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Dear Dr. Shuren and Mr. Silverman:

Public Citizen, a consumer advocacy organization with more than 300,000 members and supporters nationwide, writes urging you to take enforcement action against the medical device companies Stryker Neurovascular (Stryker) and Boston Scientific for publishing false and misleading information on their website resulting in the misbranding of the Wingspan Stent System with Gateway PTA Balloon Catheter (Wingspan Stent System), a medical device used to open narrowed arteries in the brains of patients diagnosed with intracranial stenosis (narrowing of the blood vessels) who have experienced repeated strokes and meet certain criteria.

Specifically, the Stryker website contains the following:

(1) A "disclaimer" stating, inaccurately, that the Wingspan Stent System is authorized by federal law for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≤ 50 percent stenosis that are accessible to the system. This statement contains a confusing error and omits important limitations added to the Wingspan label in August 2012.

(2) A list of published reports regarding research pertinent to the Wingspan Stent System and related products that omits the critically important results of the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) study. The SAMMPRIS study is the only large, prospective, randomized,

> well-controlled clinical trial conducted to date that tested the device. The study demonstrated a greater than twofold increase in the rate of stroke or death in subjects receiving the stent combined with aggressive medical management compared with controls who received only aggressive medical management.

In addition, Boston Scientific, which obtained initial FDA approval to market the Wingspan Stent System as a humanitarian use device in 2005[1] and currently manufactures the device on behalf of Stryker,[2] has also posted similar information on its website describing a false indication and misleadingly referring to favorable studies while omitting reference to the SAMMPRIS study.

Under federal law, a medical device that is distributed with false or misleading information in its labeling is considered misbranded.[3] We urge the FDA to take enforcement action against Stryker and Boston Scientific for manufacturing and distributing misbranded Wingspan Stent System devices.

In addition, we are disturbed to find that updated professional labeling for the device is not available through the FDA's website. The only professional labeling document that we could find posted on the FDA website dates back to 2005, the date of the device's original humanitarian device exemption (HDE) approval.[4] We urge the FDA to update its website appropriately with the current professional labeling for the Wingspan Stent System, either by updating the device's information page, which is currently archived and out of date,[5] or by adding a link to the FDA's recent "Safety Communication" describing the changes to the indication.[6]

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[1] Food and Drug Administration. Approval order for HDE application H050001 for the Wingspan Stent System. August 3, 2005. http://www.accessdata.fda.gov/cdrh_docs/pdf5/H050001a.pdf. Accessed April 3, 2014.
[2] Stryker Neurovascular. Product information: Wingspan® Stent System with Gateway® PTA Balloon Catheter. http://www.strykerneurovascular.com/products/view/8. Accessed April 3, 2014.
[3] 21 U.S.C. § 352(a).
[4] Food and Drug Administration. Wingspan Stent System with Gateway PTA Balloon Catheter – H050001. http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=h050001. Accessed April 3, 2014.
[5] *Ibid.*
[6] Food and Drug Administration. FDA safety communication: narrowed indications for use for the Wingspan Stent System. August 8, 2012. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm314600.htm. Accessed April 3, 2014.

I. Background

The Wingspan Stent System was approved by the FDA under an HDE application, number H050001, on August 3, 2005.[7] The approval was based on data from a small, historically controlled study involving 44 participants (the HDE study).[8] The initial FDA-approved indication for use was the following:

> The Wingspan Stent System … is indicated for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system.[9]

On September 7, 2011, the *New England Journal of Medicine* published online results of the randomized SAMMPRIS study, which compared aggressive medical management alone with aggressive medical management plus stenting with the use of the Wingspan Stent System in patients who had a recent transient ischemic attack or stroke attributed to stenosis of 70-99% of the diameter of a major intracranial artery.[10] The primary endpoint for the SAMMPRIS study was stroke or death within 30 days after enrollment or after a revascularization procedure with the Wingspan Stent System for the qualifying lesion during the follow-up period or stroke in the territory of the qualifying artery beyond 30 days.[11] The SAMMPRIS study was stopped early after 451 patients had enrolled, because the 30-day rate of stroke or death (the study's primary outcome measure) was significantly higher in the group that received intervention with the Wingspan Stent System compared to the control group (14.7% in the stented group, versus 5.8% in the medical-management-only group).[12]

