2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

September 19, 2018

Urgent: Important Safety Update
AFX® Endovascular AAA System

Dear Physician,

This letter provides important information related to the AFX Endovascular AAA System (AFX System) which is intended for the endovascular treatment of patients with abdominal aortic aneurysms (AAA). In previous safety updates, Endologix has provided information on the rates of Type III endoleaks and suggestions for patient surveillance and treatment. This notification provides the following additional information:

1) Update on Type III endoleak rates (Appendix 1)
2) Refined patient-tailored surveillance recommendations (Appendix 2)
3) Sizing recommendations for AFX with Duraply, which align with the AFX2 with Duraply IFU sizing recommendations (Appendix 3)
4) Recommendations for intervening through an AFX device or re-intervening on an AFX device (Appendices 4 and 5, respectively)

Please note this notice provides updated information and revisions to the Instructions for Use (IFU) to enhance patient safety. **No product return is required**. The Regulatory Agency of your country has been notified of this communication.

Update on Type III Endoleak Rates

Type III endoleaks may cause increased pressure within the aneurysm sac that could increase the risk of aneurysm rupture and patient death. Investigations into Type III endoleaks have identified the following associations:

- Inadequate component overlap at the index procedure
- Lateral movement in large or tortuous aortas leading to reduction or loss of component overlap and/or implant stability
- Use of an excessively oversized proximal extension relative to the bifurcated main body device
- Procedural factors such as extensive guidewire/catheter manipulation or aggressive balloon molding
- Off-label use (especially in highly calcified anatomy)
- Implant of other manufacturer's devices as proximal extensions

As explained in previous communications, Endologix has taken a number of actions in recent years to address Type III endoleaks with the AFX System. These have included changes to the system's Instructions for Use (IFU) as well as product modifications intended to help prevent the occurrence of Type III endoleaks such as changing from the original graft material processing referred to as Strata (AFX System with Strata) to an improved process known as Duraply™ (AFX System with Duraply™), and introduction of the AFX®2 Bifurcated Endograft System manufactured with Duraply (AFX2 System with Duraply). Endologix has been monitoring the effectiveness of these changes through its complaint monitoring system and, as shown in Appendix 1, the reported Type IIIa and IIIb endoleak estimated complaint rates at equivalent time points past 1-year have been lower for the AFX System with Duraply and AFX2 System with Duraply compared to the AFX System with Strata, which has been discontinued and was removed from the field in December 2016. Note that the estimated complaint rates are calculated based on voluntary complaint reporting and units sold, which may underestimate the true event rate on a per patient basis.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Patient-Tailored Surveillance Recommendations

As described in previous updates, all AFX patients require life-long, regular follow-up to assess the performance of their endovascular implant. Therefore, at a minimum, Endologix recommends that high- resolution CT scan imaging (contrast-enhanced and non-contrast) be performed at one month, six months, one year, and annually thereafter. Furthermore, in June 2017, Endologix issued recommendations that patients implanted with AFX Strata receive semi-annual clinical follow-up and appropriate patient-tailored imaging, if needed, commensurate with patient status and co-morbidities between annual CT scans.

In addition to these surveillance recommendations, and in line with the clinical practice guidelines published by the Society of Vascular Surgeons (SVS) and the European Society of Vascular Surgeons (ESVS) recommending personalized surveillance regimens[1,2], Endologix is providing information to assist physicians in tailoring follow-up for patients. These recommendations are provided in Appendix 2.

