Classification of Implanted Blood Access Devices for Hemodialysis (21 CFR 876.5540)

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GU Advisory Panel Meeting
June 27, 2013

Objective of This Panel Meeting

Implanted blood access devices for hemodialysis are currently Class III, but marketed through the 510(k) process. *These devices are for use in supporting or sustaining human life or for use which is of substantial importance in preventing impairment of human health, or presents a potential unreasonable risk of illness or injury.*

Is there sufficient information to establish special controls to provide adequate assurance of safety and effectiveness?

Yes → **Down-classify to Class II (510(k))**

No → **Remain as Class III and call for PMA submissions**

FDA Team Presenters

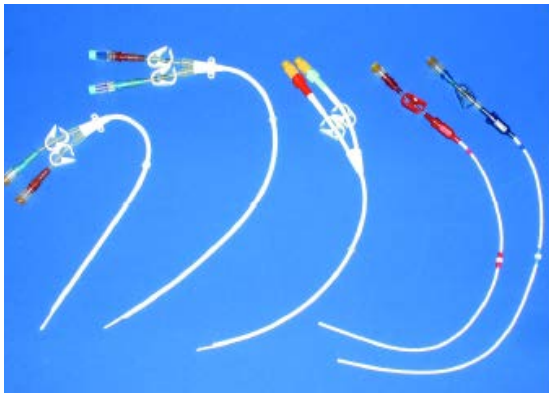
- Introduction
  - Branden Reid, Ph.D.
- Literature Review
  - Gang Chen, M.D., Ph.D.
- Device Adverse Event Reports
  - Carrie Rainis, Ph.D.
- Clinical Review and FDA's proposed recommendations for reclassification
  - Frank Hurst, M.D.

Outline

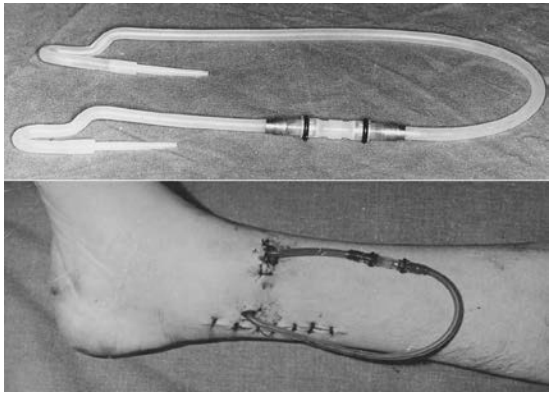
- Device introduction
- Regulatory history and industry response to 515(i) order
- Cleared indications for use
- Literature Review
- Device Adverse Event Reports
- Clinical Summary and Risks to Health
- FDA Recommendation

Device Introduction

***Identification* (21 CFR 876.5540): A blood access device and accessories is a device intended to provide access to a patient's blood for hemodialysis or other chronic uses. The device includes <u>implanted blood access devices</u>, non-implanted blood access devices, and accessories.**



Nephrol Nurs J. 2009 Mar-Apr;36(2):119-23.)



http://www.intechopen.com/books/aneurysm/vascular_access_for_hemodialysis

- The regulation is split between non-implanted and accessories in Class II, while implanted blood access devices are in Class III
- Implanted Blood Access Devices: various flexible or rigid tubes, which are surgically implanted in appropriate blood vessels and are intended to remain in the body for 30 days or more
- Examples: catheters, arterio-venous shunt cannulas and vessel tips

Regulatory History

- **1978: Initial Classification Panel Meeting**
  - Panel recommended that both implanted and non-implanted blood access devices be classified into class II
- **1981: Preamble to the proposed rule**
  - FDA agreed with the panel recommendation for non-implanted blood access devices, but FDA disagreed with the panel for implanted blood access devices and proposed that implanted blood access devices be classified into class III due to potential risks to health
- **1983: FDA classified implanted blood access devices into class III**
- **2009: FDA published a 515(i) order requiring information on the safety and effectiveness of implanted blood access devices**
  - 15 device manufacturers all recommended that implanted blood access devices be reclassified to class II

Regulatory History

- **6/2012: FDA published a proposed rule under section 513(e) proposing the reclassification of implanted blood access devices for hemodialysis from class III to class II**
  - Special Controls Guidance Document would mitigate the risks to health

- **7/2012: The Food and Drug Administration Safety and Innovation Act (FDASIA) was enacted**
  - Amended the device reclassification procedures under section 513(e) of the FD&C Act, changing the process from rulemaking to an administrative order requiring panel input
  - Changes also did not allow for finalization of the proposed reclassification and Special Controls Guidance Document proposed in June 2012
  - FDA proposes to codify the proposed special controls within the 21 CFR 876.5540 Regulation

Cleared Indications

- **Implanted hemodialysis catheters are generally indicated for use in attaining long-term vascular access for hemodialysis and apheresis. They may be implanted percutaneously and are primarily placed in the internal jugular or subclavian vein. Catheters greater than 40 cm are intended for femoral vein insertion.**
- **Additional variations in Indications for Use Statements exist for other implanted blood access device designs such as those for the fully subcutaneous catheters, coated catheters, and A-V shunt cannulaes**

Risks to Health

- ***Thrombosis in patient and catheter occlusion, or central venous stenosis:*** **Inadequate blood compatibility of the materials used in this device, blood pooling between dialysis sessions, or turbulent blood pathways could lead to potentially debilitating or fatal thromboembolism.**
- ***Adverse tissue reaction:*** **Inadequate tissue compatibility of the materials used in this device could cause an immune reaction.**
- ***Infection and pyrogen reactions:*** **An improperly sterilized device could cause a skin or bloodstream infection.**
- ***Device failure:*** **Weakness of connections or materials could lead to blood loss or device fragment embolization.**
- ***Cardiac arrhythmia, hemorrhage, embolism, nerve injury, or vessel perforation:*** **Improper placement into the heart or blood vessel could damage tissues and result in injuries.**
- ***Hemolysis:*** **Turbulence or high pressure created by narrow openings or changes in blood flow paths could cause the destruction of red blood cells.**
- ***Accidental withdrawal or catheter migration:*** **A catheter's cuff may not allow adequate ingrowth from the surrounding subcutaneous tissue, which could cause the device to dislodge or fall out with subsequent blood loss.**

Systematic Literature Review of Implanted Hemodialysis Catheters

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June 27, 2013

Outline

- Objective
- Methods
- Results on safety and effectiveness
- Study strengths and limitations
- Summary

