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# Current Knowledge of the Safety and Effectiveness of the Wingspan System

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ODE/CDRH/FDA

# Overview of the Morning Session

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- FDA Introductions
  - » Humanitarian Device Exemption (HDE) overview
  - » Purpose of meeting
  - » Introduction to the disease and treatment options
- Stryker Presentation and Q&A
- SAMMPRIS Study Presentation and Q&A
- Open Public Hearing
- Lunch

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# Overview of Humanitarian Device Exemption (HDE) Approval Process

**Lynn Henley, M.S., M.B.A.**

Investigational Device Exemption and  
Humanitarian Device Exemption Programs  
Office of Device Evaluation  
Center for Devices and Radiological Health

# Section 520(m) of the Food, Drug and Cosmetic Act

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“... to encourage the discovery and use of devices intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States.”  
[yearly]

# Intent of HDE Provisions

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Provide incentive for development of devices intended for treatment or diagnosis, **in small patient populations where otherwise a device manufacturer's research and development costs could exceed market returns**

# HDE vs. Premarket Approval Application (PMA)

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- Both are marketing approvals
- Both subject to post-market Medical Device Reporting (MDR) requirements for adverse event reporting
- Approval thresholds differ:
  - » PMA: safety and **effectiveness**
  - » HDE: safety and **probable benefit**

# Statutory Conditions

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- Approval (HDE) authorizes **marketing** of a humanitarian use device (HUD)
- IRB approval required before the device is used (except in emergency situations)
- Labeling must clearly identify device as an HUD, and that effectiveness for that indication has not been demonstrated

# Statutory Conditions

- No comparable **device** currently available (through a Premarket Notification Application [510(k)] or PMA)
- Device not otherwise available through other marketing applications
- Device:
  - » Does not pose unreasonable risk of illness or injury (i.e., **safety** is demonstrated), **AND**
  - » **Probable benefit** outweighs the risk (i.e., exempt from effectiveness requirements of a PMA) taking into account the probable risks and benefits of alternative therapies

# HUD Designation (21 CFR 814 Subpart H)

- Request submitted to FDA's Office of Orphan Products (OOPD) in Office of the Commissioner
- Designates the intended population for the device
  - » Must be <4000 per year in the U.S.
  - » If subset of a larger population, must be "medically plausible" subset
- 45 day review

# “Medically Plausible Subset”

If the disease or conditions occurs in >4,000 patients per year:

- The device could be used in a subset of the disease or condition as long as sponsor shows the subset is “medically plausible”
- A “medically plausible subset” is one in which use of the device is limited to that subset because of some inherent property of the device and/or the disease
- Sponsor must explain why the device couldn't also be used in all patients with disease or condition

# HDE Application

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- Letter granting HUD designation (from OOPD)
- Explanation why device would not otherwise be available
- Statement that no comparable device exists
- Device description

# HDE Application (continued)

- Bench and animal testing
- Clinical experience: data, literature, investigation(s), marketing experience (including experience outside the United States [OUS] or use of the same device for a different indication)
  - » Clinical trials are often not randomized or controlled due to small sample size and lack of a comparable marketed device

# HDE Application (continued)

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- Manufacturing information: Quality Systems Regulation (QSR) applies (unless elements waived)
- Labeling (physician and patient), including HUD statement (that no effectiveness demonstrated)

# Key Points

- HDE is marketing approval
- IRB approval required
- Informed Consent not required by FDA
- No requirement to submit other marketing applications
- May have multiple HDEs for same indication from different sponsors
- Labeling must include HUD statement that effectiveness has not been demonstrated

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# Rationale for Meeting

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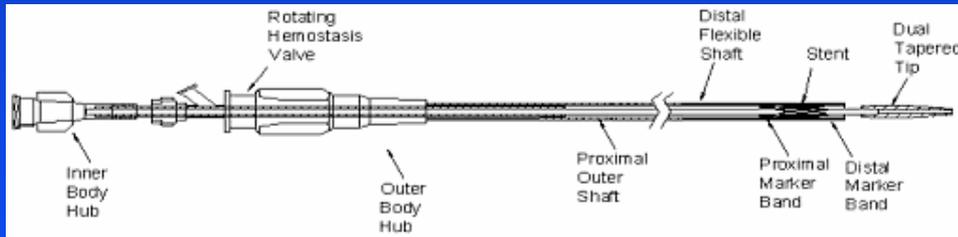
To solicit Panel's opinion on:

The **risks** and **probable benefits** of the Wingspan System for the treatment of intracranial stenosis based on the available premarket and postmarket data

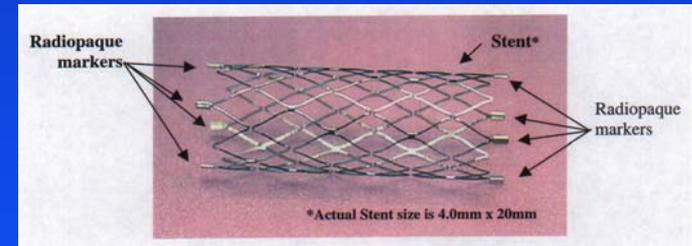
# Wingspan Stent System with Gateway PTA Balloon Catheter (Wingspan System)

- Device System Components
  - » Wingspan Stent
  - » Wingspan Delivery Catheter
  - » Gateway PTA Balloon Catheter

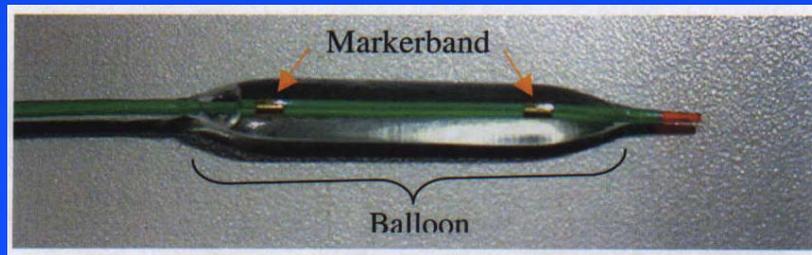
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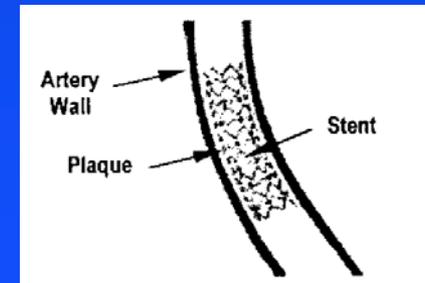
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# Regulatory History

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## Wingspan Stent System with Gateway PTA Balloon Catheter (**Wingspan System**)

- Stryker Neurovascular (formerly Boston Scientific Neurovascular)
- Humanitarian Use Device (HUD) Designation  
– 1/9/2004
- Humanitarian Device Exemption (HDE)  
H050001- approved 8/3/2005

# Regulatory History

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H050001- approved 8/3/2005

- Bench and animal testing
- Clinical study (prospective, single arm, outside US)
  - » 45 subjects
  - » Recurrent stroke
  - » 50% or greater stenosis
  - » Refractory to warfarin and/or aspirin

# Regulatory History

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Approved HDE indication:

“for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with  $\geq 50\%$  stenosis that are accessible to the system”

# Wingspan System's data

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- Pre-market: HDE study
- Post-market:
  - » Multi-center studies
  - » Single-center studies
  - » SAMMPRIS (Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis) study

# SAMMPRIS STUDY

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- Sponsor-investigator (Marc Chimowitz, MD) study
- Investigational Device Exemptions (IDE) application for an expanded indication
  - » Not required to be “refractory to medical therapy”
- Angioplasty & Stenting w/ Aggressive Medical Management vs. Aggressive Medical Management
- Enrollment stopped prematurely in April, 2011
- Ongoing follow-up per protocol

# Timeline of Events

- April 2011: Stopped enrollment in SAMMPRIS study
- April - September 2011: Ongoing data analysis by IDE Sponsor
- September 2011: SAMMPRIS Interim results published (*Chimowitz et al., New England Journal of Medicine, 2011, 365(11), 993-1003*)
- November 2011- present: FDA has interacted with IDE holder to request additional analyses and to acquire original data for FDA's independent analysis

