



U.S. Food and Drug
Administration

Center for Biologics Evaluation and Research Laboratory Quality System

Laboratory Quality Product Testing Policy (TP)

**Title: Wilate (Octapharma) von Willebrand Factor/Coagulation Factor VIII
Complex (Human)**

Document ID: 125251

Cross-Reference Code: CBXX-4.4-TP-166

Revision Level: 01

Issue Date:

Effective Date:

Total Pages: (including this cover page)

WARNING: The information contained in this document is **CONFIDENTIAL** and should not be released. See FOIA exemption regarding circumvention.

Testing Plans document how CBER currently anticipates regulating licensed products including the circumstances under which CBER testing may be used to evaluate a lot of licensed product. It is the responsibility of each Product Office to develop Lot Release Testing Plans for the licensed products under its purview.

Product Trade Name:

Wilate

**License Product Name
(Proper Name):**

von Willebrand Factor/Coagulation Factor VIII Complex
(Human)

LQDB Product ID:

002200

License Number:

1646

STN (RMS-BLA):

125251

Applicant (Supplier):

Octapharma Pharmazeutika Produktionsges.m.b.H

Signatures Required to Approve or Update Testing Plan

Director, DPQ/OVRR:

William McCormick, Ph.D.

Director, OBRR:

Ginette Michaud, M.D.
For Jay S. Epstein, M.D.

Director, DMPQ/OCBQ:

John A. Eltermann, Jr.

Center Lab Quality Mgr:

Deborah L. Jansen

Mode of Product Regulation

Based upon Product Office assessment of the product, including relevant manufacturing, safety, clinical and other considerations, determine which form of CBER review and or release of manufactured product lots is necessary.

Lot Release – Manufacturer may not distribute product until receiving lot-specific release from CBER.

Surveillance – Manufacturer may distribute product without lot-specific release from CBER. Manufacturer is required, according to the terms of the license, to periodically provide CBER with lot-specific testing information and possibly samples.

Exempt – Manufacturer is free to distribute product post-licensure without supplying any additional information or samples to CBER.

Lot Release

Protocol Review

☐

Protocol Review and
Confirmatory CBER Testing

☒

Alternative to Lot Release

Surveillance

☐

Exempt

☐

Justification for Mode of Regulation:

Briefly, describe how the indicated Mode of Regulation supports CBER's mission to ensure the purity, potency, safety, efficacy, and availability of this biological product including justification for any confirmatory CBER product testing, per 21 CFR 610.2(a). Additionally, for products on Surveillance, summarize the requirements for submission of lot-specific information and sample (if required) as described in the license.

Brief Description: Wilate is manufactured from cryoprecipitate harvested from plasma collected in the U.S. The cryoprecipitate is reconstituted in a buffer and treated with aluminum-hydroxide followed by two different chromatography steps, ultra- and diafiltration, and sterile filtration. The manufacturing process includes treatment with an organic solvent/detergent (S/D) mixture, composed of tri-n-butyl phosphate (TNBP) and Octoxynol-9, and a terminal dry-heat (TDH) treatment step [at +100°C (212°F) for 120 minutes at a specified residual moisture level of -(b)(4)-]. The process thus provides two independent and effective virus inactivation procedures, namely S/D treatment in bulk and TDH treatment of the lyophilized product in final container. Wilate is indicated for the treatment -----(b)(4)----- of spontaneous and trauma-induced bleeding episodes in severe von Willebrand disease (VWD), and in mild and moderate VWD where the use of DDAVP treatment is ineffective or contra-indicated.

Mode of Lot Release: Wilate will be released by Protocol Review and Confirmatory Testing for von Willebrand Factor activity using the von Willebrand Factor Ristocetin Cofactor Activity Assay (vWF:Rcof). Testing for vWF:RCoF activity of each lot will ensure the quality of the product as it is related to the potency and efficacy.

The following discussion forms the rationale for the testing plan for release of this biologic.

Safety and Purity – Safety and purity of the final product submitted to CBER will be evaluated from the information provided in the lot release protocol. For Lot Release Protocol review refer to Appendix 1 on page 3.

Potency and Identity – Potency and identity of the final product submitted to CBER will be evaluated from the information provided in the lot release protocol. Potency test for von Willebrand Factor, Ristocetin Cofactor Activity (VWF:RCo) will be performed on 100% of the lots submitted to assure product quality. For Lot Release Protocol review refer to Appendix 1 on page 3.

Document ID number	Test Method	Test Specifications	Testing Frequency
000220	von Willebrand Factor, Ristocetin Cofactor Activity Assay (VWF:RCo)	± 30 % of labeled potency value	100 %

Lot Testing algorithm(s):

For each Test Method listed above describe how the indicated frequency of testing supports the assurance of product quality.

The Algorithm indicating frequency of testing according to each Test Method listed above should be consistent with the need to assure safety, purity, or potency risks and support CBER's decision to implement Lot Release testing for this product.

For each method with testing frequencies other than 100%, describe how lots are pre-selected for testing, i.e. random number table, every nth lot submitted, first X lot(s) submitted per time period, decision tree, etc.

The Laboratory of Hemostasis (LH) or the Division of Product Quality (DPQ) will test every lot of Wilate, manufactured for market release, for von Willebrand Factor (VWF:RCo) Activity as well as review every Lot Release Protocol.

Conditions anticipated to require temporary over-ride of algorithm:

Specify conditions justifying algorithm over-ride; i.e. Public Health Considerations (e.g. temporary product shortage, sudden increase in demand), Operational Considerations (e.g. temporary unavailability of resources), Lot-specific Compliance Considerations (e.g. questions raised during lot release protocol review).

- Public Health Considerations (e.g. temporary product shortage, sudden increase in demand)
- Operational Considerations (e.g. temporary unavailability of resources)
- Lot-specific Compliance Considerations (e.g. questions raised during lot release protocol review)

Specifications for Review of Lot Release Protocols

Appendix 1: Specifications for tests on Final Container

Reviewed by DPQ

<i>Test</i>	<i>Specification</i>
Sterility	No growth
Endotoxin -(b)(4)-	------(b)(4)-----
General Safety	Pass
Moisture (water content)	------(b)(4)----

Reviewed by DH/OBRR

<i>Test</i>	<i>Specification</i>
Dissolution (solubility) time	-(b)(4)--
Total Protein	≤1.5 mg/mL
-(b)(4)-	-(b)(4)-
Potency VWF:RCo Activity	------(b)(4)-----