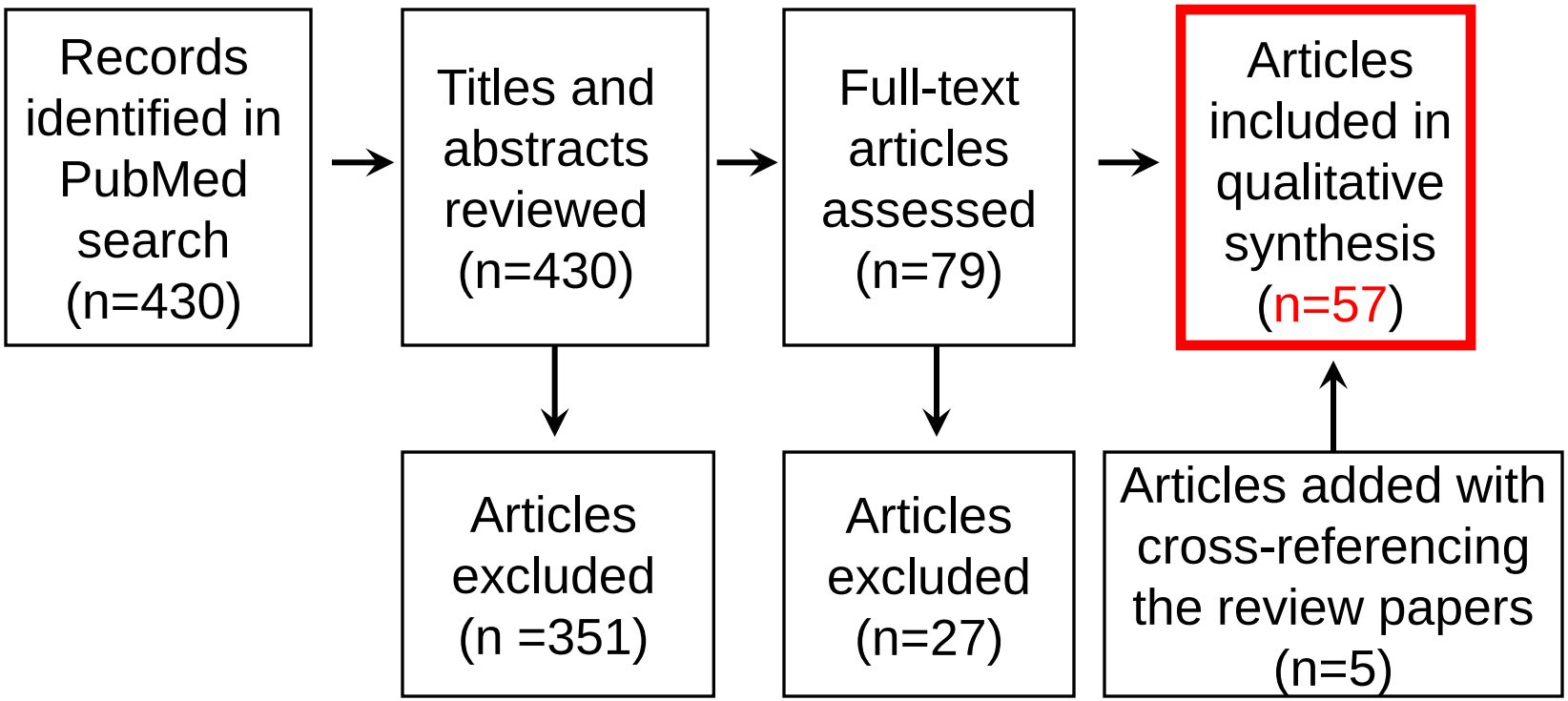
Objective

To summarize the safety and effectiveness outcomes of Implanted Hemodialysis Catheter (IHC) use reported in the literature since the year 2000

Methods

- A search of PubMed database was conducted on March 5, 2013
- All articles were limited to Human, English and Publication Date from January 1, 2000

Article Retrieval and Selection



Results

- Studies on various brands of IHC use (n=36)
  - Single-arm studies (n=27)
  - Comparative studies (n=9)
- Studies on a fully subcutaneous venous access device (n=6)
- Case series/reports of complications (n=15)

Single-arm Studies (n=27)

- 13 studies were conducted in US, 2 studies in Canada and 12 studies in European countries
- 2 cross-sectional, 12 retrospective cohort, 13 prospective cohort studies
- 3,175 patients evaluated. Sample size of the studies: 5 to 639
- 21 studies with patient gender information: 1,293 (51.6%) males, 1,214 (48.4%) females
- Mean/median age of patients in 20 studies: 52-78 years old
- Two studies were conducted in younger population with mean ages of 13.3 and 13.9 years olds

Single-arm Studies (n=27)

Effectiveness:

- Technical success rate, mean blood flow rate and primary patency rate are commonly reported effectiveness endpoints
- Technical success is usually defined as the establishment of hemodialysis access via the access vein with adequate catheter function. It was achieved in 100% of patients in 8 studies, 92.9% and 88% in two other studies.

Mean Blood Flow Rate with the Use of IHCs

Reference *	Study Location	Sample Size	Mean Blood Flow Rate (ml/min)
Conz et al., 2001	Italy	5	250±50
Di lorio et al., 2001	Italy	88	272±38
Gallieni et al., 2002	Italy	28	303±20
Falk et al., 2007	US	33	>300
Bertoli et al., 2010	Italy	25	270±17
Power et al., 2010	UK	26	300±3

** All studies were observational. In the Falk study, femoral vein was used as insertion site. The study by Power evaluated translumbar catheters.*

Primary Patency Rate with the Use of IHCs

Reference *	Study Location	Sample Size	Primary Patency Rate						
			1M	2M	3M	6M	12M	24M	36M
Funaki et al., 2001	US	24	90%	NR	NR	71%	25%	NR	NR
Falk et al., 2007	US	33	44%	29%	19%	4%	NR	NR	NR
Van Ha et al., 2007	US	97	86%	NR	64%	39%	NR	NR	NR
Bertoli et al., 2010	Italy	25	NR	NR	NR	67%	54%	NR	NR
Power et al., 2010	UK	26	NR	NR	NR	NR	73%	33%	28%

** All studies were observational. In the Falk study, femoral vein was used as insertion site. The study by Power evaluated translumbar catheters.*

NR – Not Reported

Single-arm Studies (n=27)

Safety:

- Device-related infection, thrombosis, malfunction and device survival were the most common safety endpoints evaluated and reported.
- Five studies reported a total of 10.2% to 26% of treated patients with catheter thrombosis. Two studies in Europe reported thrombosis rates of 1.16 and 1.94 per 1,000 catheter-days.
- The catheter malfunction rates were 1.7-7.4 per 1,000 catheter-days in 4 studies.

