

(cont. from page start)

Purpose: To prepare Travatan BAC Free, 0.004% Formulations for stability testing, PET, sterility validation, and method validation.
Ch. Sach 7-2-04

Experimental:

Equipment:

Mettler AX 205 DR Analytical Balance, Asset No. 515840, Rm. C128 (referred to as Balance 1)
Mettler PG 5002 Balance, Asset No. 101265, Rm. C128 (referred to as Balance 2)
Orion 520A+ pH Meter, Asset No. A2220, Rm. C128
Corning Hot Plate Stirrer, Rm. C128
Millipore 0.22 µm Filter Unit (1000 mL and 150 mL)
Laminaire Laminar Flow Hood, Asset No. 13324-00, Rm. B-132
Conner Center Clean Suite Rm. C143

Formulations:

FID	Batch	Description
107047	04-37157	TRAVATAN BAC Free, 0.004%
107337	04-37158	TRAVATAN BAC Free, 0.004%-no Zinc Chloride
107339	04-37159	TRAVATAN BAC Free, 0.004%-no Boric Acid
107340	04-37160	TRAVATAN BAC Free, 0.004%-no Sorbitol or Propylene Glycol
107343	04-37238	TRAVATAN BAC Free, 0.004%-no Boric Acid - 10X Zinc Chloride

Compounding Procedures: (see attached batch records with adjunctive data)

- A. FID 107047 Batch 04-37157 TRAVATAN BAC Free, 0.004%
1. Tare weighed a clean glass bottle with a stir bar. (Balance 2)
 2. Added about 50 % of batch water.
 3. Weighed and added the batch quantity of the following excipients to the ^{bottle} beaker: boric acid, sorbitol, 0.1% zinc chloride stock solution. Stirred the solution to dissolve these ingredients. (Balance 2)
 4. Added the batch quantity of AL-6221 0.2%/25% HCO-40/37.5% Propylene Glycol Stock Solution to the ^{bottle} beaker, and Qsed to 95% of batch weight with purified water. (Balance 2)
 5. Stirred to mix the solution. Measured the pH.
Initial pH = 4.02
 6. Adjusted pH if necessary.
Amount of 1N HCL added = N/A
Amount of 1N NaOH added = 16.4 mL
 7. Qsed to 100% of batch weight. (Balance 2) Final pH = 6.057

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bottle @ #5 7-2-04

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Verified By: Bhagwati Kobra

Date: 7/20/04

Entered By: Ch. Sach

Date: 7-19-04

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B. FID 107337 Batch 04-37158 TRAVATAN BAC Free, 0.004%-no Zinc Chloride

AS 7-2-04

1. Tare weighed a clean glass bottle with a stir bar. (Balance 2)
2. Added about 50 % of batch water.
3. Weighed and added the batch quantity of the following excipients to the ^{bottle AS 7-2-04} beaker: boric acid and sorbitol. Stirred the solution to dissolve these ingredients. (Balance 2)
4. Added the batch quantity of AL-6221 0.2%/25% HCO-40/37.5% Propylene Glycol Stock Solution to the ^{bottle AS 7-2-04} beaker, and Qsed to 95% of batch weight with purified water. (Balance 2)
5. Stirred to mix the solution. Measured the pH.
Initial pH = 4.06
6. Adjusted pH if necessary.
Amount of 1N HCL added = N/A
Amount of 1N NaOH added = 8.0ml
7. Qsed to 100% of batch weight. (Balance 2) Final pH = 6.062

