Summary of Safety and Effectiveness Data (SSED)

I. GENERAL INFORMATION

Device Generic Name:	LifeStent® and LifeStent® XL
Device Trade Name:	LifeStent® Vascular Stent System LifeStent® XL Vascular Stent System
Applicant Name and Address:	Bard Peripheral Vascular, Inc. 1625 W. 3rd Street Tempe, AZ 85281
Premarket Approval Application (PMA) Number:	P070014/S010
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	December 23, 2010
Expedited:	Not applicable

The original PMA (P070014) was approved on February 13, 2009 and is intended to improve luminal diameter in the treatment of symptomatic de-novo or restenotic lesions up to 160 mm in length in native Superficial Femoral Artery (SFA) and/or proximal popliteal arteries with reference vessel diameters ranging from 4.0 - 6.5 mm. The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the LifeStent® and LifeStent® XL Vascular Stent Systems.

II. INDICATIONS FOR USE

The LifeStent® and LifeStent® XL Vascular Stent Systems are intended to improve luminal diameter in the treatment of symptomatic *de-novo* or restenotic lesions up to 240 mm in length in native Superficial Femoral Artery (SFA) and/or proximal popliteal arteries with reference vessel diameters ranging from 4.0 – 6.5 mm.

III. CONTRAINDICATIONS

The LifeStent® and LifeStent® XL Vascular Stent are contraindicated for use in:

- Patients with a known hypersensitivity to Nitinol (nickel, titanium) and/or tantalum.
- Patients who cannot receive recommended anti-platelet and/or anti-coagulation therapy.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system.

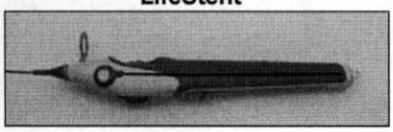
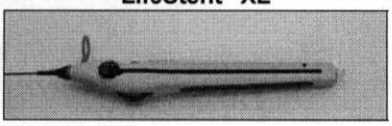
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the LifeStent® and LifeStent® XL Vascular Stent System labeling (Instructions for Use).

V. DEVICE DESCRIPTION

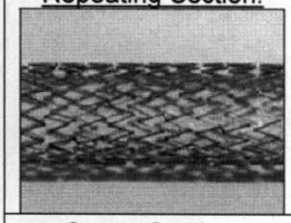
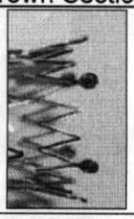
The LifeStent® and LifeStent® XL Vascular Stent Systems are designed to deliver nitinol self-expanding stents, designed to maintain patency of obstructed peripheral vascular arteries, via a sheathed delivery system.

Table 1: LifeStent® System Family Summary

System	Stent	Deployment Mechanisms
LifeStent® 	Ø6mm X 20-80mm Ø7mm X 20-80mm Contains 6 radiopaque tantalum markers on each end	Thumbwheel Rapid Deployment Lever Rapid Deployment Ring
LifeStent® XL 	Ø6mm X 100-170mm Ø7mm X 100-170mm No radiopaque markers	Thumbwheel Rapid Deployment Lever

The stents are equivalent in design with only one difference located at the crown section; the LifeStent® stent has 6 tantalum radiopaque markers on both the distal and proximal ends of the stent, while the LifeStent® XL stent does not have markers.

Table 2: LifeStent® Stent Design

Repeating Section: 	A repeat section of circumferentially distributed struts following a helical pitch/pattern. Rows of struts are connected with bridges placed every fifth strut pair and consists of 19 strut pairs per 360° repeat. Stent length is modified by increasing or decreasing the number of 19 strut pair segments within the repeating section of the stent. This section is the same for both the LifeStent® and LifeStent® XL stents.
Crown Section: 	LifeStent®: Two identical crown sections of circumferentially distributed struts located at each end of the stent. The crown section has a flared outside diameter and consists of 18 strut pairs in each crown section. These segments located at the distal and proximal ends of the stent, contain six (6) links that each terminate into a ring that holds a tantalum, disk-shaped, radiopaque marker.
	LifeStent®XL: Two identical crown sections of circumferentially distributed struts located at each end of the stent. The crown section has a flared outside diameter and consists of 18 strut pairs in each crown section. These segments are located at the distal and proximal ends of the stent.