Catheter-related Infection and Bacteremia Rate

Reference *	Study Location	Sample Size	Infection Rate **	Bacteremia Rate **
Funaki et al., 2001	US	24	**0.6**	NR
Ewing et al., 2002	UK	88	**2.4**	NR
Gallieni et al., 2002	Italy	28	**0**	NR
Cetinkaya et al., 2003	Turkey	85	**0.82**	NR
Develter et al., 2005	Belgium	157	**2.31**	**1.71**
Wang et al., 2006	US	200	**1.3**	NR
Alomari et al., 2007	US	207	**3.0**	NR
Van Ha et al., 2007	US	97	**1.4**	**1.0**
Spector et al., 2008	US	85	**1.4**	**0.3**
Mojibian et al., 2009	US	57	**1.12**	**0.56**
Bertoli et al., 2010	Italy	25	NR	**1.77**
Power et al., 2010	UK	26	**2.84**	**0.82**
Thomson et al., 2010	UK	365	NR	**1.77**
Adeb et al., 2012	US	120	**1.8**	NR
Martin-Pena et al., 2012	Spain	123	NR	**0.34**

** All studies were observational. The study by Power et al evaluated translumbar catheters. The study by Adeb et al was on pediatric patients.*

NR – Not Reported
*** per 1,000 catheter-days*

Single-arm Studies (n=27)

Safety:

- The other low frequency complications reported were fibrin sheath formation, bleeding, broken catheter, kinked or pinched catheter, catheter dislocation, pneumothorax, hemothorax, carotid artery puncture and air embolism.
- The Kaplan-Meier device survival were 62%-78% at 1-month, 25%-65% at 6-month, 13%-42% at 12-month in 5 studies.

Comparative Studies (n=9)

- 7 studies were conducted in US, 2 studies in Ireland and France. There were 3 RCTs and 6 observational studies.
- The mean blood flow rate did not differ between catheters in 5 studies comparing this endpoint.
- No significant differences in infection rates were observed in all studies except one.
- The safety and effectiveness results reported in the comparative studies for various IHCs were mostly within the range reported in the single-arm studies.

Studies on a fully subcutaneous device (n=6)

- 6 papers on 5 original studies published between 2000 and 2006. Four observational studies evaluated a total of 100 patients implanted with the device in US, Canada and Germany. One US multi-center study with a hybrid study design.
- The device-related infection rates and the rates of thrombolytic infusions or occlusions were mostly within the range reported for standard catheters. In one US study and the German study, at least 4 deaths were reported as contributed to device-related infection.

Case Series/Reports (n=15)

- One paper identified 71 patients who were referred to a dialysis access center in US primarily for a broken clamp or cracked extension tube.
- The remaining 14 papers reported 18 patients with various complications including catheter-related bacteremia, thrombosis, malfunction (fracture, leak, dislocation, migration et al), bleeding and a large squamous cell carcinoma in situ at the exit site of a prior IHC.

Study Strengths and Limitations

Strengths:

- Studies all focused on the safety and effectiveness of IHCs with the catheter names specified in most of the studies.

Limitations:

- Lack of controls, small sample size, follow-up variations, different patient population and techniques in catheter placement.
- Differences in patient selection and other uncontrolled factors between catheter groups, limited power to detect statistically significant differences due to small number of patients in each catheter group.

Review Strengths and Limitations

Strengths:

- All original reports published since 2000 that directly evaluate the safety and effectiveness outcomes of implanted hemodialysis catheter use were reviewed.

Limitations:

- Data published before year 2000 were not included.
- Potential publication bias and bias arising from selective reporting of study findings in a publication.

Summary

- Technical success can be achieved with adequate blood flow rate in most of the patients placed with IHCs.
- The catheter patency rate and device survival decreased significantly over time due to catheter-related complications.
- Catheter-related infections, thrombosis and device malfunction remain the most common complications with IHC use.

Medical Device Reports

June 27, 2013

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Division of Postmarket Surveillance
Office of Surveillance and Biometrics
Center for Devices and Radiological Health
Food and Drug Administration

Overview of MAUDE

MAUDE = Manufacturer and User Facility Device Experience database
MDR = Medical Device Report

Benefits:

- Qualitative snapshot
- "Real users" in "real world"
- Rare / unexpected events
- Long - term events
- Vulnerable population
- Off - label use
- Use errors

Limitations:

- Passive System
  - Under - reporting
  - Lack of physician awareness
- Incomplete information
- Causality not confirmed
- Reporting biases
- Inability to estimate rate
  - No "denominator" data
- Trends should be interpreted cautiously

MDRs – Search Methods

MAUDE Search:

- **Date Report Received: Jan 1st, 1998 to Mar 24th, 2013**
- **Product Codes (Procodes):**

Product Code	Name
FIQ	A-V Shunt Cannula
FKW	Vessel Tip
LFJ	Subclavian Catheter
MSD	Implanted Hemodialysis Catheter
NYU	Implanted Coated Hemodialysis Catheter

MDRs - Analysis

1. Report Review
   - No reports under FKW
   - Procodes FIQ & NYU
     - < 50 reports
     - Individually reviewed
   - Procodes MSD & LFJ
     - ~15% sampled & individually reviewed
   - Reports placed into 1 of 10 categories and aligned to Risks to Health where possible
   - Additional concerns not captured in Risks to Health
   - Text search – “corrective”, “recall”
2. Assessed Top 100 (by Product Code)
   - Event Type, Device Problem Codes (DPCs), Patient Problem Codes (PPCs)

