

SUMMARY MEMO: P060039/S059
ATTAIN STARFIX MODEL 4195

EXECUTIVE SUMMARY:

This PMA 180 Day Supplement proposes updates to the current finished product release criteria for Elution and Content Uniformity for the Attain StarFix Model 4195 lead. The Supplement also proposes minor updates to the data analysis and methodology in the Analytical Methods testing and proposes an alternate method for Related Substances. The proposed changes are being made to align release criteria with critical quality attributes of the lead; to reduce sample burden; and to improve efficiencies by consolidating use of samples.

Specifically, Medtronic proposes the following modifications related to the Model 4195 Finished Product Release criteria:

- Eliminate the Elution testing requirement for finished product release
- Update the finished product release criteria for Content Uniformity to align with current (b)(4) TS/CCI
- Add alternative method for Related Substances
- Add alternative sample preparation options to the method for Assay and Identity to derive results from Content Uniformity samples

The review team found the changes above and the data to support the changes acceptable. Therefore, I am recommending approval of this PMA supplement.

DEVICE DESCRIPTION:

The Model 4195 Attain StarFix (P060039, approved June 13, 2008) is a steroid-eluting, left ventricular deployable lobe lead (5Fr) designed for pacing and sensing via the cardiac vein. The distal tip of the Model 4195 includes a nominal dose of 30 ug of beclomethasone dipropionate (BDP).

INDICATIONS FOR USE

The Medtronic Attain StarFix® Model 4195 steroid eluting, transvenous lead with deployable lobe fixation is intended for chronic pacing and sensing in the left ventricle via the cardiac vein, when used in conjunction with an implantable pulse generator or implantable cardiac defibrillator.

DESCRIPTION OF CHANGES

This submission proposes modifications to the Model 4195 Finished Product Release criteria. The proposed changes are highlighted in **red** in the table below. The proposed changes from the current requirements are summarized in the last column of the table.

TEST	METHOD	ACCEPTANCE CRITERIA	Changes from current requirements
Description / Visual ¹	(b)(4) TS/CCI	Cardiac lead with blue outer tubing, a segment of clear tubing, a tip electrode, and a molded tip seal. The serial number prefix (b)(4) TS/CCI is (b)(4) TS/CCI. The drug is located on the Model 4195 lead tip and will appear as a white, off-white or clear residue under magnification, but may not be visible with the naked eye.	No Change
Identity / HPLC	(b)(4) TS/CCI	The retention time of the beclomethasone dipropionate (BDP) peak in the sample preparation is within (b)(4) TS/CCI of the mean retention time of the BDP peak in the system suitability injections.	Update (b)(4) TS/CCI alternative sample preparation options
Identity / UV/PDA	(b)(4) TS/CCI	The UV absorption spectra of the (b)(4) TS/CCI (b)(4) TS/CCI similar wavelengths.	Update (b)(4) TS/CCI add alternative sample preparation options
Assay / HPLC ¹	(b)(4) TS/CCI	(b)(4) TS/CCI Label Claim	Update (b)(4) TS/CCI add alternative sample preparation options
Content Uniformity / HPLC	(b)(4) TS/CCI	<p>The requirements for dosage uniformity are met if the acceptance value (b)(4) TS/CCI</p> <p>(b)(4) TS/CCI</p> <p>(b)(4) TS/CCI</p> <p>(b)(4) TS/CCI</p> <p>Acceptance criteria follow (b)(4) TS/CCI</p> <p>(b)(4) TS/CCI</p>	Revised acceptance criterion to align with current (b)(4) TS/CCI

TEST	METHOD	ACCEPTANCE CRITERIA	Changes from current requirements
Related Substances ¹	(b)(4) TS/CCI	(b)(4) TS/CCI	Add equivalent alternate method (methods employ different sample preparation instructions)
Residual Solvents	(b)(4) TS/CC	(b)(4) TS/CCI	No Change
(b)(4) TS/CC Sterility Process Review ³	(b)(4) TS/CCI	(b)(4) TS/CCI	No Change

1. Denotes test required for stability testing.

2. (b)(4) TS/CCI

3. (b)(4) TS/CCI

In addition, the Stability Study Protocol for the Model 4195 Lead will be updated to address the proposed changes in the Model 4195 Finished Product Release requirements.

There are no changes to the manufacturing site for this submission:

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 Villalba, PR USA 00766
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REASONS FOR CHANGES

The changes to the finished product release criteria ((b)(4) TS/CCI (b)(4) TS/CCI) are being made to align these criteria with the critical quality attributes of the lead, and to reduce sample burden.

The updates to the methods (add alternative method for Related Substances and add alternative sample preparation options to the method for Assay and Identity) are proposed to reduce sample burden and to improve efficiencies by consolidating samples.

In addition, there are no other changes to the analytical methods, release criteria, device design, device manufacturing, or device labeling related to these changes.

SUBSTANTIVE REVIEW

Chemistry Manufacturing and Controls (CMC)

CDER provided a review of the CMC section of this submission in a review memo dated August 27, 2014. The CMC reviewer indicated the firm aligned the release criteria for (b)(4) TS/CCI added an alternative method for related substances (which was validated to be equivalent), and added alternative sample preparation options to the assay/identity method (to derive the results from the content uniformity samples). All of the above changes were found to be acceptable. ODE agrees with this recommendation and has no further concerns.

Biopharmaceutics

CDER provided a review of the biopharmaceutics section of this submission in a review memo dated September 2, 2014. The Biopharmaceutics Reviewer indicated the drug release test is no longer required for control of the Model 4195 leads. CDER is in agreement with eliminating the drug release test specifically for this product because of the product's unique design and drug quality attributes. That is, the drug is incorporated as a dry coat at only the tip helix and covers a small surface area. There are no excipients or release rate controlling agents used, which differs from the commonly used silicone/MCRD technology among other leads. For the silicone/MCRD technology, drug release is a critical quality attribute of the formulation and thus a necessary test.

CONCLUSION AND RECOMMENDATION:

The review team found the changes above and the data to support the changes acceptable. Therefore, I am recommending approval of this PMA supplement.