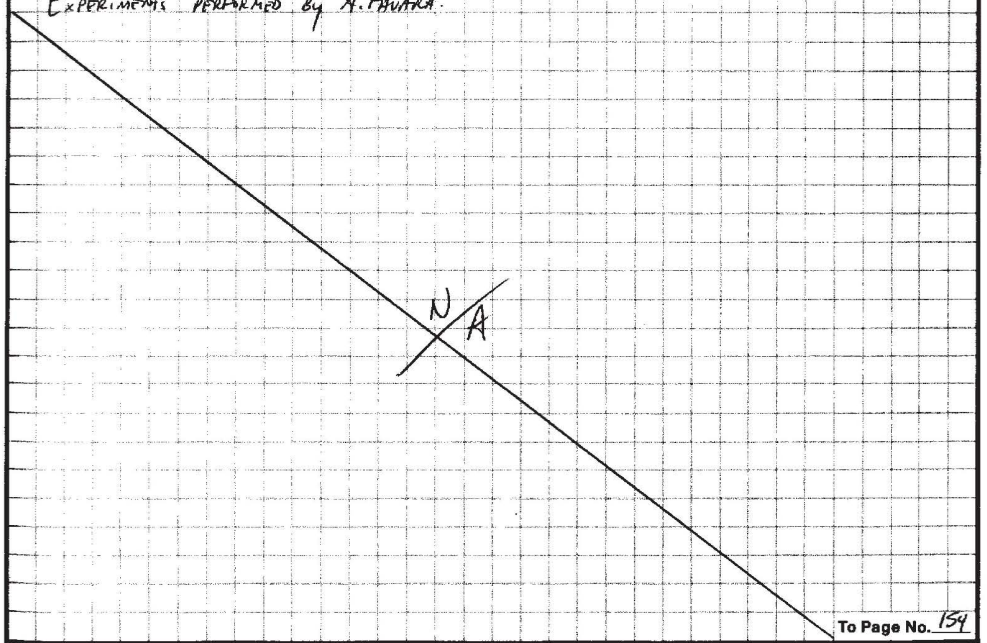
TITLE Asteliin + Steroid Experiments Book No. 1044 11/20/06 153

From Page No. N/A

(A.)
- 1050A - All Azelastine HCl added first 0.1%
- 1055 - All Azelastine HCl in solution, solution clear
- 1100 - All NaCMC added 0.2%
- 1130 - Solution clear - all is dispersed & in solution, clear

(B.)
- 1000A - NaCMC added 1.5%... clear after 25 min. mix
- 1030 - Added pinch of Azelastine HCl, does not seem to be dissolving
- 1055 - Added all of Azelastine HCl 0.1%, does not seem to be dissolving
- 100p - Azelastine HCl floating, not in solution.
- 300p - Azelastine HCl still undispersed / floating in solution and some stuck to mixing shaft.

Experiments performed by A. Fawara.



To Page No. 154

Recorded by: [signature] Date 12/05/06 Verified by: Anil Balwani Date 10/25/07

Project No. —

Book No. 1044 TITLE Astelin + Steroid Experiment 11/21/06

From Page No. 153

(A.) 1025a - Add all 15g Avicel RC-591 (1.5%)
Mix ≈15 min.
1045a - Add all Azelastine HCl (0.1%)

Result is a thick, white mixture. Azelastine HCl never goes into solution. Undissolved chunks are visible suspended in a gel-like mixture.

(B.) 1015a - Azelastine HCl 0.1% added to water, mixed for 5 minutes until dissolved.
1050a - Add Avicel RC-591 1.5% to ~~mix~~ solution #1 11/21/06 JDD, mixed for 30 minutes. Never becomes a uniform solution.

Separation occurs overnight. Top 1/3 is cloudy with some undissolved Azelastine HCl observed. Bottom 2/3 is thick, white, opaque mixture that has settled to the bottom.

Sample sent to analytical.

Experiments performed by A. Favara.

