Disappearing Orphan Devices

Marc Gewillig, MD, PhD

FAEPC, FESC, FPICS, FACC

DISCLOSURE STATEMENT OF FINANCIAL INTEREST

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

AFFILIATION/FINANCIAL RELATIONSHIP	COMPANY
• Grant/Research Support	• Medtronic
• Consulting Fees/Honoraria/Proctor	• Venus, Edwards, Medtronic, Abbott, NuMed
• Major Stock Shareholder/Equity	
• Royalty Income	
• Ownership/Founder	
• Intellectual Property Rights	
• Other Financial Benefit	

MDD to MDR

- MDD: “light touch”, high variability, “to easy”
  vulnerable fraude & corruption

- MDR: more thorough
  - Safety first !!
  - More data
    - Safety
    - Efficacy
    - Long term
  - More control: production, distribution

- ? 100% guarantee ? No risk ?

- set at level fraude & corruption

More time deadline >> 2023 >> 2024 >> 2027-8

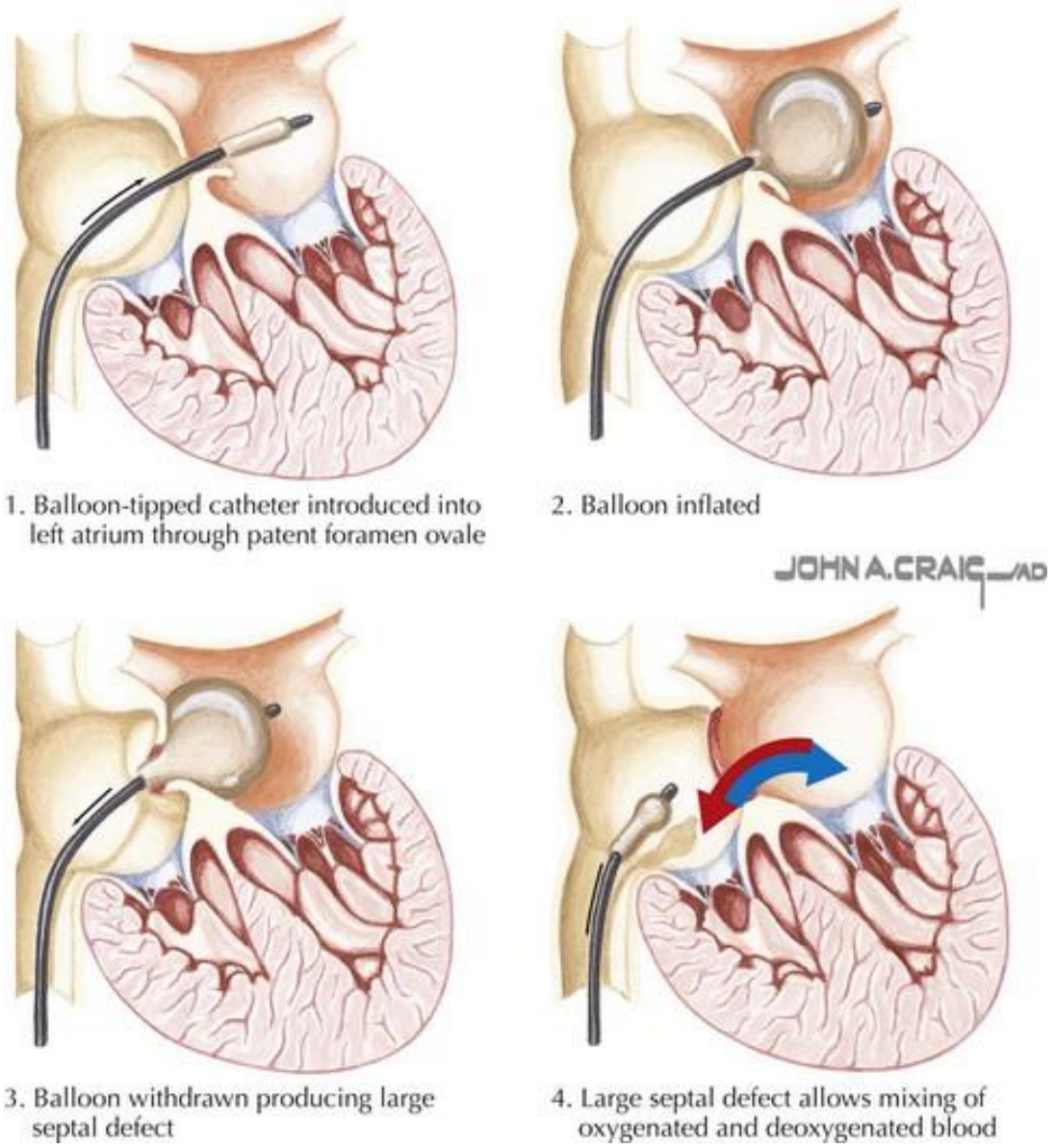
More expensive

Rashkind balloon

- Septostomy in newborn TGA
  - Bedside transumbilical on ICU
  - Since 1963: ± 1st procedure EVER !!!