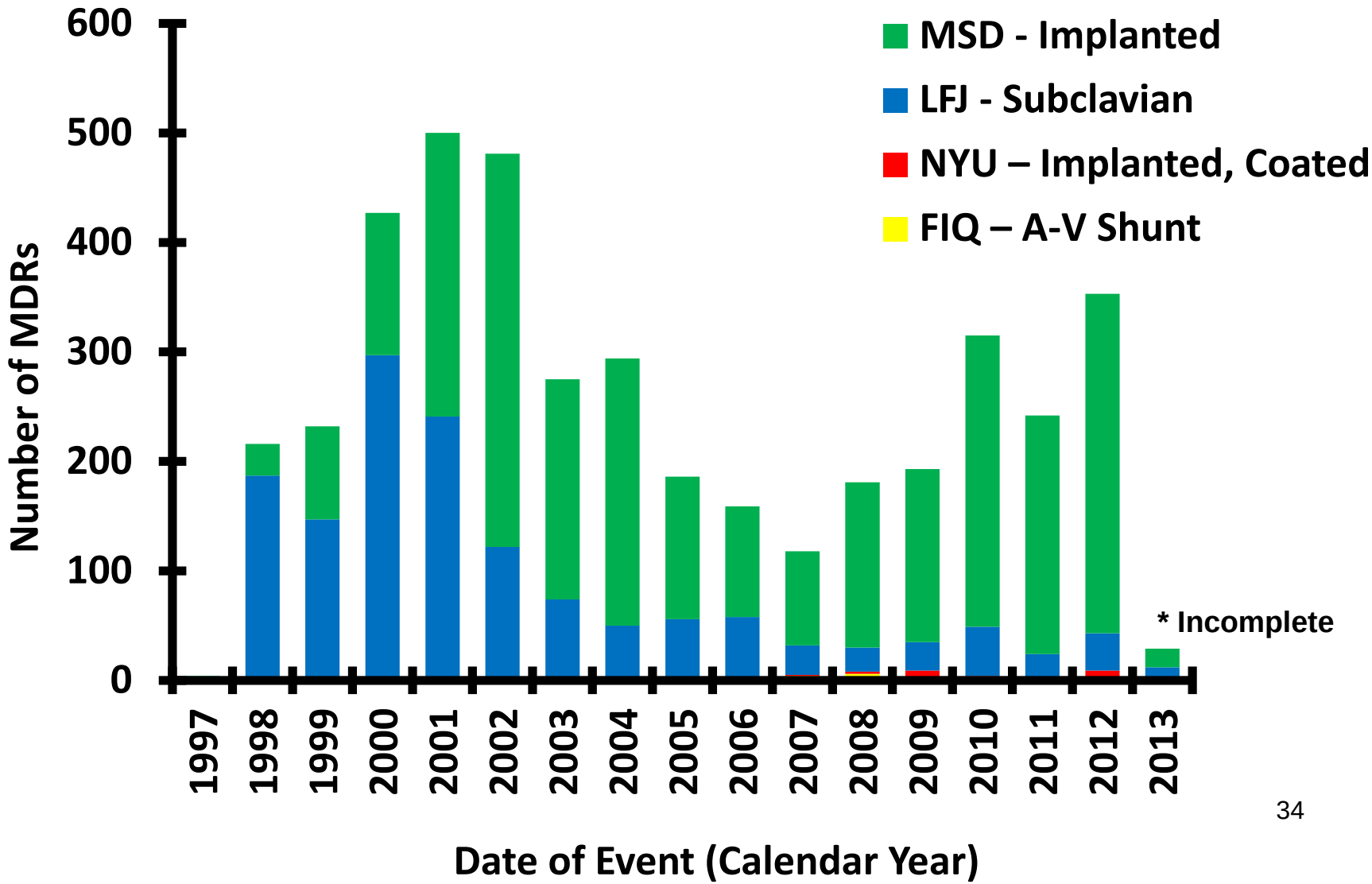
Product Code	Name
FIQ	A-V Shunt Cannula
FKW	Vessel Tip
LFJ	Subclavian Catheter
MSD	Implanted Hemodialysis Catheter
NYU	Implanted Coated Hemodialysis Catheter

MDRs - Analysis

3. Risks to Health

- ***Thrombosis in Patient and Catheter Occlusion, or Central Venous Stenosis:*** **Inadequate blood compatibility of the materials used in this device, blood pooling between dialysis sessions, or turbulent blood pathways could lead to potentially debilitating or fatal thromboembolism.**
- ***Adverse Tissue Reaction:*** **Inadequate tissue compatibility of the materials used in this device could cause an immune reaction.**
- ***Infection and Pyrogen Reactions:*** **An improperly sterilized device could cause an infection or an unclean device could cause a fever.**
- ***Device Failure:*** **Weakness of connections or materials could lead to blood loss.**
- ***Cardiac Arrhythmia, Hemorrhage, Embolism, Nerve Injury, or Vessel Perforation:*** **Improper placement into the heart or blood vessel could damage tissues and result in injuries.**
- ***Hemolysis:*** **The destruction of red blood cells due to turbulence or high pressure created by narrow openings or changes in blood flow paths.**
- ***Accidental Withdrawal or Catheter Migration:*** **A catheter's cuff may not allow adequate ingrowth from the surrounding subcutaneous tissue, which could cause the device to dislodge or fall out with subsequent blood loss.**

MDRs – Search Results



MDRs – NYU & FIQ

NYU – Implanted Coated Hemodialysis Catheter

- 510(k)s Cleared (2):
  - Palindrome Emerald Catheter
    (K060509, Tyco Healthcare Group, 2006)
  - Palindrome H, SI, HIS Chronic Catheters
    (K112477, Covidien, 2011)
- 26 reports since 2006