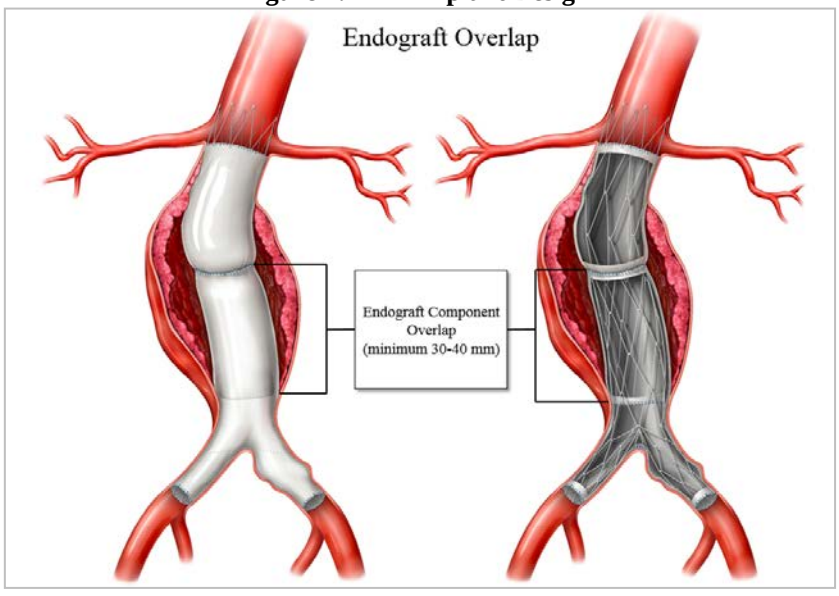
Device Sizing Recommendations

As described in previous updates, the AFX2 Sizing Algorithm may mitigate the identified contributing factors and help prevent the occurrence of Type III endoleaks. This sizing algorithm was included in the AFX2 with Duraply IFU at the time of its commercial release in February 2016 and will be added to the AFX with Duraply IFU for consistency across platforms. These sizing recommendations are provided in Appendix 3.

Guidelines on Intervention Through or Re-intervention On an AFX Device

Endologix recognizes there may be a clinical need to either perform an intervention through a previously implanted AFX device (e.g., to gain vascular access for a coronary procedure), or a re-intervention on such a device (e.g., for treatment of a Type III endoleak). As illustrated in **Figure 1**, the AFX implant has a unique endoskeleton design where the ePTFE is only attached to the most proximal and distal stent apices of the implant. The ePTFE is not attached to the stent cage throughout its entire length.

Figure 1: AFX Implant Design



Based on this unique design, Endologix has developed guidelines that should be considered in intervention/re-intervention situations to ensure that devices can be tracked through the previously implanted AFX device

[1] Chaikof, Elliot L., et al. "The Society for Vascular Surgery Practice Guidelines on the Care of Patients with an Abdominal Aortic Aneurysm." Journal of Vascular Surgery, vol. 67, no. 1, Jan. 2018, pp. 2–77.e2.
[2] Moll, F.l., et al. "Management of Abdominal Aortic Aneurysms Clinical Practice Guidelines of the European Society for Vascular Surgery." European Journal of Vascular and Endovascular Surgery, vol. 41, 2011, pp. S1–S58.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

without damage. This includes step-by-step instructions on how to best navigate the endoskeleton design of the existing AFX device in order to obtain and confirm proper wire access. These guidelines are intended to help guide the physicians and do not take the place of physician judgement. Refer to Appendix 4 and Appendix 5 for an outline of the complete intervention and re-intervention guidelines, respectively. These guidelines will be added to the product IFUs following appropriate regulatory approvals.

Your Endologix International Holdings B.V. representative will provide additional training on the key IFU changes to enable you and your team to become familiar with the updated IFU prior to formal availability. Once approved and translated, the complete, updated IFU will be provided either via hard copy upon request to Endologix Customer Service at +31 88 116 91 01 or made available in the Endologix Labeling Library, accessible as noted on the AFX System label (http://www.e-labeling.eu/, KEY-CODES: ELX10039 and ELX10028) for countries where e-labeling is accepted.

Endologix will continue to monitor the clinical experience with the AFX System, listen to physician feedback, and provide updates regarding important information collected through complaint monitoring. Endologix appreciates your review of this notification and requests that you share it within your organization, as appropriate. Adverse reactions or quality problems experienced with the use of this product may be reported to Endologix, at fieldassurance@endologix.com. If you have any questions regarding the content of this notification, please contact your Endologix representative or Endologix Customer service for the E.U. at +31 88 116 91 01 (5.00 A.M. – 6:00P.M.).