Transition Zone: 	Two identical transition zones of circumferentially distributed struts around 360 degrees. The transition zones are located between the repeat section and the crown sections at both ends of the stent and are connected to the crown sections and the repeat sections of the stent with bridges. This section is the same for both the LifeStent® and LifeStent® XL stents.

Figure 1: LifeStent® Stent Design (20-80mm lengths)

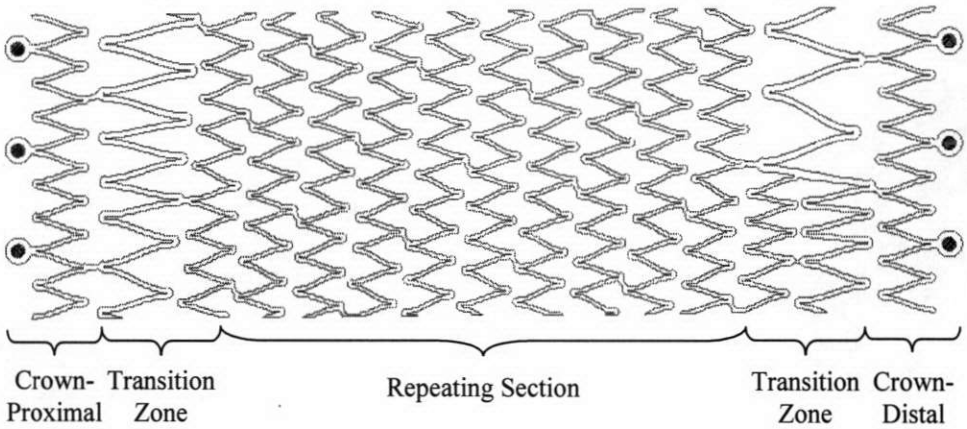
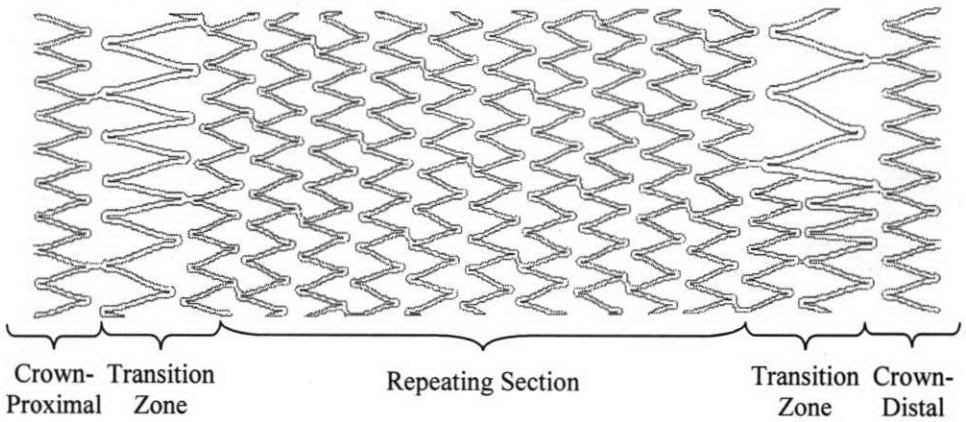


Figure 2: LifeStent® XLStent Design (100-170mm lengths)



The device is available in the following diameters and lengths:

Table 3: LifeStent® and LifeStent® XL Lengths

Diameters	*LifeStent® Lengths (mm)*					*LifeStent® XL Lengths (mm)*			
6mm	20	30	40	60	80	100	120	150	170
7mm	20	30	40	60	80	100	120	150	170

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of superficial femoral and proximal popliteal artery atherosclerotic disease:

- Non-Invasive Treatment (exercise and/or drug therapy)
- Minimally Invasive Treatment (balloon angioplasty, endovascular stent placement, directional atherectomy)
- Surgical Treatment (surgical by-pass)

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 LifeStent® and LifeStent® XL Vascular Stent Systems were introduced into the European Union (EU) market in the winter of 2006. Additionally, the LifeStent® and LifeStent® XL Stent System have been cleared for use within the Biliary Tree in the United States beginning in December of 2005 and April of 2006, respectively. The stent systems approved for this PMA are identical with the systems cleared for use in the Biliary Tree. In August 2008, the LifeStent® Biliary Stent System device was recalled. Specifically, some of the devices exhibited a gap between the tip of the delivery system and the primary sheath such that the guidewire lumen could be visible. The corrective and preventative actions implemented appear to have adequately addressed the tip-to-sheath gap issue. The LifeStent® and LifeStent® XL delivery systems were evaluated in the E-TAGIUSS confirmatory clinical study. In February 2009, the LifeStent and LifeStent XL Vascular Stent Systems were approved for the treatment of symptomatic *de-novo* or restenotic lesions up to 160 mm in length in native Superficial Femoral Artery (SFA) and/or proximal popliteal arteries.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects (e.g., complications) that may occur and/or require intervention with the use of this device include, but are not limited to:

- Allergic/anaphylactoid reaction
- Amputation
- Aneurysm
- Angina/coronary ischemia
- Arterial occlusion/thrombus, near the puncture site
- Arterial occlusion/thrombus, remote from puncture site
- Arterial occlusion/restenosis of the treated vessel
- Arteriovenous fistula
- Arrhythmia
- By-pass Surgery
- Death related to procedure

- Death unrelated to procedure
- Embolization, arterial
- Embolization, stent
- Fever
- Hemorrhage/bleeding requiring a blood transfusion
- Hematoma bleed, remote site
- Hematoma bleed at needle, device path: nonvascular procedure
- Hematoma bleed, puncture site: vascular procedure
- Hypotension/hypertension
- Incorrect positioning of the stent requiring further stenting or surgery
- Intimal injury/dissection
- Ischemia/infarction of tissue/organ
- Liver failure
- Local infection
- Malposition (failure to deliver the stent to the intended site)
- Open surgical repair
- Pain
- Pancreatitis
- Pulmonary embolism/edema
- Pneumothorax
- Pseudoaneurysm
- Renal failure
- Respiratory arrest
- Restenosis
- Septicemia/bacteremia
- Stent Fracture
- Stent Migration
- Stroke
- Vasospasm
- Venous occlusion/thrombosis, remote from puncture site
- Venous occlusion/thrombosis, near the puncture site

For the specific adverse events that occurred in the clinical studies conducted to support the original indication, please see Section X of the original SSED.

IX. SUMMARY OF PRECLINICAL STUDIES

No new preclinical studies were submitted or required for the approval of the expanded indication proposed in this PMA supplement. Please see the original SSED for details.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a retrospective analysis involving 285 patients for the treatment of long segment lesions in order to expand the Indication for Use of the LifeStent® and LifeStent® Vascular Stent Systems. These retrospective data were the basis for the PMA Supplement approval decision to expand the indication for use to include treatment of lesions up to 240 mm in length.

A. Study Design

Retrospective Analysis of LifeStent® Vascular Stent Systems in the Treatment of Long Segment Lesions: Study Overview

This study consisted of a post-hoc analysis of four sources of data: (1) a pivotal IDE clinical trial (RESILIENT: IDE G040023; "RESILIENT"), (2) a multi-center, non-randomized, observational study conducted in Europe ("ELODIE I"), (3) the routine clinical practice of a United States (U.S.) physician ("US Series"), and (4) the routine clinical practice of a European Union (EU) physician ("EU Series"). In total, two-hundred-eighty-five (285) patients with one or more implanted LifeStent® devices were identified and included in the analysis. There were a total of 46 lesion segments in this analysis with lesion lengths beyond 160 mm.

