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A rare device approval for Xvivo

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The FDA yesterday bestowed the rare accolade of a humanitarian device exemption (HDE) approval on Xvivo Perfusion's lung transplant technology. HDEs are roughly the medtech equivalent of orphan drug approvals, and are awarded to devices that treat conditions affecting fewer than 4,000 people in the US each year.

The first half of this year was devoid of HDE approvals, despite a rapid uptick in the rate at which first-time premarket approvals (PMAs) were handed out (*FDA grants twice as many device approvals in half the time, July 25, 2014*). With only two HDEs awarded in 2013 and none at all in 2012 (see table below), the fact that the Xvivo system has achieved the distinction points to the value the FDA places on the technology. The company's shares are up 12% today on the Stockholm exchange.

Improving the odds

The technology could well be very important. The shortage of donor organs for transplant is a pressing concern: according to the FDA, 1,754 lung transplants were performed in the US in 2012, after which a further 1,616 potential recipients remained on the waiting list.

The agency is therefore open to devices that might improve the odds. The Xvivo Perfusion System preserves donated lungs that do not initially meet the criteria for lung transplantation, allowing time for a more detailed assessment of the organs. After a more in-depth evaluation the original decision is sometimes overturned, and the lungs are passed as fit for implantation. Currently, only one in five donated lungs is suitable for transplant, the FDA says.

The system comprises an cardiac bypass system including a pump, heater and cooler, and a ventilator; it keeps the lungs at body temperature and continuously perfuses the tissue with Xvivo's sterile solution to remove waste products. The ventilator enables the airways to be examined with a bronchoscope.

The device went before an FDA advisory committee in March (*Event – Xvivo tech aims to breathe new life into transplants, February 17, 2014*). The gastroenterology and urology devices panel voted 10-0 on all three votes in favour of safety, "probable benefit" and overall risk-benefit profile.

HDEs vs PMAs, 2005-2014		
Year	**Number of HDEs**	**Number of PMAs**
2005	2	32
2006	2	42
2007	4	28
2008	4	30
2009	1	18
2010	1	22
2011	5	43
2012	0	41
2013	2	23
2014 to date	2	18
Total	**23**	**297**

The Xvivo system was not the first HDE approval this year; the FDA quietly conferred one last month on

Terumo’s Lvis product line, used in the embolisation of intracranial aneurysms.

HDEs, being intended to address unmet needs, carry a lower burden of proof when it comes to efficacy than PMAs, the other main regulatory route for innovative technologies. An HDE application does not have to contain clinical data demonstrating that the device is effective – though it must show that the probable benefit to health outweighs the risks, as well as satisfying several other conditions.

Xvivo submitted data from two clinical trials to support safety. Both compared lung transplant patients who received non-ideal donor lungs preserved using Xvivo’s device with patients who received ideal donor lungs preserved using conventional techniques. Both trials showed that recipients of the ideal and non-ideal lungs had similar survival rates up to 12 months after transplant and similar rates of organ rejection. Xvivo will supplement this with a post-approval study.

Lengthy process

Even though relatively little evidence is needed, very few devices manage to achieve this kind of approval – the last decade has seen 23 HDE approvals compared with 297 first-time PMAs, data compiled by *EvaluateMedTech* show.

And this is no quicker than standard PMA approach. Since 2005, it has taken an average of 18.1 months to shepherd a device down the PMA path, but 23.6 months to obtain an HDE. The FDA awards few HDEs, but it takes its time to review the products.

Quite right too; often the technologies are so novel that the agency has to create new categories for them, which is why the *EvaluateMedTech* device classification for the Xvivo system has yet to be decided. It is reassuring to know that devices with no forerunners receive a lot of the FDA’s time and attention.

HDE approvals of the last five years						
Device name	**Company**	**EMT device classification - level 1**	**EMT device classification - level 3**	**Number**	**Decision date**	**Review time (months)**
NeuRx RA/4	Synapse Biomedical	Anesthesia & Respiratory	Other Respiratory Therapeutic Devices	H070003	17 July, 2008	11.0
Levitronix CentriMag right ventricular assist system	Thoratec	Cardiology	Ventricular Assist Devices	H070004	October 7, 2008	17.3
Infuse/Mastergraft posterolateral revision device	Medtronic	Orthopedics	Bone Fillers	H040004	October 10, 2008	37.1
IBV valve system	Olympus	General & Plastic Surgery	Other Surgical Instruments & Accessories	H060002	October 24, 2008	31.2
Reclaim deep brain stimulation for obsessive compulsive disorder	Medtronic	Neurology	Deep Brain Stimulation Devices	H050003	February 19, 2009	39.7
Melody transcatheter pulmonary valve and Ensemble delivery system	Medtronic	Cardiology	Transcatheter Heart Valves	H080002	January 25, 2010	16.9
cPAX aneurysm treatment system	NeuroVasx	Neurology	Neurovascular Devices	H100002	January 4, 2011	8.3
NeuRx diaphragm pacing system	Synapse Biomedical	Anesthesia & Respiratory	Other Respiratory Therapeutic Devices	H100006	September 28, 2011	11.5
Elana Surgical KitHUD	Elana	Cardiology	Atherectomy Devices	H080005	October 3, 2011	33.9
BSD-2000 hyperthermia system	BSD Medical	Radiology	Hyperthermia Devices	H090002	November 18, 2011	29.8
Berlin Heart EXCOR paediatric ventricular assist device	Berlin Heart	Cardiology	Ventricular Assist Devices	H100004	December 16, 2011	17.8
Argus II retinal prosthesis system	Second Sight Medical Products	Ophthalmics	Other Ophthalmic Prosthetic Devices	H110002	February 13, 2013	21.4
Liposorber LA-15	Kaneka	Blood	LDL Therapeutic Devices	H120005	October 10, 2013	13.2
Low-profile visualized intraluminal support device (Lvis and Lvis Jr)	Terumo	Neurology	Neurovascular Devices	H130005	July 25, 2014	Unknown
Xvivo perfusion system	Xvivo Perfusion	TBD	TBD	H120003	August 13, 2014	25.1

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