



**FOOD AND DRUG ADMINISTRATION**  
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

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MEMORANDUM

**From:** Laura Wood, OBRR/DH/LH

**Through:** Timothy Lee, Ph.D., Acting Lab Chief, OBRR/DH/LH

**To:** The file of STN 125351/0,  
Natalya Ananyeva, Ph.D., Committee Chairperson, OBRR/DH/LH  
Jie He, RPM, OBRR/DBA/RPMB

**Company:** Nycomed Danmark ApS (Nycomed)

**Product:** Fibrin Sealant Patch (TachoSil)

**Subject:** Final review of adventitious agent safety evaluation for the fibrinogen component supplied by CSL Behring GmbH

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**Summary**

TachoSil is a whitish sponge of equine collagen, coated with fibrinogen and thrombin of human origin. The collagen sponge serves as a flexible and mechanically-stable carrier for the active substances. Riboflavin is added to the human protein components during manufacture as a yellow colorant to indicate the active side of the patch. Both the fibrinogen and thrombin are provided -----(b)(4)-----  
-----.

Separate BLA's have been submitted to CBER for the fibrinogen and thrombin components. The fibrinogen component is called Fibrinogen Active Substance -(b)(4)-, and is provided to Nycomed as a -----(b)(4)-----  
----- fibrinogen,  
------(b)(4)----- human albumin, -----(b)(4)----- L-arginine hydrochloride, ---(b)(4)---  
--- sodium chloride -----(b)(4)----- sodium citrate.

Despite some minor differences regarding final manufacturing procedures and strength, Fibrinogen Active Substance -(b)(4)- is comparable to -----(b)(4)-----  
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----- (b)(4) -----. The same viral reduction study results are quoted for Fibrinogen Active Substance as for ---- (b)(4) ----.

**Viral Reduction Table**

The following table is taken from **Table 3.2.A.2.3.2-1: Mean (log<sub>10</sub>) virus inactivation/reduction for Fibrinogen Active Substance - (b)(4) -**:

[  
--(b)(4)--  
]

**Information request:**

During review, the following information request was communicated to Nycomed:

1. Concerning Table 3.2.A.2.3.2-1 in the original submission:

----- (b)(4) -----  
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----- (b)(4) -----  
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2. Concerning Table 2 in your package insert, submitted in Amendment 6:

- A. The PRV and HSV reductions cannot be combined. They may be listed separately.
- B. As in Table 3.2.A.2.3.2-1, the ----- (b)(4) ----- step reductions cannot be combined. Therefore, the total log<sub>10</sub> reductions should be:
  - ≥ 9.6 for HIV

- $\geq 11.2$  for BVDV
- 4.4 for CPV
- $\geq 6.7$  for HAV

These changes were requested in conjunction with other changes in the package insert. The changes were made. The  $1.6 \log_{10}$  PRV reduction was mentioned in a footnote underneath the table.

### **Conclusion**

The appropriate changes were made and the package insert is acceptable from a CMC perspective.