AS 7-2-04

AS 7-2-04

C. FID 107339 Batch 04-37159 TRAVATAN BAC Free, 0.004%-no Boric Acid

AS 7-2-04

1. Tare weighed a clean glass bottle with a stir bar. (Balance 2)
2. Added about 50 % of batch water.
3. Weighed and added the batch quantity of the following excipients to the ^{bottle AS 7-2-04} beaker: sorbitol and 0.1% zinc chloride stock solution. Stirred the solution to dissolve these ingredients. (Balance 2)
4. Added the batch quantity of AL-6221 0.2%/25% HCO-40/37.5% Propylene Glycol Stock Solution to the ^{bottle AS 7-2-04} beaker, and Qsed to 95% of batch weight with purified water. (Balance 2)
5. Stirred to mix the solution. Measured the pH.
Initial pH = 5.965
6. Adjusted pH if necessary.
Amount of 1N HCL added = N/A
Amount of 1N NaOH added = N/A
7. Qsed to 100% of batch weight. (Balance 2) Final pH = 5.953

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End of day Ad. Sub 7-2-04

AS 7-6-04

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Filter: REF LN11118:78

- Filters used: 1 Liter Millipore Filter Unit Lot H2NND3007 Expires Oct. 2005
150 mL Millipore Filter Unit Lot H4CN79786 Expires Mar. 2007
1. Filter 1000mL of Batch 04-37157-2 ^{AS 7-6-04} 04-37157 using a 1 Liter Filter Unit. Label as Lot 04-37157-2 and print Lot Report. Cap Filter unit under laminar flow hood.
 2. Filter 150mL of Batch 04-37157 using a 150mL Millipore Filter unit. Label as Lot 04-37157-3 and print Lot report. Cap Filter unit under laminar flow hood.

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Date

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Date

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REF LN11118:79

Filter (cont):

3. Filter Batch 04-37158 using two 1 Liter Millipore Filter Units. (1000mL each unit).
Label as Lot 04-37158-1 and print Lot report. Cap Filter unit.

4. Filter Batch 04-37159 using two 1 Liter Millipore Filter Units. (1000mL each unit).
Label as Lot 04-37159-1 and print Lot report. Cap Filter units.

AS 7-6-04

PET submission of Lot 04-37157-3:

Submit Lot 04-37157-3 for PET, USP. Date submitted 7-6-04 by Adrian Sauceda
LIMS Submission ID: 100076642

AS 7-6-04

Sterility Validation:

Deliver Lot 04-37157-2 to Kathleen Alford for sterility validation.
Delivered on 7-6-04 by Adrian Sauceda (1 Liter delivered)

AS 7-6-04

Method Validation:

Deliver Lot 04-37158-1 and Lot 04-37154-1 to Louann Cruz of Analytical
Chemistry for Method Validation. Two Liters of each Lot delivered on 7-6-04
by Adrian Sauceda.

AS 7-6-04

Lot Disposition Report:

Print Lot Disposition Reports for Lots 04-37157-2, 04-37157-3, 04-37158-1
and 04-37159-1. Place with adjunctive data.

End of day Ad. Sauceda 7-6-04

AS 7-7-04

Fill: (In Conner Center Clean Suite)

Fill 4mL spp bottles with 2.5mL of Batch 04-37157. Fill 800 bottles.
HDPE closures used. Label ziplock bags as Lot 04-37157-1 to
store bottles. Bottles not labeled at this time since most will be
used for stability testing. See lot report for packaging information.

*Note: Remainder of Batch 04-37157 stored in refrigerator for later use.

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Date

Entered By:

Date

(cont. from page 79) AS 7-8-04

D. FID 107340 Batch 04-37160 TRAVATAN BAC Free, 0.004%-no Sorbitol or Propylene Glycol

AS 7-8-04

1. Tare weighed a clean glass beaker with a stir bar. (Balance 2)
2. Removed the stir bar. Weighed and added the batch quantity of HCO-40 directly in the beaker. (Balance 1)
3. Added about 50 % of batch quantity of purified water.
4. Stirred for at least 15 minutes until HCO-40 is dissolved.
5. Weighed and added the batch quantity of the following excipients to the beaker: boric acid and 0.1% zinc chloride stock solution. Stirred the solution to dissolve these ingredients. (Balance 1)
6. Weighed the batch quantity of AL-06221 using a spatula. (Balance 1)
The spatula was placed in the bottle with the end containing AL-06221 immersed in the solution.
7. QSeD to 95% of batch weight with purified water. (Balance 2)
8. Covered the opening with parafilm to minimize evaporation. Stirred overnight to dissolve the AL-06221.