Yours Sincerely,

Matt Thompson, MD
Chief Medical Officer

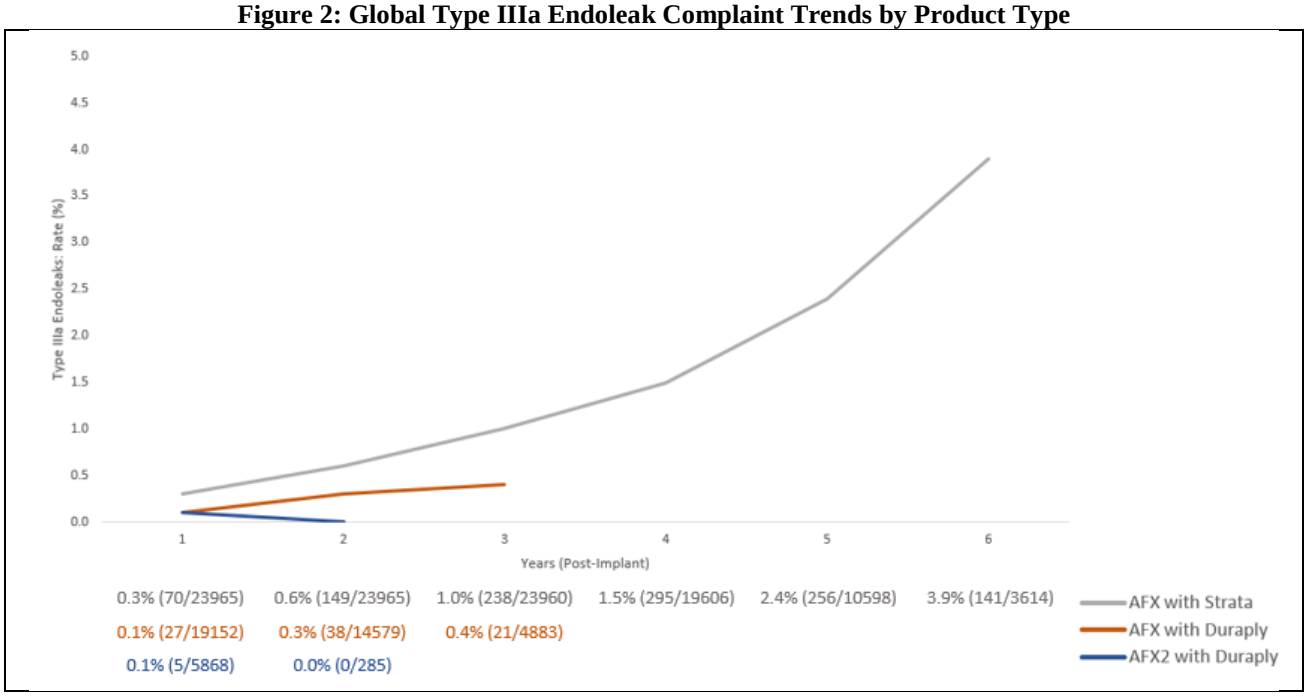
2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Appendix 1: Type III Endoleak Update

As explained above, Endologix has been monitoring the effectiveness of the 2013-2016 IFU and product changes through its complaint monitoring system. **Table 1** and **Table 2** below provide the number of Type IIIa and IIIb events reported to Endologix that have been observed within the respective durations of implantation. Follow up continues to accrue with events reported across all time points. **Figure 2** and **Figure 3** below display the global Type IIIa and Type IIIb endoleak complaint trends for AFX with Strata, AFX System with Duraply, and AFX2 System with Duraply. As shown in these figures, the reported Type IIIa and IIIb endoleak complaint rates past 1-year have been lower for the AFX System with Duraply and AFX2 System with Duraply compared to the AFX System with Strata, at equivalent time points. Additionally, it appears the Type IIIa endoleak rate for the AFX System with Strata continues to increase. Therefore, continued vigilance in patient surveillance and re-intervention in the case of loss of component overlap remains important. Note that the estimated complaint rates are calculated based on voluntary complaint reporting and units sold, which may underestimate the true event rate on a per patient basis. This underestimate may be greater for the more recent versions (i.e., AFX System with Duraply and AFX2 System with Duraply), which may have a larger hospital inventory as compared to the AFX System with Strata, which is no longer available. In particular, as there are only an estimated 285 patients at risk at 2-years for the AFX2 System, these particular data should be interpreted with caution.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Figure 2: Global Type IIIa Endoleak Complaint Trends by Product Type



**NOTE: Complaint rates are calculated based on voluntary complaint reporting and units sold, which may underestimate the true event rate on a per patient basis. This underestimate may be greater for the more recent versions (i.e. AFX System with Duraply and AFX2 System with Duraply), which may have a larger hospital inventory as compared to the AFX System with Strata, which is no longer available.*