Subjects received at least one commercially available LifeStent® which was identical to the current commercially available LifeStent® device. Specifically, the following analyses were undertaken:

- Estimating the patency (defined in this analysis as freedom from TVR) at 12-months post-procedure of lesions of length: 50 mm, 100 mm, 160 mm, and 240 mm (long-term effectiveness)
- Comparing the combined performance of the LifeStent® device at 30-days post-procedure to the ViVa OPC, (acute safety) and,
- Estimating the freedom from death and amputation at 12-months post-procedure in patients with long lesions treated with the LifeStent® device by calculating the rates observed in this study (long-term safety).

1. Retrospective Analysis of LifeStent® Vascular Stent Systems in the Treatment of Long Segment Lesions: Clinical Inclusion and Exclusion Criteria

No pre-specified Inclusion Criteria other than those attributed to the individual studies themselves were applied to this post-hoc analysis. All RESILIENT study patients, and all patients collected as part of the US series were compiled for this analysis. Additionally, only those patients in the ELODIE study and the EU series with lesion segments or stented segments > 160 mm in length who were treated with LifeStent® were compiled for this analysis.

No pre-specified Exclusion Criteria other than those specified by the individual studies themselves were applied to this post-hoc analysis.

2. Retrospective Analysis of LifeStent® Vascular Stent Systems in the Treatment of Long Segment Lesions: Follow- up Schedule

No pre-specified Follow-up Schedules other than those attributed to the individual studies themselves were applied to this post-hoc analysis. All RESILIENT study patients, and all patients collected as part of the US series were compiled for this analysis. Additionally, only those patients in the ELODIE study and the EU series with lesion segments or stented segments > 160 mm in length who were treated with LifeStent® were compiled for this analysis.

3. Retrospective Analysis of LifeStent® Vascular Stent Systems in the Treatment of Long Segment Lesions: Clinical Endpoints

The primary safety and effectiveness endpoints assessed in this study were:

- Acute Safety, defined as the estimate of freedom from death, amputation, or TVR at 30-days post-procedure for all patients (compared to the ViVa OPC); and,
- Long-term Safety, defined as the estimate of freedom from death or amputation at 12-months post-procedure in patients with total lesions lengths ≥ 160 mm; and,
- Effectiveness, defined as the estimate of freedom from Target Vessel Revascularization (TVR) at 12-months post-procedure in lesions of length 50 mm, 100 mm, 160 mm, 200 mm, and 240 mm.

B. Accountability of PMA Cohort

All patients with lesion segments or stented segments > 160 mm in length were included in the retrospective analysis. There was a total of 46 lesion segments in this analysis with lesion lengths beyond 160mm.

C. Patient Demographics and Baseline Parameters

Retrospective Analysis of LifeStent® Vascular Stent Systems in the Treatment of Long Segment Lesions: Study Population Demographics

Characteristics of the subjects and lesions analyzed are provided in the tables below.

Table 4: Retrospective Analysis of LifeStent - Long-Segment Lesions Subject and Lesion Characteristics

Characteristic	RESILIENT	ELODIE I	US Series	EU Series	TOTAL
Age at Procedure (years)					
N reported	198	11	66	10	285
Mean	68.4	71.8	72.6	73.9	69.7
St Dev Range	10.2	8.63	10.9	5.53	10.3
	20.7 – 88.2	53.9 - 85.6	36.3 - 96.8	63.9 - 83.1	20.7 – 96.8
Gender (% male)	69.2	45.5	60.6	44.4	65.5
N reported*	198	11	66	9	284
Race (% Caucasian)	88.9	100	77.3	100	86.6
N reported	198	3	66	10	277
Hypertension (%)	85.4	72.7	84.9	100	85.3
N reported	198	11	66	10	285
Hypercholesterolemia (%)	80.3	54.6	75.8	80.0	78.3
N reported	198	11	66	10	285
Smoking (%)	25.8	36.4	60.6	0.0	33.3
N reported	198	11	66	10	285
CAD (%)	56.6	27.3	57.6	30.0	54.7
N reported	198	11	66	10	285
DM (%)	38.9	0.00	50.0	30.0	39.7
N reported	198	11	66	10	285
Rutherford Category of Target Limb					
N reported	198	11	NR	10	219
Class 1 (%)	3.5	0		0	3.2
Class 2 (%)	40.4	45.5		10.0	39.3
Class 3 (%)	56.1	36.4		60.0	55.3
Class 4 (%)	0.0	0		0	0
Class 5 (%)	0.0	18.2		30.0	2.3
Indication of Target Limb					
N reported	198	11	71	10	290
Claudication (%)	100	90.9	49.3	70.0	86.6
Critical Limb Ischemia (%)	0	9.1	50.7	30.0	13.4
ABI of Target Limb					
N reported	183	NR	51	10	244

