SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Drug Eluting Coronary Stent System
Premarket Approval Application (PMA) Supplement Number:	P070015/S128
Device Trade Name:	XIENCE V® and XIENCE nano® Everolimus Eluting Coronary Stent System
PMA Supplement Number:	P110019/ S075
Device Trade Name:	XIENCE PRIME® Everolimus Eluting Coronary Stent System XIENCE PRIME® LL Everolimus Eluting Coronary Stent System XIENCE Xpedition® Everolimus Eluting Coronary Stent System XIENCE Xpedition® SV Everolimus Eluting Coronary Stent System XIENCE Xpedition® LL Everolimus Eluting Coronary Stent System XIENCE Alpine™ Everolimus Eluting Coronary Stent System
Device Procode:	NIQ
Applicant's Name and Address:	Abbott Vascular 3200 Lakeside Drive Santa Clara, CA 95054
Date of Panel Recommendation:	None
Date of FDA Notice of Approval:	September 23, 2015

This is a bundled Premarket Approval (PMA) Supplement for P070015 and P110019 for the XIENCE Family of Everolimus Eluting Coronary Stent Systems (XIENCE Family of Stents). The XIENCE Family of Stents includes the XIENCE V Stent System, approved under P070015 on July 2, 2008, the XIENCE nano, approved on May 24, 2011 under P070015/ S054, the XIENCE PRIME and XIENCE PRIME LL Stent System (XIENCE PRIME Stent System) approved on November 1, 2011 under P110019, and XIENCE Xpedition, XIENCE Xpedition SV, and XIENCE Xpedition LL (XIENCE Xpedition Stent System) approved on December 21, 2012 under P110019/S025 and XIENCE Alpine™ (XIENCE Alpine Stent System) approved September 3, 2014 under P110019/S070.

The Summary of Safety and Effectiveness Data (SSED) to support the indications is available on the CDRH website (http://www.accessdata.fda.gov/cdrh_docs/pdf7/P070015b.pdf and http://www.accessdata.fda.gov/cdrh_docs/pdf11/P110019b.pdf) and is incorporated by reference herein. This bundled PMA supplement, P070015/S128 and P110019/S075 was submitted to request approval for an expanded indication to include patients with diabetes mellitus.

II. INDICATIONS FOR USE

XIENCE V and XIENCE nano Everolimus Eluting Coronary Stent System

The XIENCE V and XIENCE nano Everolimus Eluting Coronary Stent System is indicated for improving coronary luminal diameter in patients, including those with diabetes mellitus, with symptomatic heart disease due to *de novo* native coronary artery lesions (length ≤ 28 mm) with reference vessel diameters of 2.25 mm to 4.25 mm. Additionally, the XIENCE V stent system is indicated for treating *de novo* chronic total coronary occlusions.

XIENCE PRIME and XIENCE PRIME LL Everolimus Eluting Coronary Stent System

The XIENCE PRIME and XIENCE PRIME LL Everolimus Eluting Coronary Stent System is indicated for improving coronary luminal diameter in patients, including those with diabetes mellitus, with symptomatic heart disease due to *de novo* native coronary artery lesions (length ≤ 32 mm) with reference vessel diameters of ≥ 2.25 mm to ≤ 4.25 mm. Additionally, the XIENCE PRIME stent system is indicated for treating *de novo* chronic total coronary occlusions.

XIENCE Xpedition, XIENCE Xpedition SV and XIENCE Xpedition LL Everolimus Eluting Coronary Stent System

The XIENCE Xpedition, XIENCE Xpedition SV and XIENCE Xpedition LL Everolimus Eluting Coronary Stent System is indicated for improving coronary artery luminal diameter in patients, including those with diabetes mellitus, with symptomatic heart disease due to *de novo* native coronary artery lesions (length ≤ 32 mm) with reference vessel diameters of ≥ 2.25 mm to ≤ 4.25 mm. In addition, the XIENCE Xpedition stent system is indicated for treating *de novo* chronic total coronary occlusions.

XIENCE Alpine Everolimus Eluting Coronary Stent System

The XIENCE Alpine Everolimus Eluting Coronary Stent System is indicated for improving coronary artery luminal diameter in patients with symptomatic heart disease, including those with diabetes mellitus, due to *de novo* native coronary artery lesions (length ≤ 32 mm) with reference vessel diameters of ≥ 2.25 mm to ≤ 4.25 mm. Additionally, the XIENCE Alpine stent system is indicated for treating *de novo* chronic total coronary occlusions.

III. CONTRAINDICATIONS

The XIENCE Family of Stents is contraindicated for use in patients:

- Who cannot receive antiplatelet and / or anticoagulant therapy
- With lesions that prevent complete angioplasty balloon inflation or proper placement of the stent or stent delivery system
- With hypersensitivity or contraindication to everolimus or structurally-related compounds, cobalt, chromium, nickel, tungsten, acrylic polymers~~, and~~ or fluoropolymers

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the XIENCE V, XIENCE PRIME, XIENCE Xpedition and the XIENCE Alpine labeling.

V. DEVICE DESCRIPTION

XIENCE Family of Everolimus Eluting Coronary Stent Systems Summary

The XIENCE Family of Everolimus Eluting Coronary Stent Systems (EECSS) is a device / drug combination product consisting of a Cobalt Chromium (CoCr) alloy stent coated with a formulation containing everolimus, the active ingredient, embedded in a non-erodible polymer mounted on a delivery system. The XIENCE V is offered in sizes 2.5 mm to 4.0 mm diameter and the XIENCE nano is offered in the 2.25 mm diameter. The stent platform and delivery system of the XIENCE V and XIENCE nano are identical to the MULTI-LINK VISION and MULTI-LINK MINI VISION, respectively. The XIENCE V was approved under P070015; and the XIENCE nano Stent System is a line extension to the XIENCE V Stent System, which was approved under P070015/S054.

The XIENCE PRIME and XIENCE PRIME LL were approved under P110019 and are available in the 2.25 mm to 4.25 mm diameters. The XIENCE PRIME LL is available in longer stent lengths compared to XIENCE V, which include 33 mm and 38 mm for the 2.5mm to 4.25 mm stents. The stent is coated with a formulation containing everolimus, the active ingredient, embedded in a non-erodible polymer, which is identical to the XIENCE V Everolimus Eluting Coronary Stent System; however, there are minor differences between the stent designs and delivery systems. The XIENCE Xpedition, XIENCE Xpedition LL and XIENCE Xpedition SV

and XIENCE Alpine EECSS are line extensions to the XIENCE PRIME Stent System, which were approved under P110019/S025 and P110019/S070, respectively, with a modified delivery system.

See the Device Component Description sections below for additional information on the XIENCE Family of Stents.