Following publication of the SAMMPRIS results, Public Citizen petitioned the FDA to remove the Wingspan Stent System from the market.[13] On March 23, 2012, the FDA convened its Neurological Devices Panel of the Medical Devices Advisory Committee to discuss the most current knowledge regarding the safety and effectiveness of the Wingspan Stent System for the treatment of intracranial stenosis, including the results of the recent SAMMPRIS study. The panel members overwhelmingly agreed that there was no evidence of benefit for use of the

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[7] Food and Drug Administration. Approval order for HDE application H050001 for the Wingspan Stent System. August 3, 2005. http://www.accessdata.fda.gov/cdrh_docs/pdf5/H050001a.pdf. Accessed April 3, 2014.
[8] Food and Drug Administration. Summary of safety and probable benefit: Wingspan Stent System with Gateway PTA Balloon Catheter, HDE Number: H050001. http://www.accessdata.fda.gov/cdrh_docs/pdf5/H050001b.pdf. Accessed April 3, 2014.
[9] *Ibid.*
[10] Chimowitz MI, Lynn MJ, Derdeyn CP, et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. *N Engl J Med.* 2011;365:993-1003.
[11] *Ibid.*
[12] *Ibid.*
[13] Carome MA, Sorscher S, Wolfe SM, Kessler L. Public Citizen petition to the FDA to withdraw approval of the humanitarian device exemption for the Wingspan Stent System. December 21, 2011. http://www.citizen.org/documents/petition-to-fda-to-withdraw-approval-of-wingspan-stent-system-122111.pdf. Accessed April 3, 2014.

Wingspan system for most patients with transient ischemic attacks or stroke due to intracranial atherosclerotic stenosis when compared to a program of aggressive comprehensive medical management as was administered in the SAMMPRIS study.[14,15] However, some panelists suggested that for a certain specific set of patients, Wingspan Stent System remains an important option.[16]

Rather than withdraw the Wingspan Stent System from the market, the FDA on August 8, 2012, decided to allow the device to remain on the market under a narrowed indication for use.[17,18] In doing so, the agency again relied primarily on the results the small, historically controlled HDE study.[19] The FDA also relied on a sub-analysis of the SAMMPRIS results, which showed (unsurprisingly) that when only a subset of 33 subjects meeting a narrow set of criteria were examined, the difference in harm between groups was no longer statistically significant, although there was no evidence from this subgroup analysis that subjects treated with the Wingspan Stent System did better than those receiving aggressive medical management alone.[20]

The FDA issued a safety communication on August 8, 2012, informing health care providers and patients of the newly narrowed indication. The communication stated the following:[21]

> Wingspan is now approved only for patients who are between 22 and 80 years old AND who meet ALL of the following criteria:
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> - who have had two or more strokes despite aggressive medical management;

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[14] Food and Drug Administration. Transcript: Meeting of the Center for Devices and Radiological Health Medical Devices Advisory Committee, Neurological Devices Panel, March 23, 2012. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/NeurologicalDevicesPanel/UCM300900.pdf. Accessed April 3, 2014.

[15] Food and Drug Administration. FDA safety communication: narrowed indications for use for the Wingspan Stent System. August 8, 2012. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm314600.htm. Accessed April 3, 2014.

[16] *Ibid.*

[17] *Ibid.*

[18] Stade NK. Food and Drug Administration response to Citizen Petition docket number FDA-2011-P-0923. August 8, 2012. http://www.citizen.org/documents/1992_and_1994_fda_response_to_petition_on_wingspan_stent_system.pdf. Accessed April 3, 2014.

[19] *Ibid.*

[20] *Ibid.*

[21] Food and Drug Administration. FDA safety communication: narrowed indications for use for the Wingspan Stent System. August 8, 2012. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm314600.htm. Accessed April 3, 2014.

