1.0 Device Identification and General Information

i) Document Number: MS-0102

ii) Device trade names: CardioCel Cardiovascular Patch and VascuCel Vascular Patch

iii) Manufacturer's name and address:

Legal manufacturer name:	LeMaitre Vascular, Inc.
Address:	63 Second Avenue, Burlington, MA. 01803, USA

iv) SRN: US-MF-000016778

v) Basic UDI-DI: CardioCel 08406631CardioCelUW; VascuCel 08406631VascuCelGM

vi) Device Item Codes, Descriptions, Basic UDI

Catalogue Number	Product Name	Dimensions
EC0202	CardioCel Adapted Collagen Scaffold	2x2 cm
EC0404	CardioCel Adapted Collagen Scaffold	4x4 cm
EC0508	CardioCel Adapted Collagen Scaffold	5x8 cm
EC0614	CardioCel Adapted Collagen Scaffold	6x14 cm
EC0404N	CardioCel Neo Adapted Collagen Scaffold	4x4 cm
EC0508N	CardioCel Neo Adapted Collagen Scaffold	5x8 cm
EV0880	VascuCel Bioscaffold Patch	0.8x8cm
EV1014	VascuCel Bioscaffold Patch	1x14cm
EV2080	VascuCel Bioscaffold Patch	2x8cm

vii) Medical device nomenclature GMDN Code / Description: 35273 **CND Code / Description:** P07020101 **EMDN Code / Description:** 57889

viii) Class of device

Manufacture Name	MDR Classification	Rule
CardioCel Cardiovascular Patch	III Implantable	8 & 18
VascuCel Vascular Patch	III Implantable	8 & 18

ix) Year when the first certificate (CE) was issued covering the device.

Device Name	Date of Initial CE Mark	Authority
CardioCel Cardiovascular Patch	13-AUG-2013	MDD 93/42/EEC
VascuCel Vascular Patch	07-MAR-2019	

x) Authorised representative if applicable; name and the SRN

EU Authorized Representative:	LeMaitre Vascular GmbH Otto-Volger-Str. 5 a/b 65843, Sulzbach/Ts Germany
SRN:	DE-AR-000013539

xi) NB's name (the NB that will validate the SSCP) and the NB's single identification number

BSI Group The Netherlands B.V. Identification Number: 2797
Say Building, John M. Keynesplein 9, 1066 EP Amsterdam, Netherlands

2.0 Intended use of the device

i) Intended purpose: The CardioCel cardiovascular patch is intended for use as a patch in cardiac defects and vascular defects. The patch material is a permanent implant used to repair damaged arteries or cardiac tissue.
The VascuCel Vascular patch is intended for use as a patch in peripheral vascular reconstruction. The patch material is a permanent implant used to repair damaged arteries.

ii) Indication(s) and target population(s) Indication:

- The CardioCel cardiovascular patch is indicated for use in the repair of cardiac and vascular defects including intracardiac defects, septal defects, valve and annulus repair, and great vessel reconstruction.
- The VascuCel Bioscaffold Patch is indicated for use as a patch material in the treatment of carotid artery disease during carotid endarterectomy, aneurysms during femoral artery repairs, and vessel repair during arteriovenous access revisions.

Target Population:

The CardioCel cardiovascular patch is designed for patients of any gender, age or ethnicity in need of permanent implantation repairing congenital heart deformities and other cardiac deformities or defects arising from cardiac related injury or malfunction, where repair using patch material is clinically indicated. There is no data for the use of this device on pregnant women.

The VascuCel vascular patch is designed for patients of any gender, age or ethnicity in need of vascular repair. There is no data for the use of this device on pregnant women or children. It is the surgeon's discretion on whether to use it on this population.

iii) Contraindications and/or limitations

- Contraindicated in patients with known or suspected hypersensitivity to bovine collagen and bovine pericardium.