XIENCE V and XIENCE nano—Device Component Description

The device component consists of the MULTI-LINK VISION or MULTI-LINK MINI VISION stent mounted onto the MULTI-LINK VISION or MULTI-LINK MINI VISION stent delivery system (SDS), respectively. The device component characteristics are summarized in **Table 1.**

Table 1 XIENCE V Stent System Product Description

	XIENCE V Rapid-Exchange (RX) Stent System	XIENCE V Over-the-Wire (OTW) Stent System
Available Stent Lengths	8, 12, 15, 18, 23, 28	8, 12, 15, 18, 23, 28
Available Stent Diameters (mm)	2.25*, 2.5, 2.75, 3.0, 3.5, 4.0	2.5, 2.75, 3.0, 3.5, 4.0
Stent Material	A medical grade L-605 cobalt chromium (CoCr) alloy MULTI-LINK VISION or MULTI-LINK MINI VISION stent	
Drug Component	A conformal coating of a non-erodible polymer loaded with 100 μg/cm^2 of everolimus with a maximum nominal drug content of 181 μg on the largest stent (4.0 x 28 mm)	
Delivery System Working Length	143 cm	143 cm
Delivery System Design	Single access port to inflation lumen. Guide wire exit notch is located 30 cm from tip. Designed for guide wires ≤ 0.014".	Sidearm adaptor provides access to balloon inflation/deflation lumen and guide wire lumen. Designed for guide wires ≤ 0.014".
Stent Delivery System Balloon	A compliant, tapered balloon, with two radiopaque markers located on the catheter shaft to indicate balloon positioning and expanded stent length.	
Balloon Inflation Pressure	Nominal inflation pressure: 8 atm (811 kPa) for 2.25, 2.5 and 2.75 mm diameters; 9 atm (912 kPa) for 3.0, 3.5, and 4.0 mm diameters Rated Burst Pressure (RBP): 16 atm (1621 kPa) for all sizes	
Guiding Catheter Inner Diameter	≥ 5 F (0.056")	
Catheter Shaft Outer Diameter (nominal)		

	2.25 – 3.0 mm	3.5 – 4.0 mm
Distal:	0.032"	0.035"
Proximal:	0.026"	0.026"

	2.5 mm	2.75 x 8 - 3.5 x 18	3.5 x 23 - 4.0 x 28
Distal:	0.032"	0.034"	0.036"
Proximal:	0.042"	0.042"	0.042"

*The 2.25 mm diameter XIENCE V EECSS is only available on the RX platform.

XIENCE PRIME and XIENCE PRIME LL —Device Component Description

The XIENCE PRIME and the XIENCE PRIME LL device component characteristics are summarized in **Table 2 and Table 3.**

Table 2 XIENCE PRIME and XIENCE PRIME LL Reference Vessel Diameter and Stent Length

	REFERENCE VESSEL DIAMETER (RVD)	LESION LENGTH
XIENCE PRIME	≥ 2.25 mm and ≤ 4.25 mm Stent Diameter: 2.25, 2.5, 2.75, 3.0, 3.5, 4.0 mm	≤ 22 mm Stent Length: 8, 12, 15, 18, 23
XIENCE PRIME LL	≥ 2.5 mm and ≤ 4.25 mm Stent Diameter: 2.5, 2.75, 3.0, 3.5, 4.0 mm	> 22 mm, and ≤ 32 mm Stent Length: 28, 33 and 38 mm

Table 3 XIENCE PRIME Stent System Product Description

	XIENCE PRIME Stent System	
	XIENCE PRIME	XIENCE PRIME LL
Available Stent Lengths (mm)	8, 12, 15, 18, 23	28*, 33, 38
Available Stent Diameters (mm)	2.25, 2.5, 2.75, 3.0, 3.5, 4.0	2.25**, 2.5, 2.75, 3.0, 3.5, 4.0
Stent Material	A medical grade L-605 cobalt chromium CoCr alloy identical to the material used in the XIENCE V stent	
Drug Component	A conformal coating of a non-erodible polymer loaded with 100 μg/cm^2 of everolimus with a maximum nominal drug content of 232 μg on the large stent (4.0 x 38 mm)	
Delivery System Working Length	143 cm	
Delivery System Design	Single access port to inflation lumen; guide wire exit notch is located 25.5 cm from tip; designed for guide wires ≤ 0.014".	
Stent Delivery System Balloon	A compliant, tapered balloon, with two radiopaque markers located on the catheter shaft to indicate balloon positioning and expanded stent length	

<table>
<tr><td></td><td colspan="2">XIENCE PRIME Stent System</td></tr>
<tr><td></td><td>XIENCE PRIME</td><td>XIENCE PRIME LL</td></tr>
<tr><td>Balloon Inflation Pressure</td><td colspan="2">Rated Burst Pressure (RBP): 18 atm (1824 kPa)
<table><tr><th>Stent Diameter (mm)</th><th>In vitro Stent Nominal Pressure (atm)</th></tr><tr><td>2.25</td><td>8</td></tr><tr><td>2.5</td><td>8</td></tr><tr><td>2.75</td><td>8</td></tr><tr><td>3.0</td><td>10</td></tr><tr><td>3.5</td><td>10</td></tr><tr><td>4.0</td><td>10</td></tr></table></td></tr>
<tr><td>Guiding Catheter Inner Diameter</td><td colspan="2">≥ 5 F (0.056”)</td></tr>
<tr><td>Catheter Shaft Outer Diameter</td><td colspan="2">Distal: 0.034” (0.86 mm)
Proximal: 0.031” (0.79 mm)</td></tr>
</table>

* The 28 mm length stent was studied in the XIENCE PRIME Core Size Registry. The results of the Core Size Registry are presented in Tables 9.1-2 to 9.1-3.

**The 2.25 mm diameter stent for XIENCE PRIME LL is only available in the 28 mm stent length.

XIENCE Xpedition—Device Component Description

The XIENCE Xpedition Family of Stent Systems includes:

- The XIENCE Xpedition SV EECSS (stent diameter 2.25, stent lengths 8, 12, 15, 18, 23, 28 mm)
- The XIENCE Xpedition EECSS (stent diameters 2.5, 2.75, 3.0, 3.25[1], 3.5, 4.0 mm, stent lengths 8, 12, 15, 18, 23, 28 mm)
- The XIENCE Xpedition LL EECSS (stent diameters 2.5,2.75, 3.0, 3.25, 3.5, 4.0 mm, stent lengths 33, 38 mm)

The device component characteristics are summarized in **Table 4**.

[1] The 3.25 mm stent diameter is only available for the XIENCE Xpedition Stent System and not for the XIENCE PRIME Stent System.