- whose most recent stroke occurred more than seven days prior to planned treatment with Wingspan;

- who have 70-99 percent stenosis due to atherosclerosis of the intracranial artery related to the recurrent strokes; and

- who have made good recovery from previous stroke and have a modified Rankin score of 3 or less prior to Wingspan treatment. The Rankin scale is used to measure the degree of disability in stroke patients. Lower scores indicate less disability.

The Wingspan Stent System should not be used for:

- the treatment of stroke with an onset of symptoms within seven days or less of treatment; or

- for the treatment of transient ischemic attacks (TIAs).

The safety communication also advised neurologists to "[b]ecome familiar with the design and results of the SAMMPRIS trial."[22]

II. False and Misleading Statements on strykerneurovascular.com

Stryker maintains a "Product Information" page for the Wingspan Stent System on its website, strykerneurovascular.com.[23] Stryker purports on the page that the company "has attempted to provide useful materials about studies that reflect, in a fair and balanced way, the relevant data on the product and disease state." In spite of this statement, Stryker's product information page contains the following false and misleading statements and omissions:

A. Selective reference to study results to misleadingly conceal important safety risks

The product information page contains a list of studies involving research pertinent to the Wingspan Stent System and related products. This list includes the original historically controlled HDE study and five presumably uncontrolled registry studies.[24] The list also includes the WASID study (the historical study involving patients treated with aggressive medical management alone, used to provide the historical control group for the HDE study). Finally, the website references the SSYLVIA study, which involved the NEUROLINK stent system, now no longer marketed.[25,26]

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[22] *Ibid*.
[23] Stryker Neurovascular. Product information: Wingspan Stent System with Gateway PTA Balloon Catheter. http://www.strykerneurovascular.com/products/view/8. Accessed April 3, 2014.
[24] *Ibid.*
[25] SSYLVIA Study Investigators. Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA): study results. *Stroke.* 2004 Jun;35(6):1388-92.

While the links to these studies are currently broken, publications of all but two of the studies can be located easily by cutting and pasting the study title into the widely used biomedical literature database, PubMed.gov. PubMed.gov provides links to the full text of each of the referenced articles, which in each case have been made available by the publisher for public viewing free of charge.

Presented without consideration of the SAMMPRIS results, these references misleadingly indicate that the Wingspan Stent System is safe and effective at preventing stroke and death, without acknowledging that the device demonstrated clear safety risks and a lack of effectiveness among the subjects enrolled in the SAMMPRIS study.

B. A "disclaimer" describing a false and misleading indication for the Wingspan Stent System that is broader than the current indication

The Stryker product information page also includes the following false description of the FDA-approved indication for the Wingspan Stent System:[27]

> Disclaimer *Humanitarian Device. The Wingspan® Stent System with Gateway® PTA Balloon Catheter is authorized by Federal Law for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≤ 50 percent stenosis that are accessible to the system. The effectiveness of this device for this use has not been demonstrated. The Gateway PTA Balloon Catheter is indicated for balloon dilation of the stenotic portion of intracranial arteries prior to stenting for the purpose of improving intracranial perfusion. IRB Review Required.

This "disclaimer" appears to include a confusing error, suggesting that the FDA-approved indication is for patients with intracranial vessels with ≤ 50 percent stenosis, rather than ≥ 50 percent stenosis, the requirement in the original FDA-approved indication.

More significantly, it fails to include the following restrictions on the indication announced by the FDA on August 8, 2012:

- 22 to 80 years old;
- two or more strokes despite aggressive medical management;
- most recent stroke occurred more than seven days prior to planned treatment with Wingspan;
- 70-99% stenosis due to atherosclerosis of the intracranial artery related to the recurrent strokes; and

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[26] Gartenberg AJ, Peleg A, Dhruva SS, Redberg RF. Presumed safe no more: lessons from the Wingspan saga on regulation of devices. *BMJ.* 2014;348:g93 doi:10.1136/bmj.g93

[27] Stryker Neurovascular. Product information: Wingspan Stent System with Gateway PTA Balloon Catheter. http://www.strykerneurovascular.com/products/view/8. Accessed April 3, 2014.

- good recovery from previous stroke and a modified Rankin score of 3 or less prior to Wingspan treatment.