3.0 Device Description

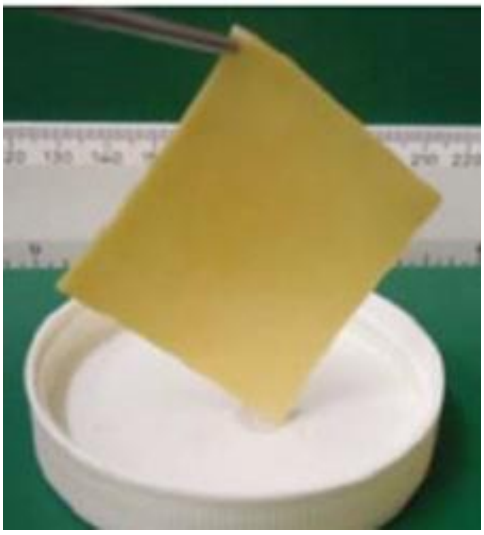
i) Description of the device

The CardioCel Bioscaffold Patch (figure 1) and VascuCel Bioscaffold Patch (figure 2) are biological scaffolds prepared from bovine pericardium using the ADAPT® Tissue Processing Technology. The devices are sterile, off white, moist, pre-cut, flat sheets of acellular collagen, presented sterile in a solution of propylene glycol and sealed in a container impermeable to air and moisture. The CardioCel Bioscaffold Patch and VascuCel Bioscaffold Patch are supplied in a range of sizes. The CardioCel Neo label is applied to products that are of 0.25-0.40 mm thickness and is

available in 2 sizes: 4cm x 4cm and 5cm x 8cm (all flat).

The CardioCel Bioscaffold Patch and VascuCel Bioscaffold Patch are manufactured from bovine pericardium that is solely sourced from herds originating in Australia from Bos Taurus breeds, including Hereford, Poll Hereford, Angus, Murray Grey, Shorthorn, Charolais, Limousin and Simmental. Australia, never having a case of transmissible spongiform encephalopathies (TSE) affecting animals, is considered by the World Organisation for Animal Health (www.oie.int) to be a negligible risk for bovine spongiform encephalopathy (BSE) and scrapie. The CardioCel Bioscaffold Patch and VascuCel Bioscaffold Patch are comprised of bovine pericardium tissue engineered, crosslinked in diluted glutaraldehyde (GA) solution, and treated with the ADAPT anti-calcification process, which has been shown to mitigate calcification in both small and large animal studies. No medicinal substance is added to the CardioCel Bioscaffold Patch or VascuCel Bioscaffold Patch. The detoxified and inert scaffold functions as a regenerative platform for cellular repair. The pericardial tissue is handled in accordance with ISO 22442-2:2020 Medical devices utilising animal tissues and their derivatives Part 2-Controls on sourcing, collection and handling.

The CardioCel Bioscaffold Patch is designed for permanent implantation in humans, indicated for the treatment of cardiac and vascular defects including intracardiac defects, septal defects, valve and annulus repair, great vessel reconstruction, and peripheral vascular reconstruction. The VascuCel Bioscaffold Patch is also designed for permanent implantation in humans, indicated for use as a patch material in great vessel repair, peripheral vascular reconstructio. The choice of device depends on the size and location of the surgical site. The CardioCel Bioscaffold Patch and VascuCel Bioscaffold Patch are designed to be cut to shape and implanted by a freehand suturing technique. The devices can be trimmed to the required matching shape and size.

Figure 1: CardioCel & CardioCel Neo	**Figure 2: VascuCel**
	

ii) Reference to previous generations: The product is a mature product currently on the market for a well-established intended use.

iii) There are no novel design features, indications, claims, or target populations for the subject device.

iv) Description of any accessories which are intended to be used in combination with the device: No accessories are supplied with this device.

v) Description of any other devices and products which are intended to be used in combination with the device: No other devices or products are intended to be used in combination with this device.

4.0 Risks and Warnings

i) Residual risks and undesirable effects

- Residual risk evaluation is conducted as part of our FMEAs and risk management procedure. We have concluded that the benefits outweigh any residual risks and that the risk has been reduced as far as possible.

ii) Potential Complications:

Adverse Events listed in IFU	Rate %	Source from CER
Bleeding	NR	State of the Art Device data
Calcification	0.44 0.09-0.35 0.14	Non-clinical data State of the Art Device data
Death	1.2 0.2	State of the Art Device data
Degeneration of the implants	NR	State of the Art Device data
Dilatation	NR	State of the Art Device data
Flow obstruction	NR	State of the Art
Formation of clinically significant fibrous tissue	NR	Non-clinical data State of the Art Device data
Haemolysis	NR NR	State of the Art Device data
Infection	Minor NR 0.4 0 Adult NR 0.21 3.3	Minor Non-clinical data State of the Art Device data Adult Non-clinical data State of the Art Device data
Infective endocarditis	6.6	Device data
Inflammation	NR	Non clinical data State of the Art
Myocardial infarction	NR 1.6	State of the Art Device data
Patch rupture	NR	Non clinical data
Pericardial adhesions	NR	State of the Art
Pseudoaneurysm formation	NR	State of the Art
Restenosis	3.1	Device data
Stenosis	4.3 1.5	State of the Art Device data
Stroke	2.4 1.6	State of the Art Device data
Thromboembolism	0.88	Device data