Table 4 XIENCE Xpedition, XIENCE Xpedition SV, and XIENCE Xpedition LL Product Description

<table>
<tr><td></td><td colspan="3">XIENCE Xpedition Stent System</td></tr>
<tr><td></td><td>XIENCE Xpedition SV</td><td>XIENCE Xpedition</td><td>XIENCE Xpedition LL</td></tr>
<tr><td>Available Stent Lengths (mm)</td><td>8, 12, 15, 18, 23, 28</td><td>8, 12, 15, 18, 23, 28</td><td>33, 38</td></tr>
<tr><td>Available Stent Diameters (mm)</td><td>2.25</td><td>2.5, 2.75, 3.0, 3.25, 3.5, 4.0</td><td>2.5, 2.75, 3.0, 3.25, 3.5, 4.0</td></tr>
<tr><td>Stent Material</td><td colspan="3">A medical grade L-605 cobalt chromium CoCr alloy identical to the material used in the XIENCE V and XIENCE PRIME stent</td></tr>
<tr><td>Drug Component</td><td colspan="3">
<table>
<tr><th>Stent Design</th><th>Diameters (mm)</th><th>Stent Length (mm)</th><th>Surface Area (cm^2)</th><th>Target Drug Amount (µg)</th></tr>
<tr><td>Small</td><td>2.25, 2.5, 2.75, 3.0, 3.25</td><td>8</td><td>0.3972</td><td>40</td></tr>
<tr><td>Small</td><td>2.25, 2.5, 2.75, 3.0, 3.25</td><td>12</td><td>0.6048</td><td>60</td></tr>
<tr><td>Small</td><td>2.25, 2.5, 2.75, 3.0, 3.25</td><td>15</td><td>0.7431</td><td>74</td></tr>
<tr><td>Small</td><td>2.25, 2.5, 2.75, 3.0, 3.25</td><td>18</td><td>0.8815</td><td>88</td></tr>
<tr><td>Small</td><td>2.25, 2.5, 2.75, 3.0, 3.25</td><td>23</td><td>1.0891</td><td>109</td></tr>
<tr><td>Small</td><td>2.25, 2.5, 2.75, 3.0, 3.25</td><td>28</td><td>1.3658</td><td>137</td></tr>
<tr><td>Small</td><td>2.5, 2.75, 3.0, 3.25</td><td>33</td><td>1.5734</td><td>157</td></tr>
<tr><td>Small</td><td>2.5, 2.75, 3.0, 3.25</td><td>38</td><td>1.8501</td><td>185</td></tr>
<tr><td>Medium</td><td>3.5, 4.0</td><td>8</td><td>0.4979</td><td>50</td></tr>
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<tr><td>Medium</td><td>3.5, 4.0</td><td>23</td><td>1.4099</td><td>141</td></tr>
<tr><td>Medium</td><td>3.5, 4.0</td><td>28</td><td>1.7415</td><td>174</td></tr>
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<tr><td>Medium</td><td>3.5, 4.0</td><td>38</td><td>2.3219</td><td>232</td></tr>
</table>
</td></tr>
<tr><td>Delivery System Working Length</td><td colspan="3">145 cm</td></tr>
</table>

<table>
<tr><th></th><th>XIENCE Xpedition Stent System</th></tr>
<tr><td>Delivery System Design</td><td>RX: Single access port to inflation lumen; guide wire exit notch is located 25.5 cm from tip; designed for guide wires ≤ 0.014”.
OTW: Sidearm adaptor provides access to balloon inflation/deflation lumen and guide wire lumen; designed for guide wires ≤ 0.014”.</td></tr>
<tr><td>Stent Delivery System Balloon</td><td>A compliant, tapered balloon, with two radiopaque markers located on the catheter shaft to indicate balloon positioning and expanded stent length</td></tr>
<tr><td>Balloon Inflation Pressure</td><td>Rated Burst Pressure (RBP): 18 atm (1824 kPa)
<table><tr><th>Stent Diameter (mm)</th><th>In vitro Stent Nominal Pressure (atm)</th></tr><tr><td>2.25</td><td>10</td></tr><tr><td>2.5</td><td>10</td></tr><tr><td>2.75</td><td>10</td></tr><tr><td>3.0</td><td>10</td></tr><tr><td>3.25</td><td>10</td></tr><tr><td>3.5</td><td>10</td></tr><tr><td>4.0</td><td>10</td></tr></table></td></tr>
<tr><td>Guiding Catheter Inner Diameter</td><td>≥ 5 F (0.056”) for 2.25 – 3.5 mm sizes
≥ 5 F (0.056”) for 4.0 x 8-33 mm sizes
≥ 6 F (0.066”) for 4.0 x 38 mm sizes</td></tr>
<tr><td>Catheter Shaft Outer Diameter</td><td>Distal: 0.034” (0.86 mm)
Proximal (RX): 0.028” (0.71 mm)
Proximal (OTW): 0.045” (1.14 mm)</td></tr>
</table>

XIENCE Alpine—Device Component Description

The XIENCE Alpine Family of Stent Systems includes:

1. stent diameter 2.25, stent lengths 8, 12, 15, 18, 23, 28 mm
2. stent diameters 2.5, 2.75, 3.0, 3.25[2], 3.5, 4.0 mm, stent lengths 8, 12, 15, 18, 23, 28, 33, 38 mm

The device component characteristics are summarized in **Table 5**.

[2] The 3.25 mm stent diameter is only available for the XIENCE Xpedition and XIENCE Alpine Stent Systems and not for the XIENCE PRIME Stent System.

Table 5 XIENCE Alpine Product Description

<table>
<tr><td></td><td colspan="2">XIENCE Alpine Stent System</td></tr>
<tr><td>Available Stent Lengths (mm)</td><td>8, 12, 15, 18, 23, 28</td><td>8, 12, 15, 18, 23, 28, 33, 38</td></tr>
<tr><td>Available Stent Diameters (mm)</td><td>2.25</td><td>2.5, 2.75, 3.0, 3.25, 3.5, 4.0</td></tr>
<tr><td>Stent Material</td><td colspan="2">A medical grade L-605 cobalt chromium CoCr alloy identical to the material used in the XIENCE V, XIENCE PRIME, XIENCE Xpedition stents</td></tr>
<tr><td>Drug Component</td><td colspan="2">
<table>
<tr><th>Stent Design</th><th>Diameters (mm)</th><th>Stent Length (mm)</th><th>Surface Area (cm^2)</th><th>Target Drug Amount (μg)</th></tr>
<tr><td>Small</td><td>2.25, 2.5, 2.75, 3.0, 3.25</td><td>8</td><td>0.3972</td><td>40</td></tr>
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<tr><th></th><th>XIENCE Alpine Stent System</th></tr>
<tr><td>Delivery System Design</td><td>RX: Single access port to inflation lumen; guide wire exit notch is located 25.5 cm from tip; designed for guide wires ≤ 0.014”.
OTW: Sidearm adaptor provides access to balloon inflation/deflation lumen and guide wire lumen; designed for guide wires ≤ 0.014”.</td></tr>
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Proximal (RX): 0.029” (0.71 mm)
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</table>

