

SECTION 7.0
XIENCE V EECSS PROPOSED POST APPROVAL STUDY

The following section summarizes both the continued access trial and the US post approval clinical study for the XIENCE™ V Everolimus Eluting Coronary Stent System (EECSS). These studies are comprised of the SPIRIT IV continued access clinical trial and XIENCE V USA post-approval clinical study. The SPIRIT IV clinical trial is currently ongoing and patients are being enrolled. The XIENCE V USA post-approval study will commence upon commercial approval (PMA approval) of the XIENCE V EECSS. Patients in both studies will be followed out to five years. Additional post-approval studies will be conducted outside the United States.

7.1 SPIRIT IV Clinical Trial (Continued Access Trial): Summary of Ongoing Study

This section summarizes the study design and number of subjects enrolled as of October 1, 2007 into the SPIRIT IV clinical trial. SPIRIT IV (study number 05-368) is a prospective, randomized, active-controlled, single-blinded, multi-center, clinical study evaluating the safety and efficacy of the XIENCE V EECSS for the treatment of *de novo* lesions ≤ 28 mm in length in native coronary artery vessels with RVD ≥ 2.5 mm to ≤ 4.25 mm, at up to 70 clinical sites in the United States.

7.1.1 Study Design

Up to 3690 subjects will be enrolled (Table 7-1) in the SPIRIT IV clinical trial. The first subject was enrolled in August 2006 and enrollment remains on-going. A total of 1,929 subjects at 51 investigational sites were enrolled on or before October 1, 2007. Subject randomization is 2:1 with 2460 subjects to receive the XIENCE V EECSS and 1230 subjects to receive the TAXUS EXPRESS²™ PECCS.

Table 7-1 Randomization Ratio and Sample Size

Treatment Group	Randomization Ratio	Sample Size
XIENCE V	2	2460
TAXUS	1	1230

Ischemia driven major adverse cardiac event (MACE) at 270 days is the primary endpoint. Secondary endpoints include¹:

- Ischemia driven target vessel failure (TVF) at 30, 180, 270 days, and 1, 2, 3, 4, and 5 years
- Ischemia driven target lesion revascularization (TLR) at 30, 180 and 270 days, and 1, 2, 3, 4, and 5 years
- Ischemia driven target vessel revascularization (TVR) at 30, 180 and 270 days, and 1, 2, 3, 4, and 5 years
- Ischemia driven MACE at 30, 180 days and 1, 2, 3, 4, and 5 years
- Acute Success (clinical device and clinical procedure)

Treatment of up to three *de novo* native coronary artery lesions is permitted, with a maximum of two lesions per epicardial vessel is allowed after successful pre-dilatation. Stent overlap is also allowed for XIENCE V subjects with lesions > 22 mm. In order for a patient to be included in the study, the target lesion/vessel must meet the requirements of the protocol. If the subject has received brachytherapy in any epicardial vessel or if the target lesion/vessel meets any of the exclusion criteria, the patient will be excluded from the study.

The analytical population for this study will be comprised of the intent-to-treat (ITT) population for the primary analysis. Subjects are scheduled for a clinical follow-up at 30, 180 and 270 days, and 1, 2, 3, 4 and 5 years following the index procedure. Follow-up visits include the collection of adverse event data, summarized and

¹ Abbott Vascular is currently working with FDA to extend the primary endpoint and add additional secondary endpoints.

adjudicated by the clinical events committee (CEC).

Safety is being assessed on a continuous basis in SPIRIT IV. Events are reviewed by the clinical safety monitors. Serious adverse events are reviewed and adjudicated by an independent CEC. The data safety monitoring board (DSMB) has regularly scheduled meetings. The DSMB reviews unblinded data provided by an independent third party. An independent review by the DSMB after the enrollment of 1200 subjects did not reveal any concerns that would impact continuation of the trial.

7.2 XIENCE V USA Post Approval Trial: Summary of Proposed Study

This section summarizes the study design of the XIENCE™ V Everolimus Eluting Coronary Stent System (EECSS) USA Post Approval Study. The XIENCE V USA (study number 06-374) is a prospective, open-label, multi-center, observational, single-arm registry designed to evaluate the continued safety and efficacy of the XIENCE V EECSS during commercial use in real world settings. Specifically, the XIENCE V USA will evaluate clinical outcomes in a cohort of real world patients receiving the XIENCE V EECSS during commercial use by various physicians with a range of coronary stenting experience, patient compliance with adjunctive antiplatelet therapy and major bleeding complications, clinical device and procedural success during commercial use, and patient health status (symptoms, physical function, and quality of life) by the Seattle Angina Questionnaire.

7.2.1 Study Design

Approximately 5000 XIENCE V patients will be consecutively enrolled at up to 275 sites in the United States of America. Academic Research Consortium (ARC) defined stent thrombosis at 1 year is the primary endpoint. Secondary endpoints include:

- Stent thrombosis at 24 hours, 30, 180 days and at 2, 3, 4 and 5 years
- Composite rate of death, myocardial infarction (MI), and revascularization (percutaneous coronary intervention [PCI] and coronary artery bypass graft [CABG]) at 30, 180 days and at 1, 2, 3, 4 and 5 years
- Composite rate of cardiac death, MI attributed to the target vessel, and target lesion revascularization (TLR) at 30, 180 days and at 1, 2, 3, 4 and 5 years
- Death (cardiac death, vascular death, non-cardiovascular death) at 30, 180, days and at 1, 2, 3, 4 and 5 years
- MI (both Q-wave and non Q-wave) at 30, 180 days and at 1, 2, 3, 4 and 5 years
- Revascularization (both PCI and CABG) at 30, 180 days and at 1, 2, 3, 4 and 5 years
- Target vessel revascularization (both PCI and CABG) (TVR) at 30, 180 days and at 1, 2, 3, 4 and 5 years
- TLR (both PCI and CABG) at 30, 180 days and at 1, 2, 3, 4 and 5 years
- Compliance and therapy interruptions with prescribed adjunctive antiplatelet therapy at 14, 30, 180 days and at 1, 2, 3, 4 and 5 years
- Major bleeding complications at 14, 30, 180 days and at 1, 2, 3, 4 and 5 years
- Clinical device and procedural success
- Patient health status (symptoms, physical function, and quality of life) at baseline, 180 days, and 1 year as assessed by the Seattle Angina Questionnaire

The treatment strategy will be determined by the investigator. It is recommended that each enrolling investigator review the XIENCE V EECSS Instructions for Use and assess the contraindications, warnings and precaution sections with respect to risks and benefits for treating potential patients. In order for a patient to be included

in the study, they (or their legal representative) must agree to participate in this study by signing the Institutional Review Board approved informed consent form and only XIENCE V EECSS stent(s) is (are) implanted into patient's coronary vasculature during the index procedure. If informed consent is unobtainable or stent(s) other than XIENCE V is (are) implanted, the patient will be excluded from the study.

The analytical population for this study will be comprised of patients who received only XIENCE V EECSS during the index procedure. Clinical follow-up will occur at 14, 30, 180 days and 1, 2, 3, 4, and 5 years. The investigator or designee may conduct follow-up as telephone contacts or office visits.

All serious adverse events will be reviewed by an independent DSMB to ensure public safety throughout the 5-year follow-up. An independent clinical events committee will review and adjudicate according to ARC definitions for the following: death, MI, revascularization, and stent thrombosis. Major bleeding complications and unexpected adverse device effects will also be adjudicated.

Please refer to the XIENCE V USA Post-Approval Study protocol included in Attachment 7A for additional details regarding the study design.