Thrombosis	1.2 0	State of the Art Device data

NR= no rate

iii) Warnings and precautions

Warnings

1. Use of the device following a compromise in sterility may result in infection.

Precautions

1. Device damage by exposure to chemicals, freezing, extreme heat, or chemical sterilization by the user has not been investigated. Therefore, the long-term surgical outcome after exposure is unknown.
2. Store the package right-side up.
3. The outside of the jar is not sterile and must not be placed in the sterile field.
4. Do not use the device if the tamper-evident seal is broken.
5. Do not use the device if the Freeze indicator has been tripped.
6. Do not use the device if there is evidence of damage to, or leakage from, the jar, or if the solution appears turbid as sterility of the product may have been compromised.
7. Do not expose the patch to any solutions, chemicals, antibiotics, antimycotics, or other drugs except for the storage solution or sterile physiological saline, as irreparable damage to the patch may result that is not apparent under visual inspection.
8. Prior to surgery, prospective patients or their representatives should be informed about possible complications which may be associated with the use of this device.
9. As with any surgical procedures, infection is a possible complication. Monitor patient for infection and take appropriate therapeutic action.

iv) Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable.

Sales by year and region:

Complaints by Region /Year	**2019**	**2020**	**2021**	**2022**	**2023**	**Total**
Total Sales	1,743	7,569	11,246	7,360	8,525	36,443
Total Complaints	6	24	36	40	87	193
Total Complaint Rate	0	0.317%	0.320%	0.543%	1.021%	0.530%
EU	**2019**	**2020**	**2021**	**2022**	**2023**	**Total**
Complaints	0	3	13	3	4	23
Sales	203	1,785	5,355	1,854	2,896	12,093
Rate (complaints/sales)	0	0.168%	0.243%	0.162%	0.138%	0.190%
US	**2019**	**2020**	**2021**	**2022**	**2023**	**Total**
Complaints	5	21	15	24	28	93
Sales	1,471	5,288	5,399	4,983	4,905	22,046
Rate (complaints/sales)	0.340%	0.397%	0.278%	0.482%	0.571%	0.422%
APAC	**2019**	**2020**	**2021**	**2022**	**2023**	**Total**
Complaints	1	0	8	13	55	77
Sales	69	496	492	523	724	2,304
Rate (complaints/sales)	1.449%	0.000%	1.626%	2.486%	7.597%	3.342%

**Up to December*

The complaints per type/category are summarized in the table below:

Complaint Category	2019	2020	2021	2022	2023	Total	Complaint Rate
Low temp. exposure	0	1	2	14	51	68	0.187%
Jar damage	5	6	21	14	14	60	0.165%
Patch thickness	0	3	1	10	1	15	0.041%
Stenosis	0	0	10	0	2	12	0.033%
High temp. exposure	0	10	0	0	0	10	0.027%
Outer box damaged	0	0	1	0	6	7	0.019%
Packaging issue (seal dislodged)	0	0	0	0	5	5	0.014%
Patch shrinkage	0	4	0	0	0	4	0.011%
Packaging issue (patch in the lid)	0	0	0	1	2	3	0.008%
Wet packaging	0	0	0	0	2	2	0.005%
Medical complications	0	0	0	0	2	2	0.005%
No device failure	1	0	0	0	0	1	0.003%
Packaging issue (missing patch)	0	0	0	1	0	1	0.003%
Labeling issue	0	0	1	0	0	1	0.003%
Defective temperature indicator	0	0	0	0	1	1	0.003%
User error	0	0	0	0	1	1	0.003%

The top complaint categories for the subject devices were low-temperature exposure (n=68), Jar damage (n=60), and patch thickness (n=15). There were 54 complaints in total as detailed above in the table.

Corrective and Preventative Actions:

Corrective and preventive actions are handled as defined in SOP14-001 CAPA. During the reporting period of 01 January 2019 to 31 December 2023 (based on CER data), 1 CAPA was opened for the subject devices. This CAPA was completed and closed on 29 September 2023. A summary of the CAPA opened during the reporting period is in the table below.

CAPA Number/initiated	CAPA Summary	Status
2022-030/ 07 Oct 2022	Low-temperature exposure - the freeze indicator was exposed to a temperature of 0c or less. The SOP was updated and a label was added to note “Do Not Freeze”	Closed, 29 Sep 2023

Field Safety Corrective Actions:

There were 0 field action notifications sent out by LeMaitre for the CardioCel and VascuCel Patch product family during the reporting period of 01 January 2018 to 31 December 2023 (based on CER data).