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Table 4: Retrospective Analysis of LifeStent - Long-Segment Lesions Subject and Lesion Characteristics					
Mean	0.72		0.61	0.41	0.69
St Dev	0.20		0.22	0.18	0.22
Range	0.24 - 1.45		0 - 1.34	0.1 - 0.67	0 – 1.45

* One patient did not report gender
NR- Not Reported

Table 5: Retrospective Analysis of LifeStent - Long-Segment Lesions Lesion and Stent Characteristics					
Characteristic	**RESILIENT**	**ELODIE I**	**US Series**	**EU Series**	**TOTAL**
N Patients	198	11	66	10	285
N Treated Limbs	198	11	72	10	291
N Treated Lesions	212	16	72	10	310
Individual Lesion Length					
N reported	212	16	72	10	310
Mean (mm)	66.0	108.8	152.6	214.0	93.1
St Dev Length	35.7	44.7	104.5	109.6	75.1
Mean N per Limb	1.1	1.5	1.1	1.0	1.1
Percent Stenosis (max per limb):					
N reported	198	11	0	10	219
Mean	87.8	92.7		96.0	88.5
St Dev	11.3	9.05		6.99	11.2
Range	50 - 100	80 - 100		80 - 100	50 - 100
N Total Lesion Lengths:					
< 50 mm	62	1	9	0	72
50 – <100 mm	93	0	19	0	112
100 – <160 mm	37	6	15	3	61
160 – <200 mm	5	1	3	4	13
200 – 240 mm	1	2	8	0	11
≥ 240 mm	0	1	18	3	22
Total Lesion Lengths:					
N	198	11	72	10	291
Mean	70.6	158.2	152.6	214	99.15
St Dev	37.7	57.8	104.5	109.6	77.3
Range	10 - 202	30 - 240	16 - 360	140 - 500	10 - 500
N Total Stented Lengths:					
< 60 mm	40	0	NR	0	40
60 – < 110 mm	71	0	NR	0	71
110 – < 170 mm	73	1	NR	1	75
170 – < 210 mm	7	7	NR	5	19
210 – < 250 mm	5	0	NR	1	6
≥ 250 mm	2	3	NR	3	8
Total Stent Lengths:					
N	198	11	NR	10	219
Mean	104.5	204.5		244.4	115.9
St Dev	55.4	53.2		125.1	69.4
Range	30 - 340	160 - 290		160 - 574	30- 574
TASC Classification	NR			NR	
N Grade A (%)		1 (9.1%)	23 (39.0%)		24 (34.3%)
N Grade B (%)		3 (27.3%)	11(18.6 %)		14 (20.0%)
N Grade C (%)		7 (63.6%)	6 (10.2%)		13 (18.6%)
N Grade D (%)		0 (0%)	19 (32.2%)		19 (27.1%)
Total		11	59		70

* For lesion characteristics, core lab data were used when available; the site reported data were used otherwise. Five (5) patients did not have lesion characteristics reported by the core lab
NR- Not Reported

D. Safety and Effectiveness Results

Retrospective Analysis of LifeStent® Vascular Stent Systems in the Treatment of Long Segment Lesions: Outcomes

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1. Safety Results

The primary acute safety endpoint of the LifeStent® and LifeStent® XL Vascular Stent Systems at 30 days post-procedure showed that the freedom-from rates were higher than the ViVa OPC (88%). The 30-day freedom-from-death, amputation and TVR rate was 99.6% with a standard error of 0.34% (95% CI: 97.59% - 99.95%).