N/A

To Page No. 155

Recorded by:	Date	Verified by:	Date
John S. Wilcomb	12/05/06	Kal Balwani	10/25/07

Project No. —

TITLE Astelin + Steroid Experiment Book No. 1044 11/22/06

From Page No. 154

(A.) Azelastine HCl 0.15% added to water, mixed for 5 minutes until dissolved and clear.
Avicel RC-591, 1.5% added next, mixed for 30 minutes, does not mix evenly.
Again separation is observed.
Half the sample settles to bottom and is opaque white.
Top half is cloudy, but translucent.

(B.) Avicel RC-591, 1.5%, added to water
mixed for 15 minutes, resulting in a thick, opaque mixture.
A sample of this is submitted to analytical.

Experiments performed by A. Favara.

N/A

To Page No. N/A

Recorded by:	Date	Verified by:	Date
John S. Wilcomb	12/05/06	Kal Balwani	10/25/07

Project No. —
56 Book No. 1044 TITLE Methocel Solution Experiments 02/12/07

From Page No. 1048+184... Experiments Begun By A. Fauvrn.

Viscosity Measurement of Methocel Solutions

① Methocel ES (Lot # TB0901240) @ 5%

Measure 50 mL p. water, heat to 80°C. Add Methocel (5g) and stir until dispersed. Add 50 mL of cold p. water. Continue to mix until solution is clear. Allow to reach room temperature. Measure viscosity using B Rock Field Viscometer

Visc. Reading: 0.2 × 100 (Factor) = 20 cps

② Methocel ES (Lot # TB0901240) @ 25%

~~Vis~~ 05/03/07

Created with similar procedure, except quantities doubled for ease of addition.

Visc. Reading: 3.0 × 100 (Factor) = 300 cps

③ Methocel K100LVCR (Lot # TJ2012N31) @ 2.5%

Created with similar procedure to #2

Visc. Reading: 7.6 × 100 = 760 cps

④ Methocel K100LVCR (Lot # TJ2012N31) @ 10%

Created with same procedure

Viscosity Reading: ERROR ∴ Visc > 10,000 cps

⑤ Methocel K100MCR (Lot # UB11012N32) @ 2.5%

Created with same procedure

Viscosity Reading: ERROR ∴ visc > 10,000 cps

⑥ Methocel K100MCR (Lot # UB11012N32) @ 10%

Could not be produced.

To Page No. ____

Recorded by: John J. Williams IV Date 02/13/07 Verified by: a/f Date 24 Oct 07

Project No. —
TITLE Astelin 03-33 Pump Cleaning Eval. Book No. 1044 157

03/01/07

From Page No. N/A

Report No: PPD-07-07P Version: 00

Purpose: To determine if the current pump cleaning procedure provided to the consumer with Commercial Astelin is suitable for Formulation # 03-33.

Packaging: Batch 03-33-03c, 30 mL - Fill HDPE V-Bottom with Valois Splash Ring Pump. (34.5 mL, HDPE, Code # G1834, Lot # 0000002836).

Experiment: (Part 1) Remove dust caps & clips from 20 bottles of Azelastine HCl Solution 0.1% w/v, Form. 03-33, Batch 03-33-03c. In a hood actuate each pump at least 6 times or until a fine spray appears. Label half the bottles "upright" and the other half "prone." Number each set 1 through 10. Store the ten bottles upright in a 40°C/Ambient RH chamber. Store the ten bottles prone in the same chamber. After 2 weeks storage, remove bottles and attempt to actuate each.

Observations: All 20 samples performed in similar fashion. Nothing notable observed during w/e spraying, all samples performed normally. Initial 03/26/07

Samples were re-capped, neck-clips were replaced, and all samples were placed in 40°C/Ambient storage chamber AQ in room #142.

These samples will be retrieved after 2 weeks and each will be actuated (or at least attempted). If the pumps will not actuate, the patient instructions from the commercial product will be followed.

To Page No. 158

Recorded by: John J. Williams IV Date 03/05/07 Verified by: C. Yingze Date 3/26/07

PTX0142-00023