Little insight into long-term trends

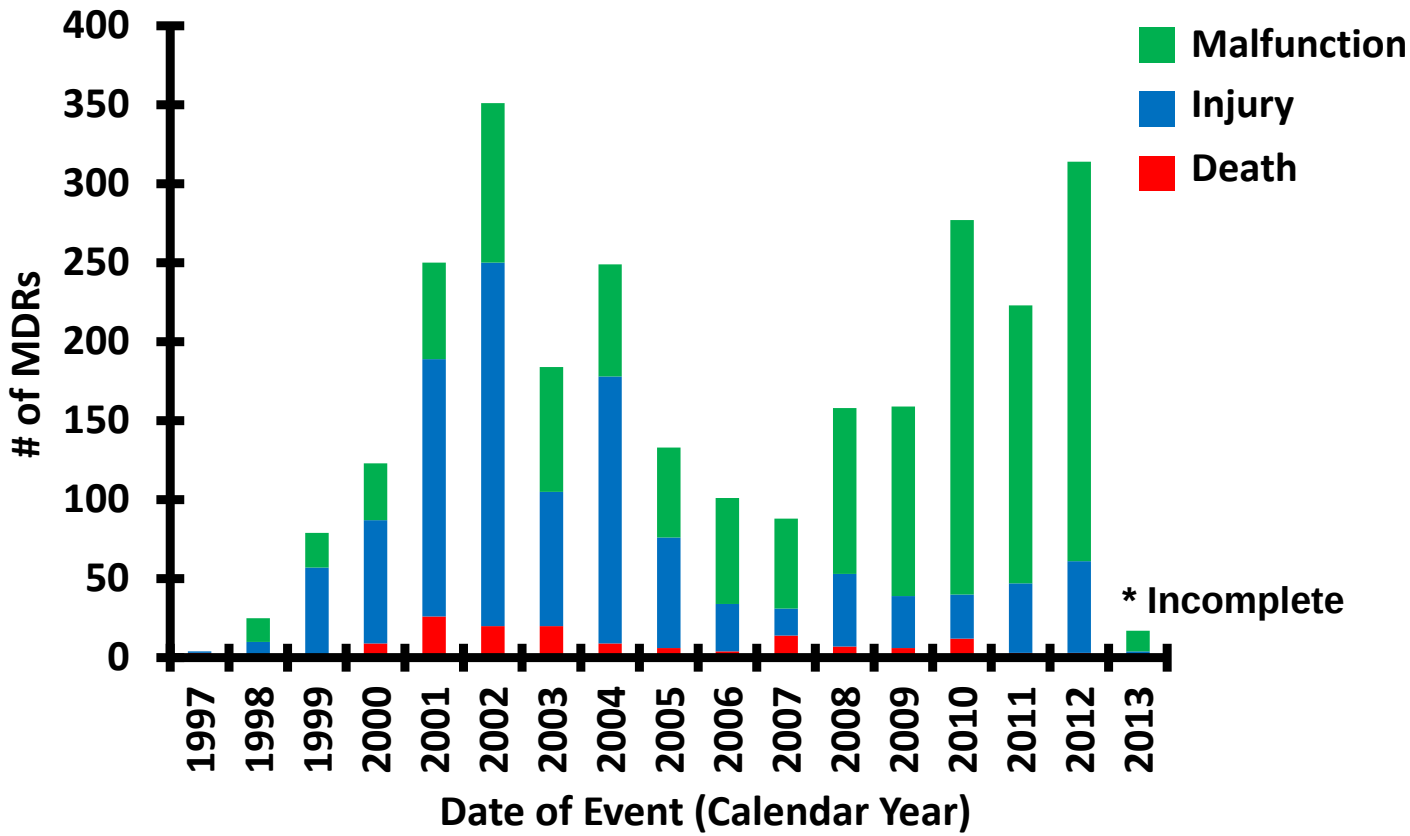
FIQ – A-V Shunt Cannula

- 18 MDRs
- Last MDR received 2008
- Decline in clinical use / market
  - Arteriovenous grafts & fistulae

MDRs – MSD

(Implanted Hemodialysis Catheter)

- Number of MDRs in early 2000's and 2010-12 similar
- Severity of events reported declined over this period
- Increased malfunctions - breaks, leaks, dislodgements



Recalls – MSD

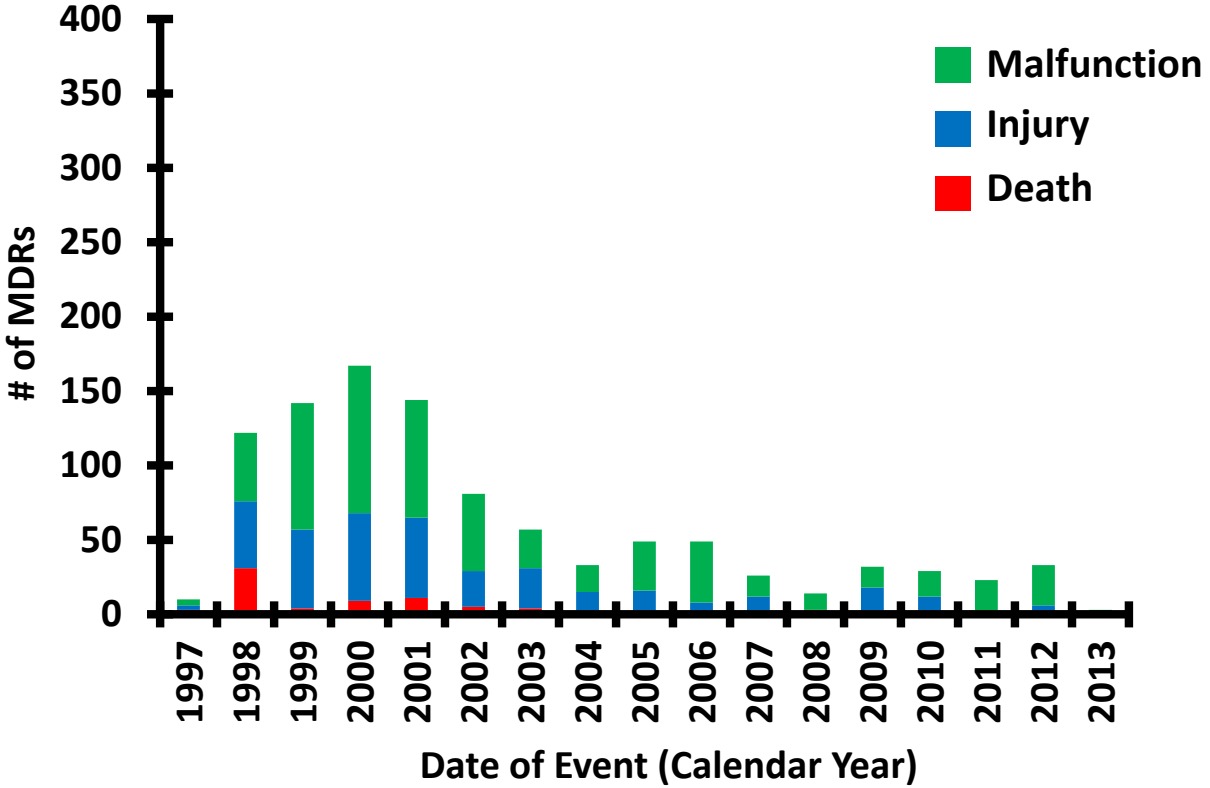
(Implanted Hemodialysis Catheter)

Date	Public Reason For Recall	Class
2011	The securement **cuff** on catheter could detach from the shaft.	II
2011	Complaints for breakage of the tunneler **sleeve** during product use.	II
2011	Complaints indicating breakage and/or separation of the **stylet**.	I
2011	Packaged with the incorrect valved peelable **introducer**.	II
2011	Separation of the **luer connector** from the extension tube.	II
2010	Potential for a cross-**lumen** leak.	II
2009	Catheter **tubing** could separate from the **hub/bifurcation**.	II
2009	**Mislabeled** as right are actually left.	II
2008	**Cuff** may be inadequately attached to the catheter.	II
2008	**Tips** may not have been adequately welded to the catheter body.	II

