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Date Received: _____
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Assigned by: _____
Completed date: _____
Reviewer Initials: _____
Supervisory Concurrence: _____

Intercenter Request for Consultative or Collaborative Review Form

To: Dr. David Krause
Center: CDRH
Division: ODE/DSORD/PRSB
Mail Code: HFZ-410
Consulting Reviewer Name:
Building/Room #: Corporate Building (CORP)
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From: Nannette Cngungun
Center: CBER/OBRR
Division: DBA
Mail Code: HFM-392
Requesting Reviewer: Natalya Ananyeva, Ph.D.
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RPM/ Mail Code: Jic 11c, HFM-380
Requesting Reviewer's Concurrence
Supervisor's Name: Tim Lee

APPROVED

By Natalya Ananyeva at 1:23 pm, Jul 07, 2009

Receiving Division: If you have received this request in error, you must contact the request originator by phone immediately to alert the request originator to the error.

Date of Request: 7/7/09
Submission/Application Number: BL 125351.0

Requested Completion Date:
Submission Type: Original BLA

Type of Product: Device-biologic combination

Submission Receipt Date: June 6, 2009

Official Submission Due Date: April 5, 2010

Name of Product: Fibrin Sealant Patch

Name of Firm: Nycomed

Intended Use: (b)(4) and as an adjunct to hemostasis in cardiovascular surgery

Brief Description of Documents Being Provided (e.g., clinical data – include submission dates if appropriate): Electronic submission

Documents to be returned to Requesting Reviewer? No.

Complete description of the request. Include history and specific issues, (e.g., risks, concerns), if any, and specific question(s) to be answered by the consulted reviewer. The consulted reviewer should contact the request originator if questions/concerns are not clear. Attach extra sheet(s) if necessary:

Type of Request: Consultative Review

Fibrin Sealant Patch from Nycomed, Denmark, is a ready-to-use wound sealant product consisting of two active substances - human fibrinogen and human thrombin – coated onto a collagen sponge. The proposed trade name is TachoSil. The Collagen Sponge serves as a flexible and mechanically-stable carrier for the active substances to ensure

their in-place position. Human Fibrinogen Active Substance and Human Thrombin Active Substance are supplied by (b)(4). Fibrin Sealant Patch is a combination product where the Collagen Sponge is classified as a Medical Device.

The Collagen Sponge is formed by Collagen (b)(4) horse tendons. This Collagen (b)(4) is a highly conserved protein among all mammalian species. The starting material horse tendons are supplied by certified horse (b)(4) species slaughterhouses (b)(4) audited and approved by Nycomed.

Collagen Sponge has been routinely manufactured as a licensed product for the Nycomed predecessor products (proprietary names -TachoComb and TachoComb H – on the European market). In the production of Fibrin Sealant Patch clinical trial material, no critical changes in the manufacturing process of Collagen Sponge were made. Some improvements were implemented from the first clinical batches up to present. With the expansion of TachoSil production capacity, an expansion of production capacity for Collagen Sponge was also included.

Consultative review is requested from CDRH to comment on the following:

- Tendon Supplier Qualification Requirements (should it be also addressed to CVM?)
- Collagen Sponge Manufacturing Process (from (b)(4) Horse Tendons to preparation of Collagen Sponge Strips)
- Implemented Improvements
- Expansion of the Production Capacity
- Control of Collagen Sponge quality (including adhesiveness)
- Adventitious Agents Safety Evaluation
- The Coating Process
- Effect of the (b)(4) on Collagen Sponge characteristics