It also fails to include the following contraindication:

> The Wingspan Stent System should not be used for:
>
> - the treatment of stroke with an onset of symptoms within seven days or less of treatment; or
> - for the treatment of TIAs.

This Stryker webpage therefore provides a falsely broader indication for the Wingspan Stent System than is currently authorized by the FDA.

The Stryker website also contains a page that lists the current accurate "Indications for Use." However, this information can be reached only by first visiting the "Product Information" page, which contains the inaccurate disclaimer, and then clicking on "View Prescriptive Information" (the page containing "Indications for Use" does not have its own separate URL).

III. False and Misleading Statements Available Through BostonScientific.com

Boston Scientific currently manufactures the Wingspan Stent System for Stryker Neurovascular. Both companies are therefore responsible for publishing accurate information about the device's indication and risks.

Boston Scientific currently hosts a PDF document on its website titled "Wingspan Stent System with Gateway PTA Balloon Catheter." This document summarizes the results of the HDE study and provides the following false indication for use:

> **Humanitarian Device.** The Wingspan Stent System with Gateway PTA Balloon Catheter is authorized by United States Federal law for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system. The effectiveness of this device for this use has not been demonstrated.
>
> **Wingspan Stent System Indications For Use**
> The Wingspan Stent System with Gateway PTA Balloon Catheter is indicated for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system.[28]

[28] Boston Scientific. Wingspan Stent System with Gateway PTA Balloon Catheter. http://www.bostonscientific.com/templatedata/imports/collateral/Neuro/spec_wingspan_gw_01_us.pdf. Accessed April 3, 2014.

Nowhere in the document does Boston Scientific describe the safety risks discovered in the SAMMPRIS study, or provide the new, narrowed indication for use authorized by the FDA. This document therefore provides a false indication for the device and misleadingly conceals known safety risks.

IV. Current Professional Labeling Not Available Through the FDA's Website

Finally, we are disturbed to note that updated professional labeling for the Wingspan Stent System is not available through the FDA's website. Instead, the FDA provides 1) a safety communication, 2) a device approval page with links to a professional labeling document dated back to 2005, the date of the original HDE approval for the device,[29] and 3) an archived information page that does not describe the device's current indication.[30] While this last page includes a disclaimer stating that the information is archived and may be out of date, the inaccurate page is likely still visited by many members of the public, as it appears as the second result when the search term "wingspan stent system" is entered into the popular Internet search engine Google.[31] Updated professional labeling information also is not available through the websites of Stryker and Boston Scientific.

V. Requested Action

Given the serious, life-threatening safety risks of the Wingspan Stent System and the lack of sound evidence demonstrating effectiveness, it is imperative that the FDA take immediate action to ensure that complete and accurate information regarding the device is disseminated to health care providers, patients, and the public by Stryker, Boston Scientific, and the agency itself. The FDA should immediately:

(1) take enforcement action against Stryker and Boston Scientific for manufacturing and distributing misbranded Wingspan Stent System devices; and

(2) update its website appropriately with the current professional labeling for the Wingspan Stent System, either by updating the device's information page, which is currently

[29] Food and Drug Administration. Wingspan Stent System with Gateway PTA Balloon Catheter – H050001. Updated August 9, 2005. http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=h050001. Accessed April 3, 2014.
[30] *Ibid.*
[31] Google. Results of search for "wingspan stent system." https://www.google.com/#q=wingspan+stent+system. Accessed April 3, 2014.

archived and out of date,[32] or by adding a link to the FDA's recent "Safety Communication" describing the changes to the indication.[33]

Thank you for your prompt attention to this important matter.

Sincerely,

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Public Citizen's Health Research Group

Michael A. Carome, M.D.
Director
Public Citizen's Health Research Group

[32] Food and Drug Administration. Wingspan Stent System with Gateway PTA Balloon Catheter – H50001. http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm078508.htm. Accessed April 3, 2014.

[33] Food and Drug Administration. FDA safety communication: narrowed indications for use for the Wingspan Stent System. August 8, 2012. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm314600.htm. Accessed April 3, 2014.