MDRs – LFJ

(Subclavian Catheter)

- Number of MDRs decreased
- Other factors - market conditions, hospital practices
- No new clearances since 1998 (started using MSD)



MDRs – Analysis Results

Group	Risk to Health	MSD* Implanted	LFJ* Subclavian	NYU Implanted, Coated	FIQ A-V Shunt
1. Thrombosis	1. Thrombosis in Patient and Catheter	7	6	1	3
2. Allergy	2. Adverse Tissue Reaction	1	0	0	2
3. Infection	3. Infection and Pyrogen Reactions	58	4	0	3
4. Break	4. Device Failure	120	98	15	1
5. Leak		115	49	6	5
6. Vascular Injury	5. Cardiac Arrhythmia, Hemorrhage, Embolism, Nerve Injury, Vessel Perforation	12	10	0	0
7. Placement		26	5	0	0
8. Hemolysis	6. Hemolysis	0	0	0	0
9. Dislodgement	7. Accidental Withdrawal or Catheter Migration	80	35	4	0
10. Other		49	14	0	4
	TOTAL	468	221	26	18

***Note:** The number of MDRs represents the total number of MDRs in each procode for the 1998 to 2013 time period. For procodes MSD and LFJ, ~15% sampling of MDRs was reviewed.*

MDRs - Summary

Overall, review of the MDR data does not raise any concerns associated with the use of these devices not already captured in the established "Risks to Health" for these products.

Clinical Summary
Risks / Proposed Special Controls
FDA Recommendation

June 27, 2013

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Division of Reproductive, Gastroenterology, Renal, and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration

Vascular Access for HD

- AVF (arteriovenous fistula)
  - Native vein-to-artery conduit
  - Not subject to FDA regulation
- AVG (arteriovenous graft)
  - Prosthetic conduit
  - Class II (special controls) under 21 CFR 870.3450
- Hemodialysis catheter
  - Non-implanted (short-term) - regulated as Class II under 21 CFR 876.5540
  - Implanted (long-term) - subject of this proposed reclassification.
    - Implanted catheters AKA “tunneled,” “chronic,” or “cuffed” catheters

KDOQI CPG

- **2.1 The order of preference for placement of vascular access in patients with kidney failure who choose HD should be (in descending order of preference):**
  - 2.1.1 Preferred: Fistulae. (B)
  - 2.1.2 Acceptable: AVG of synthetic or biological material, such as: (B)
  - 2.1.3 **Avoid if possible: Long-term catheters** (B)

Clinical Practice Guidelines for Vascular Access. NKF KDOQI Guidelines; 2006 Update

KDOQI CPG

- Use of catheters as first choice for long-term vascular access is discouraged
  - Infection
  - susceptibility to thrombosis
  - inconsistent delivery of blood flow
- Increased use of AVF (as a result)
  - 2011 - 67% of prevalent HD patients used AVF
- Although discouraged, long-term catheters are still frequently used

Clinical Practice Guidelines for Vascular Access. NKF KDOQI Guidelines; 2006 Update

Incident/Prevalent ESRD Network Data as of 12/2011; http://www.fistulafirst.org/AboutFistulaFirst/FFBIData.aspx; accessed 15 April 2013

2011 ESRD Network Data

Incident HD patients (97,942)

- 79,500 (81%) started HD with a catheter
- Only 19% of these had other maturing vascular access (17% AVF; 2% AVG)

Prevalent HD patients (376,957)

- 75,600 (20%) used a catheter
- 28,700 (7.6%) used a catheter ≥90 days

Incident/Prevalent ESRD Network Data as of 12/2011; http://www.fistulafirst.org/AboutFistulaFirst/FFBIData.aspx; accessed on 15 April 2013

Catheter Advantages

- Can be used when vascular access for hemodialysis is needed urgently
  - AVG and AVF cannot be used after placement for weeks and months, respectively.
- Can be used as a bridge while awaiting a more permanent vascular access
- Can be used in patients who may have inadequate vascular anatomy to establish a more permanent vascular access

Catheter Complications

Acute

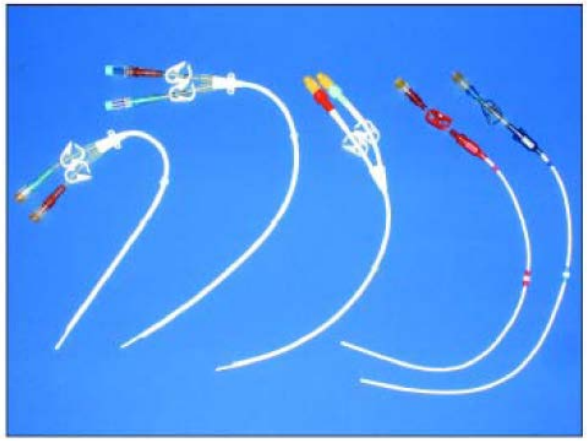
- Placement / Insertion related
  - dysrhythmia, hemorrhage, embolism, vessel / nerve injury

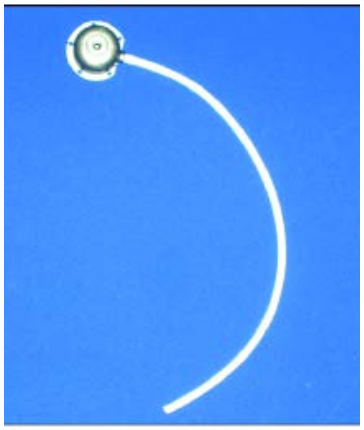
Chronic

- Thrombosis
  - Intrinsic, extrinsic, fibrin sheath, venous stenosis
- Infection
  - Local, systemic
- Mechanical dysfunction / failure
  - Migration, dislodgement, kinking, breaks, leaks
- Hemolysis
- Inadequate Dialysis