The primary long-term safety endpoint was freedom from death/amputation. The Kaplan-Meier analysis showed that the freedom-from-death/amputation rate at 12 months was 100% (lesions < 50 mm), 94.5% (lesions 50 - 100mm), 91.4% (lesions 100 - 160 mm), 63.6% (lesions 160 - 200 mm), 90.9% (lesions 200 - 240 mm) and 94.1% (lesions >240 mm).

Table 7: Retrospective Analysis of LifeStent Freedom from Death/Amputation*

	12 months (n/N**)
All Lesions	93.8% (17/291)
Lesions < 50 mm	100% (0/72)
Lesions 50 - 100 mm	94.5% (6/112)
Lesions 100 - 160 mm	91.4% (5/61)
Lesions 160 - 200 mm	63.6% (4/13)
Lesions 200 - 240 mm	90.9% (1/11)

* From the Weibull covariate-adjusted analysis
**Number starting the year

2. Effectiveness Results

The results for the primary effectiveness endpoint as defined by freedom from TVR/TLR are shown in the table below.

Table 6: Retrospective Analysis of LifeStent - Long-Segment Lesions Freedom from TLR/TVR* by Time and Lesion Length

Variable	12 months Weibull*/Kaplan-Meier (n/N**at 12 months)	24 months Weibull*/Kaplan-Meier (n/N**at 12 months)
Average of all (total) lesion lengths (= 101.1 mm)	82.4% / 79.2% (54/291)	63.3% / 62.5% (29/170)
(n= 72) < 50 mm lesions (Weibull: 50 mm)	85.4% / 83.4% (11/72)	69.0% / 68.1% (7/48)
(n= 112) 50 - <100 mm lesions (Weibull: 100 mm)	81.9% / 87.9% (12/112)	62.5% / 74.3% (9/73)
(n= 61) 100 - <160 mm lesions (Weibull: 160 mm)	76.7% / 76.5% (13/61)	53.6% / 55.2% (9/35)
(n= 13) 160 - <200 mm lesions (Weibull: 200 mm)	72.6% / 38.9% (7/13)	47.0% / 38.9% (0/2)
(n= 11) 200 - < 240 mm lesions (Weibull: 240 mm)	67.9% / 67.5% (3/11)	40.2% / NA (1/5)
(n= 22) ≥ 240 mm lesions	NA / 55.9% (8/22)	NA / 23.9% (3/7)

* From the Weibull covariate-adjusted analysis
**Number starting the year

It is important to note that this retrospective analysis was not powered to detect statistically significant differences in the performance of the LifeStent device for the treatment of long segment lesions compared to that for the treatment lesion lengths up to 160 mm. However, the safety and effectiveness results provided through this analysis were found to be clinically acceptable and powered assessments were determined to be unnecessary. Additional data will be collected in the post-marketing CONTINUUM study to confirm the performance of the LifeStent and LifeStent XL in the treatment of long segment lesions.

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XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

All of the issues associated with the long-term results of the clinical studies and long-term follow-up have been addressed in the preceding section.

XIII. PANEL MEETING RECOMMENDATION

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 Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The results of the Retrospective Analysis of LifeStent® Vascular Stent Systems in the Treatment of Long Segment Lesions show that LifeStent® can be safely implanted in patients with longer lesions (>160 mm) and can provide an effective solution to the treatment of long segment lesions with acceptable freedom from reintervention rates.

XV. CDRH DECISION

CDRH issued an approval order on December 23, 2010. The final conditions of approval cited in the approval order are described below.

The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

XVI. APPROVAL SPECIFICATION

Directions for Use: See device labeling.

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

Post Approval Requirements and Restrictions: See approval order.

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