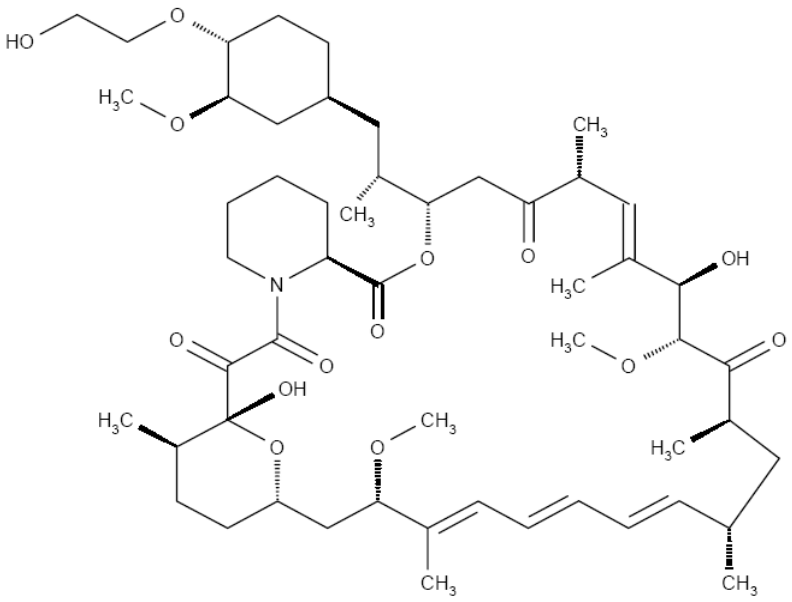
Drug Component Description for the XIENCE Family of Stents

The XIENCE Family of Everolimus Eluting Coronary Stents are coated with everolimus (active ingredient), embedded in a non-erodible polymer (inactive ingredient).

Everolimus

Everolimus is the active pharmaceutical ingredient in the XIENCE stents. It is a novel semi-synthetic macrolide immunosuppressant, synthesized by chemical modification of rapamycin (sirolimus). The everolimus chemical name is 40-O-(hydroxyethyl)-rapamycin and the chemical structure is shown in **Figure 1** below.

Figure 1 Everolimus Chemical Structure

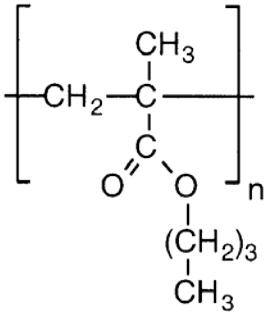
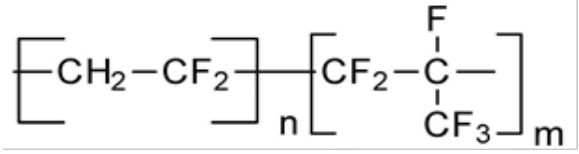


Inactive Ingredients – Non-erodible Polymer

The XIENCE V stent contains inactive ingredients including poly n-butyl methacrylate (PBMA), a polymer that adheres to the stent and drug coating, and PVDF-HFP, which is comprised of vinylidene fluoride and hexafluoropropylene monomers as the drug matrix layer containing everolimus. PBMA is a homopolymer with a molecular weight (Mw) of 264,000 to 376,000 dalton. PVDF-HFP is a non-erodible semi-crystalline random copolymer with a molecular weight (Mw) of 254,000 to 293,000 dalton. The drug matrix copolymer is mixed with everolimus (83%/17% w/w polymer/everolimus ratio) and applied to the entire PBMA coated stent surface.

The drug load is 100 $\mu g/cm^2$ for all product sizes. No topcoat layer is used. The polymer chemical structures are shown in **Figure 2** below.

Figure 2 Non-erodible Polymer Chemical Structures

PBMA	PVDF-HFP
	

Product Matrix and Everolimus Content

Table 6 XIENCE V Stent System Product Matrix and Everolimus Content

Model Number (RX)	Model Number (OTW)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (μg)
1009544-08	-	2.25	8	37
1009539-08	1009545-08	2.5	8	37
1009540-08	1009546-08	2.75	8	37
1009541-08	1009547-08	3.0	8	37
1009542-08	1009548-08	3.5	8	53
1009543-08	1009549-08	4.0	8	53
1009544-12	-	2.25	12	56
1009539-12	1009545-12	2.5	12	56
1009540-12	1009546-12	2.75	12	56
1009541-12	1009547-12	3.0	12	56

Model Number (RX)	Model Number (OTW)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (μg)
1009542-12	1009548-12	3.5	12	75
1009543-12	1009549-12	4.0	12	75
1009544-15	-	2.25	15	75
1009539-15	1009545-15	2.5	15	75
1009540-15	1009546-15	2.75	15	75
1009541-15	1009547-15	3.0	15	75
1009542-15	1009548-15	3.5	15	98
1009543-15	1009549-15	4.0	15	98
1009544-18	-	2.25	18	88
1009539-18	1009545-18	2.5	18	88
1009540-18	1009546-18	2.75	18	88
1009541-18	1009547-18	3.0	18	88
1009542-18	1009548-18	3.5	18	113
1009543-18	1009549-18	4.0	18	113
1009544-23	-	2.25	23	113
1009539-23	1009545-23	2.5	23	113
1009540-23	1009546-23	2.75	23	113
1009541-23	1009547-23	3.0	23	113
1009542-23	1009548-23	3.5	23	151
1009543-23	1009549-23	4.0	23	151
1009544-28	-	2.25	28	132
1009539-28	1009545-28	2.5	28	132
1009540-28	1009546-28	2.75	28	132

Model Number (RX)	Model Number (OTW)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (μg)
1009541-28	1009547-28	3.0	28	132
1009542-28	1009548-28	3.5	28	181
1009543-28	1009549-28	4.0	28	181