Implanted Blood Access Device Variations

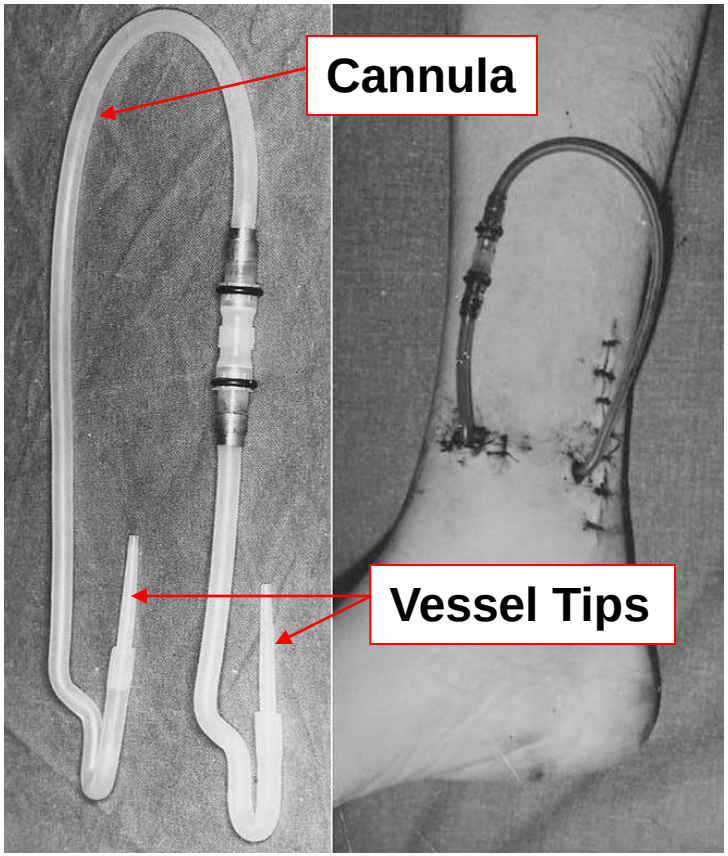
- Implanted Hemodialysis Catheters
- Coated Catheters
  - Heparin, Silver, and Heparin + Silver coatings have been cleared
- Port Catheter Systems
  - fully subcutaneous catheters
  - 1 device cleared by 510(k), but later Recalled
- A-V shunt cannulae





Ball LK. Forty years of vascular access. Nephrol Nurs J. 2009 Mar-Apr;36(2):119-23.

A-V Shunt Cannula (& vessel tips)



http://www.intechopen.com/books/aneurysm/vascular_access_for_hemodialysis

- First vascular access used for hemodialysis
  - Scribner Shunt first described in 1960
- Prone to thrombosis, infection, and dislodgement
  - Similar to catheters risks
- 1970s/1980s –became less frequently used
  - Catheters became preferred temporary vascular access for hemodialysis

Quinton W, Dillard D, Scribner BH: Cannulation of blood vessels for prolonged hemodialysis. Trans Am Soc Artif Intern Organs 6:104-113, 1960.

A-V Shunt Cannula (& vessel tips)

- Included in the Implanted Blood Access Device regulatory classification
- Have some differences compared with implanted catheters
  - External portion cannulated with needle
  - Arterial connection
- FDA believes that reclassification of these devices to Class II would be appropriate
  - Well-described risks of implanted catheters would also be relevant for these devices
  - Special Controls can be established to provide a reasonable assurance of safety and effectiveness

Clinical Summary

- Implanted blood access devices are not the optimal vascular access for hemodialysis.
- However, they are life-supporting and a necessary treatment option for a significant number of hemodialysis patients.
- The complications associated with these devices are well-described.

Risks To Health / Proposed Special Controls

Risks to Health

- Thrombosis in patient and catheter occlusion, or central venous stenosis
- Adverse tissue reaction
- Infection and pyrogen reactions
- Device failure
- Cardiac arrhythmia, hemorrhage, embolism, nerve injury, or vessel perforation
- Hemolysis
- Accidental withdrawal or catheter migration

The panel will be asked to comment on the Risks to Health and discuss whether there are additional risks that should be considered.

Risk / Mitigation

Thrombosis / Occlusion	Performance data (i.e. priming volume), Labeling (i.e. anticoagulation, obstruction management)
Adverse Tissue Reaction	Biocompatibility, Sterility, Expiration date
Infection / Pyrogen reactions	Sterility, Shelf-life, Labeling (i.e. insertion site preparation / appropriate exit site care)
Device Failure	Performance data (i.e. tensile / leak testing, recirculation, repeated clamping & chemical tolerance), Shelf-life, Labeling
Cardiac arrhythmia, Hemorrhage, Embolism, Nerve/Vessel Injury	Labeling (i.e. appropriate insertion site, insertion instructions, recommended tip location)
Hemolysis	Performance data (i.e. pressure vs. flow, mechanical hemolysis), Labeling
Withdrawal / Migration	Biocompatibility, Performance data (i.e. tensile testing), Labeling

Special Controls

- Based on the previously described Risks to Health and Mitigation Strategies, FDA is proposing Special Controls
- FDA believes that these Special Controls, in addition to general controls, can be established in order to:
  - mitigate the identified Risks to Health
  - provide reasonable assurance of the safety and effectiveness of implanted blood access devices for hemodialysis
- The FDA intends to issue a Guidance Document which will provide a more detailed description of how to comply with the proposed special controls.

Proposed Special Controls

- Components of the device must be demonstrated to be biocompatible.
- Performance data:
  - Pressure versus flow; Recirculation (forward and reverse); Priming volumes; Tensile testing of joints/materials; Air/liquid leakage testing; Repeated clamping of the catheter extensions; Mechanical hemolysis testing; Chemical tolerance to repeated exposure to commonly used disinfection agents
- Performance data must demonstrate sterility.
- Performance data must support stated shelf-life for continued sterility, package integrity, and functionality (tensile strength, repeated clamping, and leakage testing).

Proposed Special Controls

- Labeling must include the following:
  - arterial and venous pressure vs flow rates; arterial and venous priming volumes; forward and reverse recirculation; expiration date; disinfecting agents that cannot be used
  - Comprehensive insertion instructions, method/site of insertion, proper tip location, removal method, anticoagulation, management of obstruction / thrombus, and site care
  - coatings or additives (summarize performance results)
- Subcutaneous devices
  - recommended needle type, test results on repeated port use
- Coated devices
  - description of the coating/additive, duration of effectiveness, how applied, and performance testing of the coating

The panel will be asked whether the proposed Special Controls mitigate the identified Risks to Health and whether any additional or different Special Controls are recommended.

FDA Recommendation

FDA Recommendation

- In 1983, FDA noted that:
  - Implanted blood access devices for hemodialysis are part of a life-supporting system.
  - General controls / performance standards were not sufficient to provide reasonable assurance of safety and effectiveness.
- FDA recommended that implanted blood access devices be regulated as Class III
  - Device presented a potential unreasonable risk of illness or injury to the patient.
  - Data were not adequate to assure the safe and effective use of these devices.

