
180-DAY PMA SUPPLEMENT SUMMARY MEMO

Submission: P960004/S060
Company: Boston Scientific Corporation
Device: FINELINE II Sterox lead family

Change: Subassembly modifications and supplier change

INTRODUCTION

In this supplement Boston Scientific Corporation (BSC) is proposing changes to the primer formulation used on FINELINE II leads as well as to relocate manufacturing of some subassemblies in-house with minor associated design changes. The content of this 180-Day Supplement was originally submitted in 2 parts by BSC, one as an RtR Supplement and the other as a 30-Day Notice. Due to the relatedness of the RtR and 30DN submissions, FDA deemed that these changes should be combined within a single 180-Day Supplement.

RTR – Change to primer formulation, as well as minor changes to design documents of components and subassemblies. The RtR submitted as P960004/S060 was converted to a 180-Day supplement under the same submission number.

30DN – Relocate manufacturing of certain FINELINE II components in-house, rather than from an outside supplier (b)(4) Trade Secret. The contents from the 30DN that were submitted as P960004/S062, and were subsequently added to S060 by a letter logged in as S060/A001.

Device Description

The proposed changes affect FINELINE II STEROX lead family of straight and j-shaped, passive and active fixation, steroid-eluting, bipolar pacing leads. These leads were first approved in December 2000. A detailed description of the lead family starts on page 1-2 of S060 and the lead models affected are listed in Table 1-1. BSC currently uses MED-161 primer during manufacturing Terminal Front and Terminal Rear lead subassemblies which is the subject of this supplement. Pictures of these subassemblies and the locations where primer is applied were presented on page 1-4.

(b)(4) Trade Secret



BSC notes on page 2-9 that the original RtR request included that these changes would be made to both FINELINE and THINLINE lead families. (b)(4) Trade Secret



The device description, and affected component descriptions are clear and acceptable.

Summary of Proposed Modifications AND Reason for Changes

NEW PRIMER

The change is to replace (b)(4) Trade Secret primer with (b)(4) Trade Secret primer, both supplied by (b)(4) CCI as an alternate primer for certain BSC subassemblies. The primer is used to facilitate the (b)(4) Trade Secret

Use of (b)(4) Trade Secret is already approved for use on other locations of FINELINE silicone leads as well as on ACUITY and EASYTRAK leads. Replacing (b)(4) Trade Secret with (b)(4) Trade Secret for certain FINELINE primer locations increases manufacturing efficiency. There is no change to the primer requirements between the two formulations. The following locations on FINELINE leads are affected as described starting on page 1-3.

Use of (b)(4) Trade Secret will unify all primer locations to a single type for FINELINE II leads. (b)(4) TS is already used on parts of FINELINE II leads and for other lead families. This change was discussed in a real-time review teleconference conducted an IEDB reviewer on 20 May 2013 prior to this submission being combined with the 30-Day notice and converted to a 180-day supplement. The RtR minutes have been added to the DocMan record for this review. In the meeting minutes BSC provided additional detail to indicating the difference in formulation between the two primers. There is no change to the area being primed and the chemical differences do not affect the function of the primer or the specification of the resulting bond.

DESIGN DOCUMENT MODIFICATIONS

As manufacture of the Front and Rear subassemblies are moved in-house, the original vendor design documents were used as a template for new BSC internal design documents. Changes are proposed to processes to ease manufacturing, but no changes were made to materials, functional requirements, or performance (they are "functionally equivalent") as described in section 1.5 starting on page 1-5.

There are 6 reportable changes to design listed in Table 1-3:

1. Added biological testing requirement

(b)(4) Trade Secret

These changes were discussed in a real-time review teleconference conducted by an IEDB reviewer on 20 May 2013 prior to this submission being combined with the 30-Day notice and converted to a 180-day supplement. The minutes have been added to the DocMan record for this review. Within the minutes FDA questioned the firm about the larger tolerances and BSC provided acceptable justifications that the changes are very minor and they are not expected to effect performance safety or efficacy. I have reviewed the changes and agree they are minor and can be validate by the testing reviewed later in this memo.

There were 3 non-reportable changes to design listed in Table 1-4:

(b)(4) Trade Secret

I agree that the above 3 changes, as further described in the submission, would not impact device safety or effectiveness and are annual reportable.