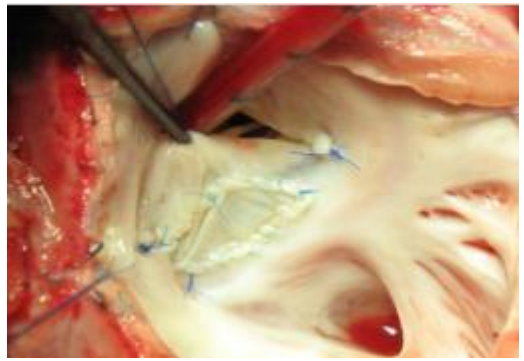
If not available:

- Cyanosis +++ minutes after birth
  - O_2 deficiency
  - brain damage
- Urgent surgery (night, B team)
- Elective caesarian



Derogation of FDA approved balloon per € country/6 months

Decellurized equine pericardial patch Matrix® Autotissue



- First CE-Mark in 2012 (for 5 years)
- 5/23 : > 16.000 Patches implanted worldwide
    - no Field Safety Corrective Actions

Decellurized equine pericardial patch Matrix® Autotissue

- Estimate process: 9 month including many extra rounds
- 230 documents (2634 pages) were uploaded
- > 811.000 €

- 2nd product of the company ...

MDD < MDR

withdrawn < 10/22			
Rashkind balloon	balloon	Edwards	septostomy in newborn
Rashkind balloon	balloon	Medtronic	septostomy in newborn
Formula 414 / 418 stents	stent	COOK	low profile premounted stent for infants
COIL MREYEFLIPPER PDA SCHL5 3MM	coils	COOK	detachable coils 3mm, 5mm, 8mm for ductus occlson
IMWC coils	coils	COOK	occlusion device
MAX/MEGA LD	stent	Medtronic	stent in PA, RVOT, CoAo
Valeo stent	stent	Bard	low profile premounted stent
Coronary cath 4,1	catheter	COOK	coronary catheter small curves for small child
Sinus Superflex DS	stent	BeMedical	stent newborn ductus
Bear Hugger	heating cushion	3M	keep infant at temperature during cath
catheter NIH-Gensini-Lehman	catheter	Medtronic	diagnostic and delivery catheters
cutting balloon 4,0 mm	balloon	Boston	cut dilation pressure resistant vessel

MDR

withdrawn < 2024-7			
Multi-Track Angiographic Catheter	catheter	Numed	angiography on wire all ages
Lunderquist Extra Stiff Support wire	guide wire	COOK	guide wire valve implantation
ATB Advance Balloon catheter	balloon	COOK	balloon
Mullins sheath	sheaths	COOK	sheath for safe delivery stent
Performer Mullins sheath	sheaths	COOK	sheath for safe delivery stent
Performer Hausdorf guiding sheath	sheaths	COOK	sheath for safe delivery stent
Mini Ghost PTA Catheter	balloon	Numed	dilation vessel - valve
Bonhoeffer Mitral Kit	balloon	Numed	dilation Mitral valve
COOK 40cm 8F pigtail drainage catheter	drain	COOK	
COOK 4 & 5F central catheters for ICU		COOK	
Si			robot surgery cardiac application
Fryderyk : all angiographic catheters	catheter	Balton	angiographic catheters
Electroda ECSS	pacing wire	Balton	temporary pacing wire
Embocure	microspheres	Balton	embolisation product
Hancock valve	surgical valve	Medtronic	surgical valve

MDR

not introduced in European market due to prohibitive costs MDR			
Z6 Rashkind	balloon	Numed	septostomy in newborn
G-Armo	stent	Numed	coarctation
Xi		Intuitive	robot surgery intra cardiac

probably withdrawn from market (pending Notified Body costs)			
Exeter snare	snare	AndraTec	snare to extract embolised foreign body
Optimus stent bare	stent	AndraTec	stent
Optimus stent covered	stent	AndraTec	covered stent
AltoSA-XL balloon	balloon	AndraTec	balloon
AltoSA-XL Gemini balloon	balloon	AndraTec	stent delivery balloon
AltoSA-SFT balloon	balloon	AndraTec	balloon
AltoSA-HP balloon	balloon	AndraTec	balloon
Temporary interruption			
EmeryGlide	guide wire MR	Nano4Imaging	MR compatible

