



FOOD AND DRUG ADMINISTRATION
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

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

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)-----

----- (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 (log₁₀) 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) -----

----- (b)(4) -----

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 log₁₀ reductions should be:
 - ≥ 9.6 for HIV

- ≥ 11.2 for BVDV
- 4.4 for CPV
- ≥ 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.