IN-HOUSE OF SUBASSEMBLIES

BSC plans to manufacture the Terminal Front and Terminal Rear assemblies in-house, as an alternate to the currently approved supplier (b)(4) Trade Secret. The use of (b)(4) Trade Secret as an alternate

to (b)(4) Trade Secret will only be made when these subassemblies are made in-house at BSC. BSC indicates that once S060 is approved and the subassembly manufacturing is moved to BSC, use of the (b)(4) Trade Secret supplier will be phased out.

This aspect of the subassembly manufacturing site location change was reviewed to similar criteria as a 30-day notice. The change is from an external supplier to an internal supplier (in-sourcing) of several device subassemblies. Adequate detail is provided to support the change as documented below in the Validation Testing and Manufacturing sections of this review memo.

- Statement of whether the changes are in response to field reports
The firm states on page 2 and within the 20 May 2013 RtR meeting minutes that the change is not being made as a result of field issues.
Changes to primer formulation and subassembly design are associated with moving the fabrication from of subassemblies from an outside supplier to in-house at BSC. In a telephone call with the BSC point of contact for this file on 27 Aug 2013, she confirmed that the changes are not being implemented due to field performance or complaints. There are no concerns regarding the reason for the changes.

- Risk Analysis
BSC provided a summary of the risk assessment in Section 2.7 of the submission, with associated hazard analyses provided in Exhibits 13 to 16. A ripple effects analysis was also provided in Exhibit 4 regarding the in-sourcing of the subassemblies. The analysis concluded the there are no new risks introduced by the changes. The analysis also determined the existing risks that are associated with the changes, and what validation testing was necessary to mitigate those risks.

The risk assessment was acceptable and I concur with the conclusion that there are no new risks and that existing risks can be mitigated with testing. The DVT testing was the same as that performed for the original design and manufacturing site as documented in the submission and telcon minutes.

- Summary of Testing to Verify/Validate Changes or rationale for not providing testing
BSC performed a set of mechanical and electrical design validation tests to support the minor design changes as well as the change to in-house manufacturing of lead subassemblies and final manufactured leads. The testing was summarized in Sections 2.2 and 2.3 and test reports were provided in Exhibit 5.

The validation testing for the primer change was summarized in section 2.2 and 2.3 including axial load durability, electrical insulation integrity, composite pull strength, dimensional checks, terminal connector testing, and connector seal integrity testing. The testing was the same as performed for the original approval and are appropriate. The 20 May 2013 teleconference minutes included test reports used to validate fabrication of the subassemblies with the modified design specifications, with acceptable results. The validation testing of the finished subassemblies and finished leads are adequate to assure that these changes can be implemented. All results met the original devices specifications. The testing supports approval of both the changes to primer/design, as well as in-sourcing of the subassemblies. Overall, the testing was appropriate and acceptable to support the proposed change.

- Sterilization
In Section 2.5, BCS summarized their sterilization assessment for the changes to design and manufacturing, with the full report provided in Exhibit 11. The analysis supported that the modifications do not impact the sterilization burden, method or validated cycle used for the original lead.

I agree with the BSC assessment that the changes do not affect sterilization. Bioburden testing was repeated as documented later in this memo, with acceptable results.

Manufacturing Facility

Part of the submission is to manufacture the Terminal Front and Terminal Rear assemblies in-house, as an alternate to the currently approved outside supplier (b)(4) Trade Secret. The information originally submitted as a 30-Day Notice in S062 to support this change was amended to the related design changes contained in S060 subject of this review. The information is comprehensive and included all of the required 30-Day Notice documentation as described in my review comments below. The parts originally produced at (b)(4) Trade Secret will now be produced at the BSC (b)(4) Trade Secret Facility, and then shipped to the BSC (b)(4) Trade Secret facility (b)(4) Trade Secret (as were the (b)(4) Trade Secret supplied parts) for use in the FINELINE II lead manufacturing line.