*** NOTE: Rates are generated by first summing all patients that have the minimum designated length of follow-up, based on the bifurcated implant sales. Then, all events that occur within the designated period among that same group of patients are summed together. The cumulative rate for each period is found by dividing the event sum by the number of at-risk patients. This approach provides cumulative complaint rates across a range of follow-up periods. Note that events known to have occurred within the designated length of follow-up, but occur in patients who have not yet reached the minimum required follow-up, are not included.*

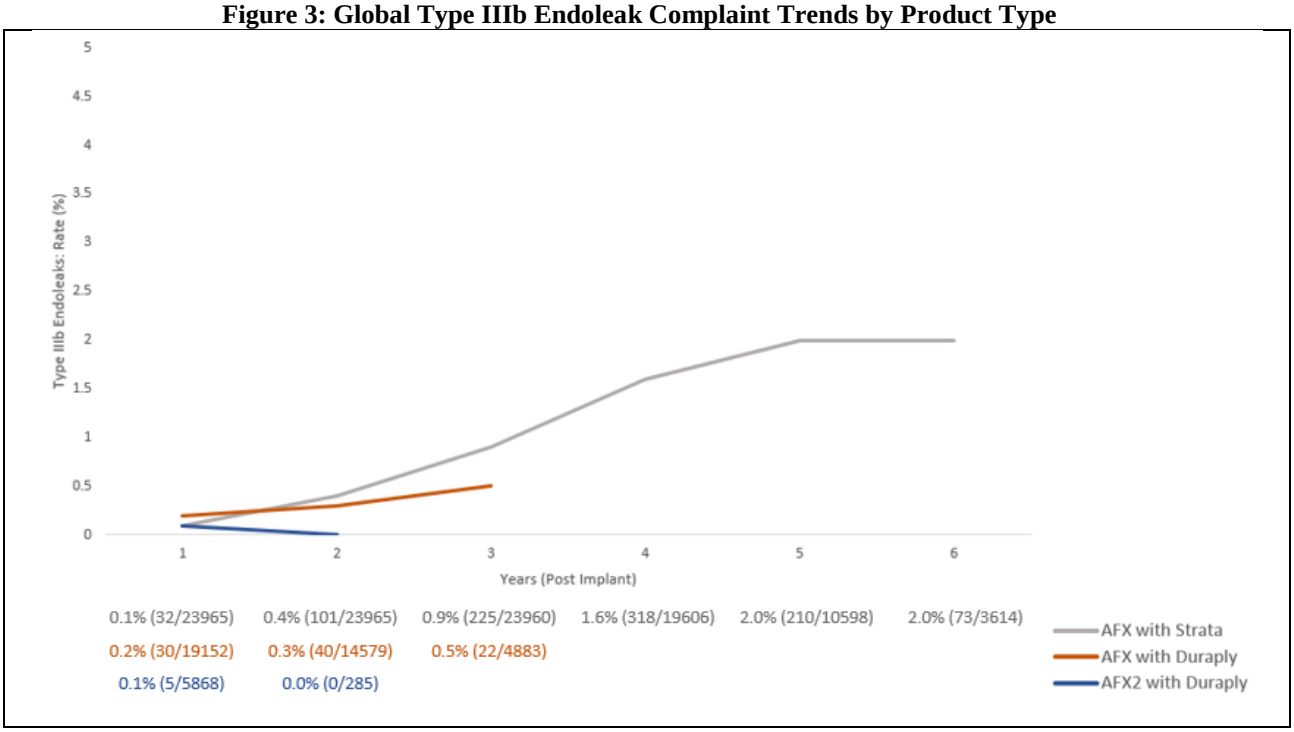
Table 1: Number of Reported Global Type IIIa Endoleaks by Duration of Implantation

	≤30 days	**> 30 days & ≤ 1 year**	**>1 year & ≤ 2 years**	**>2 years & ≤ 3 years**	**>3 years & ≤ 4 years**	**>4 years & ≤ 5 years**	**>5 years & ≤ 6 years**	**>6 years & ≤ 7 years**
AFX with Strata	28	44	80	90	95	65	35	4
AFX with Duraply	13	16	14	21	7	-	-	-
AFX2 with Duraply	1	9	0	0	-	-	-	-

The time to event above is calculated as the difference between the implantation date and event date. Note that this calculation differs from the assessment of **Figure 2.*

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Figure 3: Global Type IIIb Endoleak Complaint Trends by Product Type