Development stopped due to enormous costs in relation to the forseeable market			
Babystent	stent	Osypka	Breakable Stent
BeGrow	stent	Bentley	Breakable Stent

Company *** estimate 6/2022

Cost Comparison: MDD vs. New EU MDR

[redacted] Cost Breakdown (USD)	MDD	New EU MDR 2017/745
Technical File Review	$13,300	$58,500
Project Management Fee	$1,900	$6,500
Total Cost for review	$15,200	$65,000
Yearly costs to keep Cert.	N/A	
Administration Fee – Approx. by device	----------	$2,125
Class III Devices Testing	----------	$6,500
Report	----------	$1,083
Travel for testing	----------	$2,167
Project Management Fee	----------	$1,083
Technical Documentation Review	----------	$6,500
Total Yearly Costs	----------	$19,458
Total cost for (4) years (19,458 x 4)	----------	$77,832
Total Cost for Product for full (5) year cycle	**$15,200**	**$142,832**

>200,000 $ (2023)

Under the MDD, audits required the Notified Body to be on site a total of (4) days a year. Under the MDR, the Notified Body will be on site approximately (16) days the first year and (21) days every year after.

Comparison USA – CDN - €UR

EU MDR 2017/745	U.S. FDA	Health Canada
• Class III Device	• Class II Device	• Class IV device
• $142,832 cost every 5 years Audit, lines, post market	• One cost of $3,186 (Small Business Fee)	• One cost for license amendment of $9,964 CDN and annual license renewal cost of $381 CDN
• 18-24 month review time	• 30 day review under Special 510(k) process	• License Amendment Review – Received in 47 days.

European Union (EU) Medical Device Regulation (MDR) 2017/745 – CE Marking – Medical Devices

	QMS on-site audit	Unannounced audit	Technical documentation assessment	Technical or clinical expertise	Change notification
Customer day rates 2022 (January–June)	€2,560.00	€2,560.00	€3,200.00	€3,600.00	€320/hr for audit €400/hr for technical documentation (minimum 2 hrs)
Annual fees	€4,250.00 base rate +€500.00 per technical documentation				

All prices are minimum standard prices. Local offices may add specific additional fees or costs for travel.

Website feb 5 2023

Notified Body in €urope: problems

- NB = **Private** organisation — must make profit; FDA is government organization, non-profit
- NB has only **1 responsibility**: they must **guarantee safety of device** on market
  - no moral obligation to put good device on market within reasonable time at reasonable price — cf FDA has this obligation
- NB **Aversion of risk** — run by lawyers, not scientists nor clinicians
- **no control** on NB:
  - not in interpretation of MDR legislation
  - not on price
  - not on efficiency
  - not on transparency nor predictability of which lines will be followed — FDA is controlled by government and USA parliament
  - Recertification by national authority (2y) – European Commission (5y) — ?
- extreme **dysbalance in power** between NB-company:
  - NB can ask more questions, clinical study, …
  - no ombudsman, no referee
  - divorce very expensive — FDA is controlled; when disagreement a judge can rule …
  - power changes policies when money is around
- **Pre-consultation forbidden** — to avoid shopping; in USA is pre consultation the standard
  - **Unpredictability of process** — FDA has become very predictable after pre-consultation

MDR : ? Solutions

- MDR legislation
  - Amend
  - **Make subcategories**
    - Orphan device : MDCG Medical Device Coördination Group on Orphan Devices
      - conditional acceptance upon limited data
      - use of expert panel, registries, …

legal cycle in Europe > 7 years

- Notified Body
  - Control
  - Pre-consultation
  - Interpretation - Application of law
  - Redefine mission goals

Off-label use in Paediatric Cardiology

- off-label use of a device 63% of patients
  - 99% of stent implantations
    - On label: CP in coarctation
    - Off label: all stents in conduit, RVO, PA's , duct , arch,
  - 78% of balloon dilations off-label
    - On label: AoV, coarctation, PuV
    - Off label:
      - PA's, duct, conduit, surgical stenosis, post ductal stenosis
      - Concept of balloon interrogation, flow occlusion

Orphan device : problems

- Definition : 1 / 37,000 incidence ? (= 27/1 million)

- Off label use
  - Regulators uncomfortable with off-label: need for good definition & subclasses
  - Off-label: indication, age, size, pressure, safety class, …
  - Labeled indication for device may become “outdated” – “obsolete”
  - Different safety class: Class II vs Class III (if upgrade, then for all indications)

Disappearing Orphan Devices

Marc Gewillig, MD, PhD

FAEPC, FESC, FPICS, FACC