The location change for the subcomponents was reviewed according to criteria similar as a 30-day notice. The change is from an external supplier to an internal supplier (in-sourcing) of several device subassemblies as described above. The following information as originally submitted in S062 support the change:

- *The reason for the change was for consolidation and cost savings, and is not due to field issues. The subassemblies are manufactured with the same raw materials, but with slightly different design criteria to aid manufacturing at BSC (as described and evaluated above).*
- *BSC submitted a statement of conformity to QS/GMP regulations for the manufacturing changes.*
- *A detailed description of change control procedures and documentation change control procedures was provided.*
- *Purchasing control procedures including vendor selection, material qualification, procurement and delivery, etc. were described.*
- *Process validation and sampling information was provided to support that routine monitoring is in place and assures that the device continues to meet specifications with the new manufacturing processes at the new location.*
- *A risk assessment and testing results were presented to support the supplier change. Testing included design validation testing (mechanical, electrical, biological) as well as Operational Qualification (OQ) and Performance Qualification (PQ) testing. The testing was appropriate for the manufacturing location change and the results met all requirements and were acceptable.*

I have reviewed the above information associated with the change from an external supplier to in-house source. I found the information comprehensive and complete to support approval of the manufacturing site change for these subcomponents, as part of the 180-day supplement.

Biocompatibility

The new primer is fully encapsulated under the lead insulation, and is therefore not blood or tissue contacting. However the firm still performed biocompatibility testing per ISO 10993-1:2009 on the MED-163 primer. The testing reports were presented in Exhibit 6.

I agree that the biocompatibility testing is not required for primer, but that it is conservative and acceptable to do the testing anyway. The testing was performed per 10993 with objective, test method, acceptance criteria and results presented for each testing within the report. The testing was appropriate and acceptable and supports that use of (b)(4) Trade Secret is acceptable in FINELINE II leads.

In addition to the above testing, BSC performed "Biologic Validation" testing on the finished leads built using the new manufacturing processes. Testing included bioburden, pyrogenicity, cytotoxicity, and hemolysis and the test reports were provided in Exhibits 7-10

The testing performed was the same as used for the original device and manufacturing processes/locations. The testing procedures and acceptance criteria were presented and found acceptable. The test results met all acceptance criteria and support that the changes to design and manufacturing have not affected the device performance in these areas.

- Clinical
No clinical information or data was provided in the submission.

The minor design and manufacturing changes will not affect the device handling or clinical performance so this is acceptable.

- Statistical
Statistical information in the submission was limited to sample size justifications for the testing performed.

In all cases BSC provided acceptable rationale that the sample sizes used for bench testing provided results with prespecified statistical probability and confidence based on the risk assessment.

- Packaging Change/Description
No changes are made to the device packaging as documented on page 3-15 and within the meeting minutes.

There is no packaging concern.

- Shelf Life
No changes were made to the packaging. The firm provided a shelf life assessment in Exhibit to justify that the current 2-year shelf life remains appropriate for the modified device.

The only change to the device materials is the (b)(4) Trade Secret primer. The shelf life assessment uses an equivalency rationale with time-0 testing and shelf life testing for similar lead models that use (b)(4) Trade Secret to support that the primer change will not affect the shelf life. I agree with the rationale and that the firm proposed change does not impact the approved 2 year shelf life for FINELINE II leads

- Post Market Issues

The changes are not being implemented due to field performance issues or complaints. There are no post-market issues associated with these changes.

- Labeling
No changes were made to the labeling as documented on page 3-15 and within the meeting minutes.

There are no labeling concerns.

- Drug Component
BSC performed an assessment regarding drug stability associated with the proposed changes. The tined neck component has the same material and specifications, but will change manufacturing location and this part is directly adjacent to the drug component on passive fixation lead models. There is no change to adhesive used. An assessment regarding this manufacturing site change was provided in Exhibit 20 of S062. The results of the assessment showed no difference between the original and new part samples. The firm concludes that the manufacturing location change does not impact the tined neck component and therefore there will be no affect to the drug component which is attached to the tined neck component. The firm

concludes that the device samples currently on long term stability retention can be considered representative of the modified device.

I have reviewed the information provided and agree that the proposed changes to the tined neck component do not impact the expected performance or stability of the drug component.

RECOMMENDATION:

This documentation to support approval to utilize (b)(4) Trade Secret primer, move certain subassembly manufacturing in-house, and implement minor design changes is complete. BSC provided an acceptable risk assessment and performed appropriate mitigation testing with acceptable results. My assessment includes both my review of the information provided in S060 and S060/A001 (from S062) as well as minutes from a teleconference on 20 May 2013. The changes do not raise safety or effectiveness concerns and approval is recommended.