**NOTE: Complaint rates are calculated based on voluntary complaint reporting and units sold, which may underestimate the true event rate on a per patient basis. This underestimate may be greater for the more recent versions (i.e. AFX System with Duraply and AFX2 System with Duraply), which may have a larger hospital inventory as compared to the AFX System with Strata, which is no longer available.*

*** NOTE: Rates are generated by first summing all patients that have the minimum designated length of follow-up, based on the bifurcated implant sales. Then, all events that occur within the designated period among that same group of patients are summed together. The cumulative rate for each period is found by dividing the event sum by the number of at-risk patients. This approach provides cumulative complaint rates across a range of follow-up periods. Note that events known to have occurred within the designated length of follow-up, but occur in patients who have not yet reached the minimum required follow-up, are not included.*

Table 2: Number of Reported Global Type IIIb Endoleaks by Duration of Implantation

	≤30 days	> 30 days & ≤ 1 year	>1 year & ≤ 2 years	>2 years & ≤ 3 years	>3 years & ≤ 4 years	>4 years & ≤ 5 years	>5 years & ≤ 6 years	>6 years & ≤ 7 years
AFX with Strata	13	21	70	123	174	106	32	2
AFX with Duraply	20	13	21	22	1	-	-	-
AFX2 with Duraply	2	7	3	0	-	-	-	-

The time to event above is calculated as the difference between the implantation date and event date. Note that this calculation differs from the assessment of **Figure 3.*

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Appendix 2

Patient-Tailored Surveillance Recommendations
(To Be Added to the Product IFU)

Physicians should evaluate patients on an individual basis and prescribe their follow-up relative to the needs and circumstances of each individual patient. This is in line with personalized surveillance regimens discussed in the clinical practice guidelines published by the Society of Vascular Surgeons (SVS) and the European Society of Vascular Surgeons (ESVS). [1,2] Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or changes in the structure or position of the stent graft including reduced overlap of stent graft components) should receive follow-up at more frequent intervals than described in Section 11.1 General. In addition, enhanced surveillance should be considered for patients at higher risk of graft related complications (e.g., treated off-label, with a short seal zone, with clinical risk factors associated with Type III endoleaks).

Investigations into Type III endoleaks have identified the following associations:

- Inadequate component overlap at the index procedure
- Lateral movement in large or tortuous aortas leading to reduction or loss of component overlap and/or implant stability
- Use of an excessively oversized proximal extension relative to the bifurcated main body device
- Procedural factors such as extensive guidewire/catheter manipulation or aggressive balloon molding
- Off-label use (especially in highly calcified anatomy)
- Implant of other manufacturer's devices as proximal extensions

If any evidence of therapy failure (i.e., enlarging aneurysm, Type I or III endoleak, or graft occlusion) is observed, the patient's condition and prognosis should be reassessed. Endovascular or open re-intervention to reestablish aneurysm exclusion and/or graft patency should be considered.

---

[1] Chaikof, Elliot L., et al. "The Society for Vascular Surgery Practice Guidelines on the Care of Patients with an Abdominal Aortic Aneurysm." Journal of Vascular Surgery, vol. 67, no. 1, Jan. 2018, pp. 2–77.e2.
[2] Moll, F.l., et al. "Management of Abdominal Aortic Aneurysms Clinical Practice Guidelines of the European Society for Vascular Surgery." European Journal of Vascular and Endovascular Surgery, vol. 41, 2011, pp. S1–S58.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Appendix 3

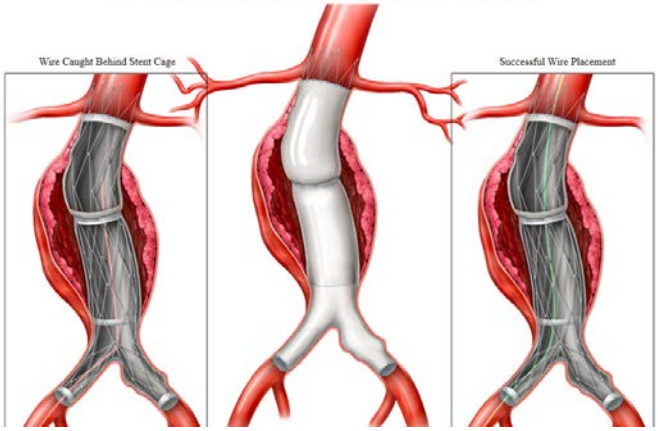
Device Sizing Recommendations ***(To Be Added to the Product IFU)***
Select the bifurcated and proximal endograft components to maximize overlap (OL) as follows: • Measure and record aneurysm length(AL) and maximum aneurysm diameter (AD) • **Select Endograft components so that the overlap (OL) is greater than the aneurysm radius (AR = AD ÷2) plus 20 mm (OL ≥AR + 20 mm)** **Note: If the recommended overlap (OL) cannot be achieved, or if AD > AL, use an infrarenal Endograft component of similar covered length and diameter to bridge to achieve the necessary overlap (OL).**
Refer to Tables 3-5 for sizing of stent graft components. When selecting a 22, 25, or 28 mm proximal extension, a diameter one size larger than the main body of the bifurcated stent graft is recommended. When selecting a 31 or 34 mm proximal extension, use only a bifurcated stent graft having a 28 mm diameter body. Under sizing or over sizing may result in incomplete sealing or compromised flow.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