Table 7 XIENCE PRIME Stent System Product Matrix and Everolimus Content

Model Number (RX)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (μg)
1011730 - 08	2.25	8	40
1011731 - 08	2.5		40
1011732 - 08	2.75		40
1011733 - 08	3.0		40
1011734 - 08	3.5		50
1011735 - 08	4.0		50
1011730 - 12	2.25	12	60
1011731 - 12	2.5		60
1011732 - 12	2.75		60
1011733 - 12	3.0		60
1011734 - 12	3.5		75
1011735 - 12	4.0		75
1011730 - 15	2.25	15	74
1011731 - 15	2.5		74
1011732 - 15	2.75		74
1011733 - 15	3.0		74
1011734 - 15	3.5		91
1011735 - 15	4.0		91
1011730 - 18	2.25	18	88
1011731 - 18	2.5		88
1011732 - 18	2.75		88
1011733 - 18	3.0		88
1011734 - 18	3.5		116
1011735 - 18	4.0		116
1011730 - 23	2.25	23	109
1011731 - 23	2.5		109
1011732 - 23	2.75		109
1011733 - 23	3.0		109
1011734 - 23	3.5		141

Model Number (RX)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
1011735 - 23	4.0		141
1011730- 28	2.25	28	137
1011731 - 28	2.5		137
1011732 - 28	2.75		137
1011733 - 28	3.0		137
1011734 - 28	3.5		174
1011735 - 28	4.0		174
1011731 - 33	2.5	33	157
1011732 - 33	2.75		157
1011733 - 33	3.0		157
1011734 - 33	3.5		199
1011735 - 33	4.0		199
1011731 - 38	2.5	38	185
1011732 - 38	2.75		185
1011733 - 38	3.0		185
1011734 - 38	3.5		232
1011735 - 38	4.0		232

Table 8 **XIENCE Xpedition, XIENCE Xpedition SV and XIENCE Xpedition LL EECSS Product Matrix and Everolimus Content**

XIENCE Xpedition™ RX US Part #	XIENCE Xpedition™ OTW US Part #	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
1074225-08	1165225-08	2.25	8	40
1074225-12	1165225-12	2.25	12	60
1074225-15	1165225-15	2.25	15	74
1074225-18	1165225-18	2.25	18	88
1074225-23	1165225-23	2.25	23	109
1074225-28	1165225-28	2.25	28	137
1074250-08	1165250-08	2.5	8	40
1074250-12	1165250-12	2.5	12	60
1074250-15	1165250-15	2.5	15	74
1074250-18	1165250-18	2.5	18	88
1074250-23	1165250-23	2.5	23	109
1074250-28	1165250-28	2.5	28	137
1074250-33	1165250-33	2.5	33	157
1074250-38	1165250-38	2.5	38	185
1074275-08	1165275-08	2.75	8	40
1074275-12	1165275-12	2.75	12	60
1074275-15	1165275-15	2.75	15	74
1074275-18	1165275-18	2.75	18	88
1074275-23	1165275-23	2.75	23	109
1074275-28	1165275-28	2.75	28	137
1074275-33	1165275-33	2.75	33	157
1074275-38	1165275-38	2.75	38	185
1074300-08	1165300-08	3.0	8	40
1074300-12	1165300-12	3.0	12	60
1074300-15	1165300-15	3.0	15	74
1074300-18	1165300-18	3.0	18	88
1074300-23	1165300-23	3.0	23	109
1074300-28	1165300-28	3.0	28	137
1074300-33	1165300-33	3.0	33	157
1074300-38	1165300-38	3.0	38	185

XIENCE Xpedition™ RX US Part #	XIENCE Xpedition™ OTW US Part #	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
1074325-08	1165325-08	3.25	8	40
1074325-12	1165325-12	3.25	12	60
1074325-15	1165325-15	3.25	15	74
1074325-18	1165325-18	3.25	18	88
1074325-23	1165325-23	3.25	23	109
1074325-28	1165325-28	3.25	28	137
1074325-33	1165325-33	3.25	33	157
1074325-38	1165325-38	3.25	38	185
1074350-08	1165350-08	3.5	8	50
1074350-12	1165350-12	3.5	12	75
1074350-15	1165350-15	3.5	15	91
1074350-18	1165350-18	3.5	18	116
1074350-23	1165350-23	3.5	23	141
1074350-28	1165350-28	3.5	28	174
1074350-33	1165350-33	3.5	33	199
1074350-38	1165350-38	3.5	38	232
1074400-08	1165400-08	4.0	8	50
1074400-12	1165400-12	4.0	12	75
1074400-15	1165400-15	4.0	15	91
1074400-18	1165400-18	4.0	18	116
1074400-23	1165400-23	4.0	23	141
1074400-28	1165400-28	4.0	28	174
1074400-33	1165400-33	4.0	33	199
1074400-38	1165400-38	4.0	38	232

Table 9 XIENCE Alpine Stent System Product Matrix and Everolimus Content

Model Number (RX)	Model Number (OTW)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
1125225-08	1145225-08	2.25	8	40
1125250-08	1145250-08	2.5		40
1125275-08	1145275-08	2.75		40
1125300-08	1145300-08	3.0		40
1125325-08	1145325-08	3.25		40
1125350-08	1145350-08	3.5		50
1125400-08	1145400-08	4.0		50
1125225-12	1145225-12	2.25	12	60
1125250-12	1145250-12	2.5		60
1125275-12	1145275-12	2.75		60
1125300-12	1145300-12	3.0		60
1125325-12	1145325-12	3.25		60
1125350-12	1145350-12	3.5		75
1125400-12	1145400-12	4.0		75
1125225-15	1145225-15	2.25	15	74
1125250-15	1145250-15	2.5		74
1125275-15	1145275-15	2.75		74
1125300-15	1145300-15	3.0		74
1125325-15	1145325-15	3.25		74
1125350-15	1145350-15	3.5		91
1125400-15	1145400-15	4.0		91
1125225-18	1145225-18	2.25	18	88
1125250-18	1145250-18	2.5		88
1125275-18	1145275-18	2.75		88
1125300-18	1145300-18	3.0		88
1125325-18	1145325-18	3.25		88
1125350-18	1145350-18	3.5		116
1125400-18	1145400-18	4.0		116
1125225-23	1145225-23	2.25	23	109
1125250-23	1145250-23	2.5		109
1125275-23	1145275-23	2.75		109
1125300-23	1145300-23	3.0		109
1125325-23	1145325-23	3.25		109
1125350-23	1145350-23	3.5		141
1125400-23	1145400-23	4.0		141
1125225-28	1145225-28	2.25	28	137
1125250-28	1145250-28	2.5		137
1125275-28	1145275-28	2.75		137
1125300-28	1145300-28	3.0		137

Model Number (RX)	Model Number (OTW)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
1125325-28	1145325-28	3.25		137
1125350-28	1145350-28	3.5		174
1125400-28	1145400-28	4.0		174
1125250-33	1145250-33	2.5	33	157
1125275-33	1145275-33	2.75		157
1125300-33	1145300-33	3.0		157
1125325-33	1145325-33	3.25		157
1125350-33	1145350-33	3.5		199
1125400-33	1145400-33	4.0		199
1125250-38	1145250-38	2.5	38	185
1125275-38	1145275-38	2.75		185
1125300-38	1145300-38	3.0		185
1125325-38	1145325-38	3.25		185
1125350-38	1145350-38	3.5		232
1125400-38	1145400-38	4.0		232

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of patients with coronary artery disease including exercise, diet, drug therapy, percutaneous coronary interventions (i.e., balloon angioplasty, atherectomy, bare metal stents, coated stents, and other drug-eluting stents), and coronary artery bypass grafting (CABG) surgery. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The XIENCE Family of Stents is commercially available in the following countries:

Sales for all XIENCE versions sold worldwide from launch (9/2006) to present (8/31/2015) is cumulatively 10, 741, 988 units.