# Timeline of Events (continued)

- December 2011: petition by Public Citizen's Health Research Group to withdraw approval of the Wingspan system
- January – February, 2012: data transfer agreements were used by FDA, IDE holder and HDE holder to facilitate transfer of a limited subset of SAMMPRIS data
  - ›› Baseline characteristics
  - ›› Primary and secondary endpoints

# Timeline of Events (continued)

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- January – March, 2012: comments to FDA from medical professional organizations and practicing physicians regarding Wingspan System (<http://www.regulations.gov/#!searchResults;rpp=25;po=0;s=fda-2011-p-0923>)
- March 23, 2012: Panel meeting

# FDA Review Team

- Chandramallika (Molly) Ghosh, Ph.D., DABT – Team leader
- Pablo Bonangelino, Ph.D. - Biostatistician
- Lawrence Rodichok, M.D. - Neurologist
- Michael Froehler, M.D., Ph.D. – Neurointerventionalist
- Aron Yustein, M.D. – Acting Deputy Director, Office of Surveillance and Biometrics (OSB)
- Cara Krulewitch, CNM, Ph.D., FACNM – Branch Chief, OSB/Division of Epidemiology (DEPI)
- Megan Gatski, Ph.D. - Epidemiologist
- Ron Kaczmarek, M.D., MPH – Epidemiologist
- Hongying Helen Jiang, PhD, MS – Epidemiologist
- Lauren J. Min, PhD, MPH –Epidemiologist
- Hui-Lee Wong, PhD, MS - Epidemiologist
- Courtney Millin, Ph.D. – Analyst, OSB/Division of Postmarket Surveillance (DPS)
- Charles Kerns, RN, BSN, MS – Branch Chief, OSB/DPS

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# Overview of Stroke due to ICAD

## IntraCranial Atherosclerotic Disease

Neurologic Devices Panel meeting  
March 23, 2012

Lawrence Rodichok MD

# Strokes due to ICAD

- 795 000 strokes per year in the US.
  - » 87% ischemic – 8-12% fatal
  - » 10% intracerebral hemorrhage – 37% fatal
  - » 3% are subarachnoid hemorrhage.
- 10% of ischemic strokes are related to stenosis of a major intracranial artery
- High risk for another stroke

# Warfarin and Aspirin Study of Intracranial Disease (WASID Study)

Risk of stroke within one year:

- For TIA:
  - » 3% with 50-69% stenosis
  - » 14% with 70-99% stenosis
- For Stroke
  - » 8% vs 23%

# Importance of time since last symptoms (WASID Study)

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- More than 17 days since QE
  - » 10% incidence of stroke
- 17 days or less since QE
  - » 17% incidence of stroke

# High Risk Population (WASID Study)

	1 year	2 year
$\leq 30$ days	22.9% (15.4-30.4%)	25% (17.2-32.9%)
$> 30$ days	9% (2.1-16.0%)	9% (2.1-16.9%)

Kasner et al. Circulation 2006;113:555-63; Fiorella, SNIS 2011

# Treatment for TIA or stroke due to intracranial stenosis

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- Surgical endarterectomy not feasible
- EC to IC bypass ineffective
- Medical therapy
  - » Anti-coagulants (warfarin)
  - » Anti-platelet agents (e.g. aspirin)
- Risk factor management

# Medical Therapy

## WASID

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- Probability of stroke, brain hemorrhage, or death
  - » Aspirin : 15%
  - » Warfarin : 17%
  
- Aspirin as effective but safer

# Treatments for ICAS after WASID

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- Interventional
  - » Angioplasty and/or
  - » Stenting
- Medical
  - » Anti-platelet agents other than aspirin
  - » Dual anti-platelet therapy
  - » Aggressive risk factor management

# Medically refractory, recurrent stroke population

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- Small population
- Treatment options limited
- Not all will be eligible for all elements of best medical management
- High risk of recurrent stroke, even with current options