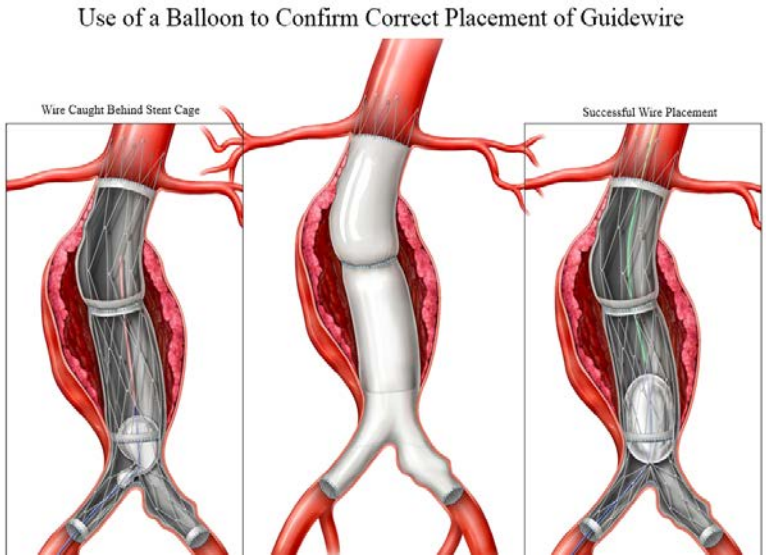
Appendix 4

Intervention Guidelines *(To Be Added to the Product IFU)*	
Intervention Guidelines (i.e., catheter-based procedures through an existing AFX device)	Prior to performing an intervention that requires a catheter to track through an existing AFX device, review this *Instructions for Use* booklet. The following instructions embody basic guidelines to consider when performing a catheter-based procedure on a patient implanted with the AFX Endovascular AAA System. These instructions are intended to help guide the physician and do not take the place of physician judgment.
General Use Information	Due to its unique endoskeleton design and because the ePTFE is not attached to the stent cage throughout its entire length (**Figure 1**), the techniques described in the sections below should be employed during an intervention that may be traversing/crossing/transferring through the AFX Endovascular AAA System. ***CAUTION:*** ***Systemic anticoagulation should be used during the intervention procedure based on hospital and physician preferred protocols. If Heparin is contraindicated, an alternative anticoagulant should be considered.*** ***CAUTION:*** ***The ePTFE graft is not attached to the stent throughout its entire length and could give the appearance of a properly placed wire or accessory, when the wire may be inadvertently placed behind a stent strut.*** ***WARNING:*** ***Excessive movement during catheter advancement may lead to cephalad movement of the existing AFX device(s), which may result in inadvertent visceral coverage.*** ***WARNING:*** ***Excessive manipulation during catheter advancement may lead to damage of the existing AFX device, which may result in a Type IIIb endoleak.***
Pre-Procedure Planning	As part of pre-procedure planning, verify that an appropriately-sized catheter or accessory device (e.g., balloons, flexible "J-tip" guidewires, pigtail catheters) have been selected to track through the previously implanted AFX Endovascular AAA System without damage. Determinants include: 1. The number of modular AFX components currently implanted may impact the flow lumen and/or endoskeleton diameter and should be considered when planning an intervention that requires transferring through the existing AFX device. NOTE: The information provided in the subsequent sections is intended to assist physicians in tracking through the existing AFX device. Follow the manufacturer's instructions for use for additional pre-procedure planning.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Intervention Guidelines *(To Be Added to the Product IFU)*	
Patient Preparation/ Arterial Access	1. Refer to institutional protocols relating to anesthesia, anticoagulation and monitoring of vital signs. 2. Position patient on imaging table allowing fluoroscopic visualization from the aortic arch to the femoral bifurcations. 3. Gain luminal access through the femoral arteries. 4. Establish adequate proximal and distal vascular control of the surgically exposed femoral artery, as needed. 5. Following the manufacturer's instructions for use, advance a flexible "J-tip" guidewire, pigtail catheter, or acceptable equivalent, into the vasculature under fluoroscopy. • NOTE: Proper device choice may limit the likelihood of tracking behind a stent strut. Reference **Figure 4**. **Figure 4: Ensure Guidewire Is Not Caught Behind Stent Strut** Ensure Guidewire is Not Caught Behind Stent Strut  ***CAUTION:*** ***Tortuosity and angulation may impact the morphology of the endoskeleton within the vasculature. Use caution when tracking devices through the existing AFX device.*** 6. Once the flexible "J-tip" guidewire or pigtail catheter reaches above the existing AFX device, slowly advance an occlusion balloon or PTA balloon over the wire and under fluoroscopy. Slowly inflate, per the manufacturer's instructions, until the balloon has been fully shaped or formed. It is recommended to use a 12mm diameter PTA balloon or an occlusion balloon that is partially inflated to ensure devices are not behind a stent strut. • Advance and retract the balloon catheter up and down the entire length of the existing AFX device to ensure there is proper luminal wire access. o NOTE: Balloon kinking during inflation or enlargement of a section of the stent cage may be a signal of a potential wire placed behind a stent strut. Reference **Figure 5**.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Intervention Guidelines *(To Be Added to the Product IFU)*	