AFGHANISTAN	CHILE	GUAM	LATVIA	OMAN	SLOVENIA
ALBANIA	CHINA	GUATEMALA KOSOVO (DNU)	LEBANON	PAKISTAN	SOUTH AFRICA
ALGERIA	COLOMBIA	HONDURAS	LIBYA	PANAMA	SOUTH KOREA
ARGENTINA	COSTA RICA	HONG KONG	LIECHTENSTEIN	PARAGUAY	SOUTH YEMEN
ARUBA	CYPRUS	HUNGARY	LITHUANIA	PHILIPPINES	SPIAN
AUSTRALIA	CZECH REPUBLIC	ICELAND	LUXEMBOURG	POLAND	SRI LANKA
AUSTRIA	DENMARK	INDIA	MACEDONIA	PORTUGAL	SWEDEN
AZERBAIJAN	DOMINICAN REP.	INDONESIA	MALAYSIA	PUERTO RICO	SWITZERLAND

BAHAMAS	ECUADOR	IRAN	MALTA	QATAR	TAIWAN
BAHRAIN	EGYPT	IRAQ	MARTINIQUE	REP. OF ARMENIA	THAILAND
BANGLADESH	EL SALVADOR ESTONIA	IRELAND	MAURITIUS	REP. OF YEMEN	TRINIDAD, TOBAGO
BARBADOS	ESTONIA	ITALY	MEXICO	REUNION	TUNISIA
BELARUS	FINLAND	ISRAEL	MOROCCO	ROMANIA	TURKEY
BELGIUM	FRANCE	JAMAICA	NEPAL	RUSSIAN FED.	UKRAINE
BOLIVIA	FREN.POLYNESIA	JAPAN	NETHERLANDS	SAMOA, AMERICAN	UNITED ARAB EMIRATES
BRAZIL	FRENCH GUYANA	JORDAN	NEW CALEDONIA	SAN MARINO	UNITED KINGDOM
BRUNEI	GEORGIA	KAZAKHSTAN	NEW ZEALAND	SAUDI ARABIA	UNITED STATES
BULGARIA	GERMANY	KOSOVO	NICARAGUA	SERBIA	URUGUAY
CAMBODIA	GREECE	KOSOVO (DNU)	NORTH MARIANA	SINGAPORE	US VIRGIN IS.
CANADA	GUADELOUPE	KUWAIT	NORWAY	SLOVAKIA	UZBEKISTAN
VENEZUELA	VIETNAM				

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the XIENCE Family of Everolimus Eluting Coronary Stents.

Adverse events (in alphabetical order) which may be associated with percutaneous coronary and treatment procedures including coronary stent use in native coronary arteries include, but are not limited to:

- Abrupt closure
- Access site hematoma or hemorrhage
- Acute myocardial infarction
- Allergic reaction or hypersensitivity to contrast agent or cobalt, chromium, nickel, tungsten, acrylic and fluoropolymers; and drug reactions to antiplatelet drugs or contrast agent
- Aneurysm
- Arterial perforation and injury to the coronary artery
- Arterial rupture
- Arteriovenous fistula
- Arrhythmias, atrial and ventricular
- Bleeding complications, which may require transfusion
- Cardiac tamponade
- Coronary artery spasm
- Coronary or stent embolism
- Coronary or stent thrombosis
- Death
- Dissection of the coronary artery

- Distal emboli (air, tissue or thrombotic)
- Emergent or non-emergent surgery
- Fever
- Hypotension and/or hypertension
- Infection and pain at insertion site
- Injury to the coronary artery
- Ischemia (myocardial)
- Myocardial infarction (MI)
- Nausea and vomiting
- Palpitations
- Peripheral ischemia (due to vascular injury)
- Pseudoaneurysm
- Renal failure
- Restenosis of the stented segment of the artery
- Shock/pulmonary edema
- Stroke/cerebrovascular accident (CVA)
- Total occlusion of coronary artery
- Unstable or stable angina pectoris
- Vascular complications including at the entry site which may require vessel repair
- Vessel dissection

Zortress®, the oral formulation of everolimus developed by Novartis Pharmaceuticals Corporation, has been evaluated in clinical trials and is approved in the United States for the prevention of organ rejection in adult kidney transplant recipients at the dose of 1.5 mg/day.

Outside the U.S., Zortress is sold under the brand name, Certican®, in more than 70 countries. Everolimus is also approved in the United States under the name of Afinitor® for patients with advanced renal cell carcinoma (cancer), after failure of treatment with sunitinib or sorafenib, at doses of 5 to 20 mg/day when taken by mouth. The following list includes the known risks of everolimus at the oral doses listed above:

- Abdominal pain (including upper abdominal pain)
- Anemia
- Angioedema
- Anorexia
- Asthenia
- Constipation
- Cough
- Delayed wound healing/fluid accumulation
- Diarrhea
- Dyslipidemia (including hyperlipidemia and hypercholesterolemia)
- Dysgeusia
- Dyspepsia
- Dyspnea
- Dysuria

- Dry skin
- Edema (peripheral)
- Epistaxis
- Fatigue
- Headache
- Hematuria
- Hyperglycemia (may include new onset of diabetes)
- Hyperkalemia
- Hyperlipidemia
- Hypertension
- Hypokalemia
- Hypomagnesemia
- Hypophosphatemia
- Increased serum creatinine
- Infections and serious infections: bacterial, viral, fungal, and protozoal infections (may include herpes virus infection, polyoma virus infection which may be associated with BK virus associated nephropathy, and/or other opportunistic infections)
- Insomnia
- Interaction with strong inhibitors and inducers of CYP3A4 or PgP
- Leukopenia
- Lymphoma and other malignancies (including skin cancer)
- Male infertility (azospermia and/or oligospermia)
- Mucosal inflammation (including oral ulceration and oral mucositis)
- Nausea
- Neutropenia
- Non-infectious pneumonitis
- Pain: extremity, incision site and procedural, back, chest, musculoskeletal
- Proteinuria
- Pruritus
- Pyrexia
- Rash
- Stomatitis
- Thrombocytopenia
- Thrombotic microangiopathy (TMA)/Thrombotic thrombocytopenic purpura (TTP)/ Hemolytic uremic syndrome (HUS)
- Tremor
- Upper respiratory tract infection
- Urinary tract infection
- Vomiting

Live vaccines should be avoided and close contact with those that have had live vaccines should be avoided. Fetal harm can occur when administered to a pregnant woman. There may be other potential adverse events that are unforeseen at this time.