Lot 7-8-04

Stirring Start time and date: 4:15 pm 7-8-04 End of day AS 7-8-04

AS 7-9-04 Stirring Stop time and date: 8:30 am 7-9-04

9. Measured the pH. Initial pH = 4.916
10. Adjusted pH if necessary.
Amount of 1N HCL added = N/A
Amount of 1N NaOH added = 0.06g

11. QSeD to 100% of batch weight with purified water. (Balance 2)

AS 7-9-04

AS 7-9-04
Filter:

Filter all 150mL of Batch 04-37160 using a 150mL Millipore Filter Unit. Label as Lot 04-37160-1 and print Lot report. Cap Filter unit under Laminar flow hood.

AS 7-9-04

PET Submission of Lot 04-37160-1:

Submit Lot 04-37160-1 for PET, USP. Date submitted 7-9-04 by Adrin Saucedo
LIMS Submission ID: 100076246

ADJUNCTIVE DATA AS 7-19-04

AS 7-9-04

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Lot Disposition Report:

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Print Lot Disposition Report for Lot 04-37160-1. Place with adjunctive data.

End of day, ed: Saucedo 7-9-04

N/A AS 7-9-04

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Verified By:

Date

Entered By:

Date

(cont. from page 80) AS 7-12-04

E. FID 107343 Batch 04-37328 TRAVATAN BAC Free, 0.004%-no Boric Acid - 10X Zinc Chloride

AS 7-12-04

1. Tare weighed a clean glass beaker with a stir bar. (Balance 2)
2. Removed the stir bar. Weighed and added the batch quantity of HCO-40 directly in the beaker. (Balance 2)
3. Added about 50 % of batch quantity of purified water.
4. Stirred for at least 15 minutes until HCO-40 is dissolved.
5. Weighed and added the batch quantity of the following excipients to the beaker: sorbitol, propylene glycol, and zinc chloride. Stirred the solution to dissolve these ingredients. (Balance 1)
6. Weighed the batch quantity of AL-06221 using a spatula. (Balance 1)
The spatula was placed in the bottle with the end containing AL-06221 immersed in the solution.
7. QSeD to 95% of batch weight with purified water. (Balance 2)
8. Covered the opening with parafilm to minimize evaporation. Stirred overnight to dissolve the AL-06221.

ok
7-13-04

Stirring Start time and date: 2:00 pm 7-12-04 End of day 7-12-04

AS 7-13-04 (Stirring Stop time and date: 8:30 am 7-13-04)

9. Measured the pH. Initial pH = 6.535
10. Adjusted pH if necessary.
Amount of 1N HCL added = 0.07g
Amount of 1N NaOH added = N/A

11. QSeD to 100% of batch weight with purified water. (Balance 2)

(C) AS 7-13-04
End of day AS 7-13-04

AS 7-13-04

Filter:

Filter Batch 04-37328 using two 1 Liter Millipore Filter units (1000 mL each unit)
Label as Lot 04-37328-1. cap Filter unit

ADJUNCTIVE DATA

AS 7-19-04

AS 7-13-04

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Method Validation:

Deliver Lot 04-37328-1 to Louann Cruz of analytical chemistry for Method Validation. Two Liters delivered by Adrian Saucedo on 7-13-04

AS 7-13-04

Lot 04-37157-1 Closures:

Under Laminar Flow hood change the closures of Lot 04-37157-1 (800 bottles) from HDPE closures to p/p closures. Print lot report.

End of day Adrian Saucedo 7-13-04

AS 7-14-04

Lot Report: Print Lot Report for Lot 04-37238-1. Place in adjunctive notebook.

Lot Disposition Report: Print Lot Disposition report for Lot 04-37238-1

Place in adjunctive notebook.

End of day AS 7-14-04 (cont. on page 82)

Verified By: 1-

Date

Entered By: sl. Saucedo

Date

7-14-04

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