U.S. FOOD & DRUG ADMINISTRATION

Inaugural RAPID Phase II/III Research Project

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SFA-**P**opliteal **E**videnc**E** **D**evelopment **(SPEED)** project

- **Rationale:**
  - While application of RAPID to unapproved technologies with greater levels of uncertainty, such as below-the-knee devices, may at first glance seem appealing, the superficial femoral artery (SFA) and proximal popliteal space is much more mature space.
  - Therefore, SPEED is ideally suited for evaluating this new registry-based systems as we already have a handle on the basic safety and effectiveness of these devices, allowing the RAPID project to be tested without risk to participating subjects.

SPEED Rationale

- Although the SFA and popliteal arteries space is a relatively mature research area, there are still many vitally **important regulatory questions** that remain **unanswered**, including:
  - Determination of a contemporary **objective performance criteria (OPC)** that is appropriate for patients with **long and heavily calcified lesions**
  - Assessment of the clinical value of newly approved modalities such as lithoplasty, innovative atherectomy devices, drug coated balloons, and a new generation of stents with novel and unique features
- Also, since many of these devices are used in combination, only a CRN such as RAPID with its potentially large data base could allow effective analysis of subgroups of patients with varying combinations and permutations of devices.
- **SPEED** would allow the FDA and all stakeholders to assess the feasibility of the RAPID project without compromising regulatory science and patient safety.

SPEED Objectives

- Develop a contemporary OPC using real world evidence (RWE).

- Potential labeling modification (e.g., longer lesions, heavy calcified lesions, diabetic patients).

  - The proposed paradigm is that industry will have access to the conglomerate of data plus their own data
  - Thus, if pre-specified statistical plan is met for a given subgroup analysis population as per examples above, a labeling modification could be requested/granted

Contains Nonbinding Recommendations

Draft – Not for Implementation

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

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Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on July 27, 2016.

Sample Size Guestimates

- Estimates derived from the Vascular Quality Initiative (VQI)
  - 14093 cases in the VQI with at least one treated artery = SFA or proximal popliteal from Jul 2015 – Jun 2016

- SPEED sample size guestimate:
  - **21000 patients with procedural** (7000 prospective and 14000 retrospective) data and
  - **4900 patients with 1 year follow-up data** (accounting for 30% lost to follow-up)

Proposed SPEED Timeline

- **May 25, 2017:** Project introduction

- **June – Sept, 2017:** Obtain legal and financial agreements/contracts to allow for multi-stakeholder collaboration (some of these already in place under RAPID phase 1 and may only need an extension)

- **Sept 2017 to March 2018:** Data Collection

  - **Prospective RWE** – Data collection using VQI for **6 months** (Sept 2017 to Mar 2018). Thus, a sample size of approximately **7000 patients** with procedural data will be available for OPC development with the respective subgroup analysis.

  - **Retrospective RWE** – Use data collected from procedures from Sept 2016 to Aug 2017, with 1 year follow-up and UDI information by March 2018. Thus, a sample size of **14000 patients** with procedural data and approximately 7000 patients with 1 year follow-up will be available for OPC development with the respective subgroup analysis. However, since the current 1 year follow-up for VQI is 70%, we estimate that **4900 patients** will have 1 year follow-up.

Proposed SPEED Timeline

Data refinement and analyses

- **April – June, 2018:**
  - Data refinement and analyses to develop a contemporary OPC using RWE
  - Data sharing with industry stakeholders for potential labeling modification (e.g., longer lesions, heavy calcified lesions, diabetic patients)

- **July – September, 2018:** Regulatory submission depending on device class (PMA, 510k)

SPEED: Potential Scenario

- Disclosures:
  - The estimated rates are based on high-level estimates, and will need to be refined based on limited off-label information gathered thus far to help better define sample sizes prospectively
  - We do not plan to power the analyses for safety, so these values are for clinical consideration and interpretation

Potential subset of indication/labeling expansions for devices under SPEED

Device type	Plain angioplasty	Bare metal stent/ covered stent
	Drug-coated Balloon	Drug-eluting stent
Lesion Characteristics	Long lesions (>140mm)	In-stent restenosis
	Calcification	Chronic Total Occlusion
	Behind the knee (P3)	
Patient Characteristics	Gender	Race
	Diabetes	

SPEED: Potential Scenario

Endpoint	Event	Estimated Rate (1 yr)	Acceptable Rate (1 yr)	Sample Size (power=90%, alpha=0.025)
Primary Safety	Major Amputations	1%*	<2%*	1539
	Clinically-significant fracture (BTK** stents)	5%*	<10%*	231
Primary Effectiveness	TLR***			
Long lesion		60%*	>50%*	263
Behind-the-knee				
Sever Calcification (based on Rocha-Singh, et al)				
In-stent restenosis				
Chronic total occlusions				

* General estimate. Detailed estimates for each category will be generated by a summer student based on current SSEDs.
** BTK = Below the knee
***TLR = Target lesion revascularization

SPEED Summary

- Develop a contemporary OPC using RWE
- Potential labeling modification (e.g., longer lesions, heavy calcified lesions)
- Generate good quality data for the treatment of claudication
  - CMS MEDCAC for lower extremity
- Demonstration project for the National Evaluation System for Health Technology (NEST)

Thank You