IX. SUMMARY OF PRECLINICAL STUDIES

A series of non-clinical laboratory studies related to the XIENCE Family of Stents were performed and the pertinent data is being leveraged from the previously approved PMAs P070015 and P110019.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a prospective analysis to establish a reasonable assurance of safety and effectiveness of percutaneous coronary intervention with the XIENCE Family of Stents for patients with diabetes mellitus in the US. Data from this analysis were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

A prospective analysis was designed to evaluate the safety and effectiveness of the XIENCE Family of Stents for patients with diabetes mellitus using one-year clinical data of diabetic patients from four AV-sponsored XIENCE stent clinical studies [SPIRIT IV (IDE G050050), SPIRIT PRIME (IDE G090068), XIENCE V USA first enrolment phase of 5,000 patients (IDE G050050), and XIENCE V USA second enrollment phase of 3,000 patients (IDE G050050)] and two external registry databases [Cleveland Clinic (CC) and the Wake Forest Baptist Medical Center (WFBMC)]. The two external databases are real-world observational registries, which are part of the National Cardiovascular Data Registry (NCDR) CathPCI registry.

A Bayesian hierarchical model was utilized to analyze the primary endpoint of target vessel failure (TVF) at 12 months, defined as a composite of cardiac death, target-vessel myocardial infarction (TVMI), or ischemia driven target vessel revascularization (ID-TVR). The TVF rate was tested against a prespecified performance goal (PG) of 14.8% (expected rate 8.6% plus a delta of 6.2%).

An "on-label" diabetic patients (including those who are treated with XIENCE 33 or 38 mm stent) from each trial/registry database were included in the analysis. Patients were considered as "on-label" diabetic if they had diabetes mellitus at baseline, had at least one XIENCE stent implanted during the index procedure, and satisfied the following criteria:

- Lesions/vessels which were treated during the index procedure:
  - Only de novo lesion
  - No chronic total occlusion lesion
  - No vessel thrombosis
  - No graft lesion
  - No bifurcation lesion
  - No left main lesion
  - At most two vessels treated, one lesion treatment per vessel
  - Reference vessel diameter between 2.25 and 4.25 mm (based on quantitative coronary angiography, visual assessment, or final balloon size pre-stent implantation)

    - Lesion length <32 mm (visual assessment)
    - If treated with a 33 or 38 mm XIENCE stent, only one 33 or 38 mm XIENCE stent treatment is allowed (overlapping with other length XIENCE stent is allowed)
- No acute myocardial infarction
- No renal insufficiency
- No staged procedure
- Left ventricular ejection fraction >30%

The statistical hypothesis was as follows:

$$H_0: \text{TVF} \geq 14.8\% \text{ vs. } H_a: \text{TVF} < 14.8\%.$$

The analysis was designed to support a claim that the TVF rate at 12 months for the XIENCE stent in on-label diabetic patients (including patients treated with a single 33 or 38 mm XIENCE stent) meets a PG of 14.8%. The study was considered to be successful if the posterior probability of a TVF rate <14.8% was greater than 0.975.

The results from the four AV-sponsored trial databases (SPIRIT IV, SPIRIT PRIME, XIENCE V USA first enrollment phase, and XIENCE V USA second enrollment phase) were considered as prior information. The two external XIENCE databases from CC and WFBMC were pooled as current data and served as the basis for statistical inference.

B. Number of Patients included in the PMA Cohort

There were 1,239 diabetic XIENCE patients included in this analysis: 451 from SPIRIT IV, 121 from SPIRIT PRIME, 185 from XIENCE V USA first enrollment phase, 192 from XIENCE V USA second enrollment phase, and 290 from pooled external databases (156 from CC and 134 from WFBMC, respectively).

Study Population Demographics and Baseline Parameters

The mean age of the diabetic population was 63 years from the pooled historical AV trials (SPIRIT IV, SPIRIT PRIME, XIENCE V USA first enrollment phase and second enrollment phase) and 65 years from the pooled two external databases (Wake Forest and Cleveland Clinic). There were 62.8% males from the pooled AV trials and 64.1% from the pooled external databases. Insulin treated diabetic patients comprised of 25.9% and 35.5% of the overall diabetic analysis population from the pooled AV trials and pooled external databases, respectively. A total of 26.6% of patients presented with unstable angina from the pooled AV trials and 57.6% from the pooled external databases. There were 23.8% and 35.9% patients who had prior MI, 34.2% and 44.8% who had prior PCI, and 10.5% and 24.5% who had prior CABG from the pooled AV trials and pooled external databases, respectively. The mean lesion length was 13.5 mm for the pooled AV trials, and 16.3 mm for the pooled external databases. There were 12.0% type C lesions in the pooled AV trials and 25.5% in the pooled external databases. There were 2.6% (32/1239) patients treated with 33 or 38 mm stents in this pooled dataset (2.5% from the pooled AV trials, and 2.8% from the pooled external databases). Compared to the pooled AV

trials, patient and lesion characteristics in the two external databases were generally more complex, likely due to their non-trial real-world settings.

C. Primary Endpoint Results

The primary endpoint of 1-year TVF rate was 8.04% based on the Bayesian binomial-normal hierarchical model where prior data from AV historical trials were taken into consideration. The 95% credible interval of TVF was between 5.23% and 11.52%. The posterior probability of a 1-year TVF rate <14.8% was >0.999, which exceeds the pre-specified success criteria (>0.975). Therefore, the analysis has met its pre-specified success criteria for the primary endpoint of 1-year TVF.

Table 11 Bayesian Analysis for the Primary Endpoint

Primary Endpoint	TVF Rate [95% Central Posterior Interval]*	Bayesian Posterior Probability (TVF < 14.8%)
1-year TVF	8.04% [5.23%, 11.52%]	> 0.999

*** The posterior mean is the Bayesian posterior average; the 95% central posterior interval is the symmetric 95% Bayesian credible interval, similar to the 95% confidence interval.**

Notes:

- The 1-year window is through 393 days (365 + 28 days).
- TVF is defined as hierarchical composite of cardiac death, target vessel MI, and ischemia-driven TVR. For the primary composite endpoint of TVF, an adjustment factor of 0.826 was applied for Cleveland Clinic to calculate the TVF rate based on the composite rate of all death/all MI/all TVR as the specifics of these events were not available from the Cleveland Clinic database.