	Figure 5: Use of a Balloon to Confirm Correct Placement of Guidewire  ***CAUTION:*** ***Balloon inflation and advancement should be performed slowly so as not to damage or dislodge the existing AFX device.*** ***WARNING:*** ***Overinflation of the balloon to ensure luminal access may create the false appearance of a wire placed behind a stent strut or may shift the main body cephalad.*** 7. During inflation and while tracking through the aortic lumen, fluoroscopic imaging in multiple planes should be used to verify that no accessory devices are behind a stent strut. 8. After verifying correct wire placement fluoroscopically, the balloon should be removed and use of alternative techniques (e.g., intravascular ultrasound) may be helpful to confirm correct wire placement. 9. Should incorrect wire placement behind a stent strut be observed, remove wire and re-advance guidewire/pigtail catheter, as described above. 10. Repeat Steps 5-8 for contralateral access, if appropriate.
Procedure – Device Advancement	1. While using continuous fluoroscopy and visualizing the entire existing AFX device, advance sheaths slowly up the ipsilateral and/or contralateral access points, as needed, and remove dilators. ***CAUTION:*** ***If the existing AFX device is at risk of being displaced cephalad while advancing devices (e.g., existing device is in severely angulated or tortuous anatomy), use of an appropriately-sized balloon on the contralateral (opposite) side may help to stabilize the existing AFX device.*** 2. Following the manufacturer's instructions for use, prepare and advance any devices necessary to complete a procedure. Once a catheter has been passed through the existing AFX device and does not lie behind a stent strut, then standard wire exchange techniques can be utilized to place a wire of appropriate diameter for the procedure. Continue to visualize the entire existing AFX device under fluoroscopy when manipulating any devices through the existing AFX device.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Intervention Guidelines ***(To Be Added to the Product IFU)***	
	CAUTION: ***Observe any cephalad movement of the existing AFX device as this may obstruct visceral vessels above the covered portion of the stent cage.*** ***CAUTION:*** ***Care should be taken when tracking accessory devices through an existing AFX device to ensure the ePTFE graft and endoskeleton is not inadvertently punctured or damaged.*** ***WARNING:*** ***Failure to visualize the entire existing AFX device when manipulating devices through the existing AFX device(s) may result in deformation.*** ***WARNING:*** ***Excessive movement when positioning devices may lead to cephalad movement, which may result in inadvertent visceral or internal iliac artery coverage.*** ***CAUTION:*** ***If the existing AFX device is displaced cephalad while advancing the device (e.g., catheter, endovascular devices), use of an appropriately-sized balloon on the contralateral (opposite) side may help to stabilize the existing AFX graft and mitigate further displacement.***
Imaging Guidelines and Post-Operative Follow-up	Procedurally, fluoroscopic imaging in multiple planes should be used to verify that no accessory devices are placed behind a stent strut. Imaging should also be used after device advancement and/or placement to ensure the existing AFX device has not been damaged or moved and that a new endoleak is not present. Upon confirmation of no negative effect to the existing AFX device, Endologix recommends that patients continue on their current imaging surveillance. Refer to Section 11 for additional imaging and post-operative follow-up guidelines.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Appendix 5

