



DEPARTMENT OF HEALTH & HUMAN SERVICES

Division of Biological Standards & Quality Control, Office of Compliance & Biologics Quality,  
Center for Biologics Evaluation & Research, Food & Drug Administration

MEMORANDUM

**From** Alfred Del Grosso, Ph.D., LACBRP/DBSQC/OCBQ HFM-682  
Tao Pan, Ph.D., LACBRP/DBSQC/OCBQ HFM-682  
Ritu Agarwal, Ph.D., LACBRP/DBSQC/OCBQ HFM-682  
Mark Levi, Ph.D., LACBRP/DBSQC/OCBQ HFM-682  
Hsiaoling Wang, Ph.D., LACBRP/DBSQC/OCBQ HFM-682  
**To** STN 125512/0  
**Through** Lokesh Bhattacharyya, Ph.D., Chief, LACBRP, OCBQ/DBSQC, HFM-682  
William M. McCormick, Ph.D., Director, OCBQ/DBSQC, HFM-680  
**Sponsor** Baxter Healthcare Corporation  
**Product** Human coagulation factor VIII, OCTANATE<sup>®</sup>, STN: 125512  
**Subject** DBSQC Review Memo for Chemistry Related Test  
Methods for Antihemophilic Factor (Recombinant),  
Porcine Sequence (OBI-1) from Baxter Healthcare  
Corporation, STN 125512

Review Summary and Recommendation

Specific Assays Reviewed and addressed in this memo include:

- 1) Water Content by ---(b)(4)---
- 2) Polysorbate 80 by ---(b)(4)-----
- 3) Chloride and Citrate by -----(b)(4)-----
- 4) Sodium and Calcium by -----(b)(4)-----
- 5) Protein Content and -----(b)(4)-----
- 6) Tris by (b)(4)
- 7) Sucrose by -----(b)(4)-----
- 8) -----(b)(4)-----
- 9) Physical and Chemical Attributes: Appearance, Reconstitution  
Time, (b)(4)



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Conclusion

The method is described in sufficient detail and has been adequately validated for its intended use.

**3. Chloride and Citrate by ----- (b)(4) -----  
Reviewer: Tao Pan, Ph.D.**

Chloride and citrate ions present in the drug product -----  
----- (b)(4) -----  
----- . A detailed SOP and  
validation report were provided for this analytical method.

**Submitted Information reviewed:**

- 3.2.P.5.1. Control of Drug Product, Specifications
- 3.2.P.5.2 Control of Drug Product, Analytical Procedures,  
AP Chloride and Citrate
- 3.2.P.5.3 Control of Drug Product, Validation of Analytical Procedures,  
VAP Citrate and Chloride
- VAP PPD 042142-01-02 Validation Report for the Analysis of Chloride and Citrate  
Ions in rp FVIII ObI-1 ----- (b)(4) ----- OBI-1 Final Drug  
Product-and ----- (b)(4) -----
- Amendment 0.28 CR-14-0193-AA-01 Supplemental Method Validation Chloride and  
Citrate Ions -b(4)---

For the final OBI-1 drug product, chloride and citrate -----  
----- (b)(4) -----  
----- , and that for  
citrate is --- (b)(4) ----- . The chloride and citrate concentrations in OBI-I final products  
were determined using an ----- (b)(4) ----- .

Method

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Conclusion: The method is described in sufficient detail and is adequately validated for its intended purpose.

**5. Protein Concentration -----(b)(4)-----**  
**Reviewer: Mark Levi, Ph.D.**

Documents reviewed:

Method Description-Protein content Assay

Method Validation Report – Protein content Assay

- 3.2.P.5.2.: “Protein and -----(b)(4)----- Content ---(b)(4)----”

- 3.2.P.5.3.: “Validation of Analytical Procedures ---(b)(4)----”

- Module 3.2.S.4.3-VR-124 “Validation of test method TQC-003-03; Analysis of -----(b)(4)----- Protein Concentration in rp-FVIII by ---(b)(4)----”

Document 119202-RPT “Supplemental Analytical Method Validation for the Analysis of ---(b)(4)----- Protein Concentration in rp-FVIII by ---(b)(4)----”



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Conclusion

Review: The method is adequately described and has been sufficiently validated.

**6. Tris by (b)(4)**

**Reviewer: Hsiaoling Wang, Ph.D.**

Submitted Documents

- Cover letters, dated Oct. 8, 2013 and Nov. 8, 2013 respectively
- 3.2.P.1 Description and Composition of Drug Product [OBI-1]
- 3.2.P.5.1 Specifications
- 3.2.P.5.2 Analytical Procedures “Tris (trishydroxymethylaminomethane)”
- 3.2.P.5.4 Batch Analyses
- 3.2.P.5.6 Justification of Specification (s) [Tris]
- SOP “Method for the Analysis of Tris in rp-FVIII (OBI) ----- (b)(4) -----, Lyophilized Finished Product, ----- (b)(4) -----”
- Validation Report for the Analysis of Tris in rp-FVIII (OBI-1) ----- (b)(4) ----- Substance, OBI-1 Final Drug Product, ----- (b)(4) -----
- 1.11.1 Quality Information Amendment 125512/0.19, received May 9, 2014
- Updated SOP M2937.04 “Method for the Analysis of Tris in rp-FVIII (OBI-1) ----- (b)(4) -----, Lyophilized Finished Product, ----- (b)(4) -----”
- 1.11.1 Quality Information Amendment 125512/0.28 (dated Aug. 13, 2014)



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Conclusion: The procedure for TRIS is adequately described and validated for the intended use.

**7. Sucrose by ----- (b)(4) -----  
Reviewer: Hsiaoling Wang, Ph.D.**

Drug Product (DP) specification for the excipient sucrose is ---(b)(4)---- The sponsor provided the method description in 3.2.P.5.2 and the validation report (SOP version 01as attachment 1 in the validation report).



4 Pages Determined to be Not Releasable: (b)(4)

**8. Physical and Chemical Attributes**

**Reviewer: Alfred Del Grosso, Ph.D**

- a. Appearance**
- b. Reconstitution Time**
- c. (b)(4)**

Specifications for Appearance (Pre-Reconstitution) is described as “white cake”, Appearance (Post-Reconstitution) is “Clear, colorless solutions, essentially free of visible particules. Reconstitution time is specified as -----(b)(4)-----  
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Documents Reviewed

- 3.2.P.5.2 Analytical Procedures “Appearance”, “Visible Particles”, “Reconstitution Time and Appearance”, “(b)(4)”
- 3.2.P.5.4 Batch Analyses
- 3.2.P.5.6 Justification of Specifications
- 3.2.P.5.3 Validation of Analytical Procedures
- AMV-RP-MVR(1)-M002/M045 Method Validation Report for the Determination of (b)(4) in rpFVIII Drug Product

Appearance of the sample before reconstitution is performed in accordance with ---(b)(4)-  
----- using a viewing station with white and dark panels and comparison to a reference photograph.

For post-reconstitution appearance and reconstitution time, -----  
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----- Comparison post-reconstitution is made against WFI or purified water. (b)(4) is determined in accordance with ---(b)(4)----- after reconstitution with -----(b)(4)-----.

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Conclusion: Procedures for “Appearance”, “Visible Particles”, “Reconstitution Time and Appearance” and “(b)(4)” are adequately described and acceptable for use.