FDA Recommendation

- Since 1983, additional evidence for safety and effectiveness has been established to support reclassification to Class II.
  - Devices have continued to evolve over time with upgraded materials and improved insertion techniques.
  - The risks are well-described
    - systematic literature review
    - MDR analysis
  - Greater premarket review experience with clearance of over 200 implanted blood access devices

Literature review – Safety / Effectiveness

Effectiveness

- Primary patency
  - 44-90% at 1 month
  - 19-64% at 3 months
  - 4-71% at 6 months
  - 25-73% at 12 months
- Blood flow
  - 245 ± 42 to 303 ± 20 ml/min
- Malfunction
  - 1.7 – 10.5 per 1,000 cath/days

Safety

- Infection
  - 0.3 - 3.5 per 1,000 cath/days
- Bacteremia
  - 0.3 - 1.77 per 1,000 cath/days
- Thrombosis
  - 0.25 - 1.94 per 1,000 cath/days
- Other
  - Breaks, Kinks, Leaks, Migration, Dislocation, Bleeding, arterial puncture, air embolism, hemothorax, pneumothorax

Medical Device Reports

- Number of reports relatively stable for recent years
  - 86 to 359 MDRs/yr (MSD) from 2002 to 2012
    - >100,000 implanted catheters in use every year
  - Increased malfunctions
    - breaks, leaks, dislodgement
  - Severity of events reported declined over time

- Review of the MDR data does not raise any new areas of concern not already captured in the previously identified “Risk to Health” categories.

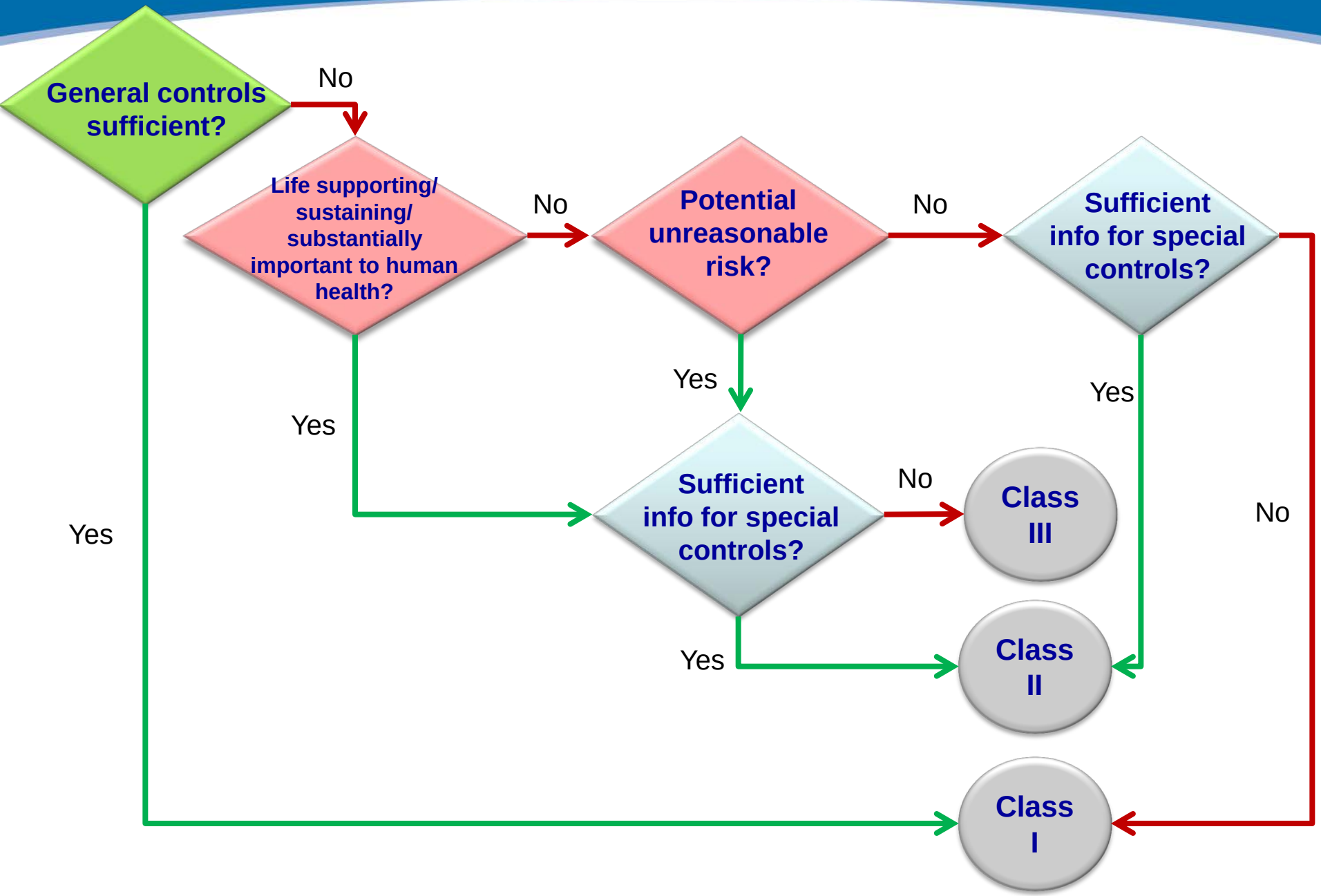
Benefit / Risk

Benefits

- Can be used when vascular access for hemodialysis is needed urgently
- Can be used as a bridge while awaiting a more permanent vascular access
- Can be used when vascular anatomy is not adequate to establish a more permanent vascular access

Risks

- Thrombosis in patient and catheter occlusion, or central venous stenosis
- Adverse tissue reaction
- Infection and pyrogen reactions
- Device failure
- Cardiac arrhythmia, hemorrhage, embolism, nerve injury, or vessel perforation
- Hemolysis
- Accidental withdrawal or catheter migration


General controls sufficient?
No
Yes
Life supporting/ sustaining/ substantially important to human health?
No
Yes
Potential unreasonable risk?
No
Yes
Sufficient info for special controls?
No
Yes
Sufficient info for special controls?
No
Yes
Class III
Class II
Class I

Proposed FDA Recommendation

- FDA has considered the available scientific literature, Medical Device Reports, FDA premarket review experience, and the Benefit vs Risk for the implantable blood access devices for hemodialysis.
  - FDA believes that the available evidence supports a reasonable assurance of safety and effectiveness.
  - FDA believes that the proposed Special Controls, in addition to general controls, would be sufficient to provide such assurance.
- Therefore, FDA recommends that these devices for hemodialysis be reclassified from Class III to Class II (General + Special Controls).