Re-intervention Guidelines ***(To Be Added to the Product IFU)***	
Secondary Intervention Guidelines (i.e., endovascular procedures to correct an existing AFX device)	Prior to performing a secondary intervention, review this *Instructions for Use* booklet, including the Intervention Guidelines in Section 12 above. The following additional warning and precautions embody basic guidelines to consider when conducting a secondary intervention on a patient implanted with the AFX Endovascular AAA System. These additional warnings and precautions are intended to help guide the physician and do not take the place of physician judgment.
General Warnings and Precautions	***WARNING:*** ***Due to the unique design of the existing AFX device, it may be difficult to achieve adequate seal for a Type III endoleak by only utilizing aortic cuffs or extensions. Specifically, the ePTFE is not attached to the stent cage throughout its entire length, thus preventing the newly placed endograft from properly sealing through its entire length.*** ***WARNING:*** ***Due to the unique design of the AFX device, only utilizing an aortic cuff or extension for the treatment of Type IIIa endoleaks may lead to a Type IIIb endoleak over time. Specifically, the aortic cuff or extension has the potential to puncture the ePTFE graft of the existing AFX device if either end interacts with the existing AFX graft material.*** ***CAUTION:*** ***Self-expanding and balloon expandable endografts used within the existing AFX device have the potential to puncture the ePTFE graft if either end interacts with the AFX graft material.*** ***CAUTION:*** ***Barbs, hooks, or anchors in the new implant may tear the existing graft material or lead to progressive tears throughout the existing AFX device. Any re-intervention should aim to prevent placement of barbs, hooks, or anchors adjacent to or within the ePTFE graft.*** ***CAUTION:*** ***The guidewire should remain in the lumen of the stent frame rather than behind the endoskeleton for the entire procedure and must be in the suprarenal aorta before any devices can be advanced and implanted within the existing endoskeleton. Care should be taken to prevent guidewire passage behind a stent strut.***
Imaging Guidelines and Post-Operative Follow Up	Procedurally, fluoroscopic imaging in multiple planes should be used to verify that no accessory devices are placed behind a stent strut (Reference **Figure 4**). Imaging should also be used after device placement to ensure the existing AFX device has not been damaged and to ensure that the reason for the re-intervention has been addressed. Assuming no additional concerns have been identified, Endologix recommends, at a minimum, that high-resolution CT scan (contrast-enhanced and non-contrast) imaging follow-up to be performed at one month, six months, one year, and annually thereafter following any re-intervention. Alternative imaging modalities such as magnetic resonance imaging, plain X-Ray or duplex ultrasound may be used in patients with impaired renal function or intolerance to contrast media. Determination of imaging techniques should be based on the physician's clinical assessment of the patient and stent graft implant, including any adjunct procedures that may have been performed in conjunction with the endovascular stent graft procedure.

2 Musick
Irvine, CA 92618
949 595 7200
endologix.com

Re-intervention Guidelines *(To Be Added to the Product IFU)*	
	Note: Additional radiological imaging may be necessary to further evaluate the stent graft in situ based on findings revealed by one of the surveillance programs. The following recommendations may be considered: • If there is evidence of poor or irregular position of the stent graft, severe angulation, kinking or migration of the stent graft on abdominal X-rays, a spiral CT or duplex ultrasound may be considered to assess aneurysm size and the presence or absence of an endoleak. • If a new endoleak or increase in AAA size is observed by spiral CT, adjunctive studies such as 3-D reconstruction or angiographic assessment of the stent graft and native vasculature may be helpful in further evaluating any changes of the stent graft or aneurysm. Spiral CT without contrast or MRI may be considered in select patients who cannot tolerate contrast media or who have renal function impairment. For centers with appropriate expertise, gadolinium or CO2 angiography may be considered in patients with renal function impairment requiring angiographic assessment.