



## MEMORANDUM

Department of Health and Human Services  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
Office of Blood Research and Review

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**To:** BLA STN 125555/0, Basil Golding MD, DHRR & Jiahua Qian, IOD/RPM Staff  
**From:** Andrey Sarafanov, PhD, DHRR/ LH  
**Through:** Mark Weinstein, PhD, IOD  
**Applicant:** Octapharma Pharmazeutika Produktionsges.m.b.H.  
**Product:** Antihemophilic Factor (Recombinant) [NUWIQ]  
**Indication** Control and prevention of bleeding episodes in adults and children with Hemophilia A  
**Subject:** Designation of STN 125555/0/43 as a Major Amendment  
**CC:** Tim Lee, PhD, DHRR/LH

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### BACKGROUND

Octapharma Pharmazeutika Produktionsges.m.b.H. (Octapharma) submitted an original Biologics License Application (BLA) under STN 125555 for Antihemophilic Factor (Recombinant) [NUWIQ], which FDA received on June 5, 2014. In this submission, NUWIQ is indicated for control and prevention of bleeding in patients with FVIII deficiency (Hemophilia A). The active ingredient in NUWIQ™ is B-domain deleted, recombinant Factor VIII (BDD-rFVIII), expressed in human cells. The deleted B-domain is (b) (4). The commercial product is a lyophilized powder in a crimp-sealed, stoppered, glass vial, available in nominal potencies of 250, 500, 1000, or 2000 international units (IU). The product is reconstituted with sterile water for injection provided in a pre-filled syringe.

The initial action due day was June 5, 2015. However, upon review and communication with Octapharma, FDA realized that in addition to the indication for control and prevention of bleeding episodes...” (i. e. on-demand), the company also desired to have an indication for prophylaxis. FDA found, however, that the submitted information in the format it received did not support the latter indication. At the late-cycle meeting (a teleconference) with Octapharma on May 4, 2015, the company maintained that the data supporting the use of NUWIQ for prophylaxis were actually included in the submission. FDA responded that these data are not in a format suitable for review by a statistical reviewer, and that if Octapharma is seeking to have NUWIQ approved for prophylaxis, they should resubmit the data in a format appropriate for review. On May 4, 2015, FDA sent a letter to the company, which described the specific requirements for resubmission. On May 8, 2015 (Amendment 43), Octapharma provided the requested data in the updated eCTD file.

### DESIGNATION OF AMENDMENT 125505/0/43 AS MAJOR

As the data in the Amendment 43 require significant amounts of time and effort to review, meeting the action due date of June 5, 2015 is not possible. SOPP 8402 defines such an amendment as a major amendment that extends the review clock. According to section V.D., a major amendment may contain a substantial amount of new data not previously submitted to the pending BLA or reviewed by the Agency, which is the case in our current situation. Based on the above, on behalf of the review committee, I recommend that the amendment 125555/0/43 be designated as a major amendment with a three month extension of the action due date.