The 1-year clinical outcomes of the XIENCE diabetic population from each of the AV trials (SPIRIT IV, SPIRIT PRIME and XIENCE V USA) and the pooled two external databases are shown in Table 11.

Table 11 One- Year Clinical Outcomes of the XIENCE Diabetic Population

	SPIRIT IV (N=451)	SPIRIT PRIME (N=121)	XV USA 5K (N=185)	XV USA 3K (N=192)	Pooled External (N=290)
TVF	7.9% (34/433)	11.8% (14/119)	7.3% (13/178)	3.6% (6/169)	8.0% (21/261)
TLF	5.5% (24/433)	5.9% (7/119)	6.7% (12/178)	2.4% (4/169)	2.4% (3/126)
Cardiac death or TVMI	3.0% (13/433)	2.5% (3/119)	3.4% (6/178)	0.6% (1/169)	0.8% (1/126)
ID-TVR	5.5% (24/433)	9.2% (11/119)	5.1% (9/178)	3.0% (5/169)	6.3% (8/126)
ID-TLR	3.2% (14/433)	3.4% (4/119)	3.9% (7/178)	1.8% (3/169)	2.4% (3/126)
Death	1.4% (6/433)	0.0% (0/119)	2.2% (4/178)	1.2% (2/169)	3.1% (8/261)
Cardiac death	0.9% (4/433)	0.0% (0/119)	1.1% (2/178)	0.6% (1/169)	0.0% (0/126)
TVMI	2.3% (10/433)	2.5% (3/119)	2.2% (4/178)	0.0% (0/169)	0.8% (1/126)
ST (ARC def/prob)	0.9% (4/431)	0.0% (0/119)	0.0% (0/175)	0.6% (1/169)	0.8% (2/261)

Notes:

- Numbers presented in this table are % (n/N).
- The 1-year window is through 393 days (365 + 28 days).
- XV USA 5K refers to the first enrollment phase of 5,000 patients in the XIENCE V USA study; XV USA 3K refers to the second enrollment phase of 3,000 patients in the XIENCE V USA study; pooled external refers to the pooled analysis of the two external databases (Cleveland Clinic and Wake Forest).
- TVF is defined as hierarchical composite of cardiac death, target vessel MI, and ischemia-driven TVR; TLF is defined as hierarchical composite of cardiac death, target vessel MI, and ischemia-driven TLR. ID-TLR= ischemia driven target lesion revascularization; ID-TVR=ischemia driven target vessel revascularization; TVMI=target vessel myocardial infarction; ST (ARC def/prob) = definite or probable stent thrombosis defined per the ARC definition.
- MI from the historical AV trials was defined per protocol and was categorized as Q-wave (development of new, pathological Q waves on the ECG) or non-Q-wave (elevation of CK levels to greater than two times the upper limit of normal and elevated CK-MB in the absence of new pathological Q waves). For the two external databases, MI was defined based on Universal MI definition per the National Cardiovascular Data Registry (NCDR) requirement.
- For the primary composite endpoint of TVF, an adjustment factor of 0.826 was applied to one of the two external databases in order to calculate the TVF rate based on the composite rate of all death/all MI/all TVR, as the specifics of these events were not available from that database.
- For other endpoints (TLF, cardiac death or TVMI, ID-TLR, ID-TVR, cardiac death and TVMI), only one of the external databases was included in the analysis, as the specific event information was not available in the other external database.

The results of this analysis support the indication for use of the XIENCE Family of Stents in patients with diabetes mellitus.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety and Effectiveness Conclusions

With regard to safety and effectiveness, the primary endpoint of target vessel failure (which consists of cardiac death, target vessel MI, and ischemia driven target vessel revascularization) is a composite of safety and effectiveness.

In the diabetic indication analysis presented herein, the posterior mean for the 1-year primary endpoint TVF was 8.04%. The 95% central posterior interval of TVF was between 5.23% and 11.52%. The posterior probability of a TVF rate <14.8% is > 0.999, which exceeds the pre-specified success criteria (>0.975). Therefore, the analysis has met its pre-specified success criterion for the primary endpoint of 1-year TVF. These 1-year clinical data from the internal AV trials and external databases support the safety and effectiveness of the XIENCE Family Stents in the treatment of diabetic patients with coronary artery disease.

B. Benefit-Risk Conclusions

The probable benefits of the device are also based on the data analysis conducted to support PMA approval as described above.

Percutaneous revascularization with coronary stent placement has been widely used as an alternative to medical or surgical treatment in selected patients with symptomatic coronary artery disease. The major limitations of PTCA (including but not limited to acute closure, intimal dissection, and restenosis) are overcome to a significant extent with coronary stents. The XIENCE Family of Stents is designed to improve luminal diameter and maintain arterial patency. Available clinical study data support acceptable event rates in diabetic patients treated with everolimus-eluting stents (EES). Diabetic patients benefit from treatment with EES because the use of bare metal stents is associated with the high rates of restenosis and target lesion revascularization.

Additional factors to be considered in determining probable risks associated with using this device are those associated with percutaneous coronary diagnostic procedures (including

angiography and IVUS) and treatment procedures. These risks are discussed in detail in Section VIII, "POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH" of this SSED.

XIENCE stent treatment in diabetic patients demonstrated acceptable rates of TVF, the individual components of TVF (cardiac death, MI, and target lesion revascularization) and stent thrombosis.

In conclusion, based on the 1-year data, the probable benefits of the devices in the XIENCE Family of Stents in the treatment of coronary artery disease in diabetic patients outweigh the probable risks.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The results of the prospective analysis of a diabetic population from four AV historical trials (SPIRIT IV, SPIRIT PRIME, XIENCE V USA first enrollment phase, XIENCE V USA second enrollment phase) and two external registry databases (CC and WFBMC) met the pre-specified success criteria based on a Bayesian analyses. The posterior mean for the primary endpoint of 1-year TVF rate was 8.04%, with 95% credible interval between 5.23% and 11.52%. The posterior probability of a TVF rate <14.8% is > 0.999, which exceeds the pre-specified success criteria (>0.975). These 1-year clinical data from internal AV trials and external databases support the safety and effectiveness of the XIENCE Family of Stents in the treatment of diabetic patients with coronary artery disease.

XIII. CDRH DECISION

CDRH issued an approval order on September 23, 2015. There were no conditions of approval cited in the approval order.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.