5.0 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

i) **Summary of clinical data related to equivalent device, if applicable:** NA

ii) **Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable**

The following clinical investigations were conducted on CardioCel prior to preparation of

the CER. These clinical investigations were identified either via searches of clinical trials databases or supplied by the manufacturer; the clinical investigations discussed in this section do not necessarily overlap with those found in the literature. When, however, an overlap of patient groups is identified, efforts are made to avoid duplication of data. This data set was appraised for relevance following MDCG 2020-6 and an overview of these data is provided below as considered relevant to this clinical evaluation.

1. Phase II Study to demonstrate the safety, efficacy and clinical performance of CardioCel in paediatric patients with congenital cardiac anomalies (2013) Note: This study, published by Neethling W. et al. in 2013, shares the same initial patient group of 30 patients as Neethling W. et al. 2020. Both studies reported analyses of outcomes from the same initial patient group who received treatment with CardioCel. The first analysis of the data reported immediate and short-term outcomes (up to 12- month follow-up) and the second analysis reported medium- to long- term outcomes at up to 10- years follow-up.

Objective(s): To evaluate the safety, efficacy, and clinical performance of CardioCel in correcting congenital cardiac anomalies in paediatric patients. The rationale for this study was to assess the anti- calcification efficacy of CardioCel during a Phase II Clinical Trial.

The performance of the device was assessed by documentation of:

- early (< 30 days) morbidity;
- time related incidence of device related complications (i.e. device failure, thromboembolism, structural leak, infections, device related re operation and replacement); and
- haemodynamic performance of the device (Echocardiography). The secondary objectives were to evaluate design features such as:
    - handling characteristics;
    - shape and sizing characteristics; and
    - implant complications.

Methodology:

Thirty paediatric patients at a single centre in South Africa underwent insertion of CardioCel for correction of congenital cardiac defects. Patients were selected with anatomy and symptoms sufficient to warrant application of CardioCel as a bio-prosthetic substitute during surgical repair procedures during open heart surgery. Specifically, this involved ASD, VSD, atrioventricular septal defect (AVSD), aortic root enlargement and RVOT reconstruction. Early follow-up procedures included the collection of peri- and post-operative data. Post-operative assessment was via echocardiograph at 6 and 12 months post- operation, and magnetic resonance imaging (MRI) on 10 randomly selected patients at 12 months. Further follow up data up to 36 months became available in an extension study for diagnoses, functional class, and specific procedures.

Results:

The first implant was performed on 29th April 2008 and the last on 1st September 2009. Overall, five (17%) patients died due to non-graft related factors; one (3.3%) patient was completely lost to follow-up; and one other patient presented for six-month data, however, subsequently failed to present at 12 months. Of the two (6.6%) patients lost to follow up, geographical relocation and travelling difficulties were cited as reasons for the lack of follow up. Further detail regarding follow-up is shown in Table 9 below.

There were five deaths; two patients died within the first 30 postoperative days (early mortality): One patient who was diagnosed with a hypoplastic aortic arch, coarctation and transposition of the great arteries died 3 days postoperatively due to acute respiratory distress syndrome due to transfusion- related lung injury. A second patient died as a result of pulmonary hypertensive crisis after correction of a truncus arteriosus. Three patients

died >3 months postoperatively (late mortality): 1 patient (aged 3 months) died of a bilateral chylothorax and septicaemia. A second patient (aged 18 months) contracted community-acquired pneumonia and died of sepsis and low pulmonary perfusion. A third patient (aged 5 years) died 3 months postoperatively in a community hospital of cardiac arrest. Of the 5 patient deaths, echocardiography assessment identified a residual leak in one patient at 6 and 12- month follow-up.

These events were considered to be non-graft related.

The results from the echocardiographs revealed anatomically intact and haemodynamically stable repairs without any visible calcification of the patch. There were no signs of calcification observed in MRIs of the 10 patients randomly selected for the assessment. There was no evidence of device calcification, infection, thromboembolic events. Although subjectively measured, device characteristics, including handling, shape, size and peri operative complications were rated as acceptable in the majority of cases. In patients with congenital heart disease, followed for 12 months, CardioCel demonstrated durable efficacy and favourable haemodynamic properties. No graft-related morbidity or mortality was observed. Nineteen patients were evaluated after 18 months, 12 patients after 24 months and six patients after 36 months of follow-up. All patients were free of patch-related complications or adverse events.

Echocardiographic results showed intact haemodynamics with no evidence of visible calcification of the CardioCel patch at the 18, 24- and 36-month evaluation.

TABLE 9 DIAGNOSIS, NYHA FUNCTIONAL CLASSES, AND SURGICAL PROCEDURES

Diagnosis	**N** (%)
Ventricular Septal Defect Repair (VSD)	13 (43)
Atrioventricular Septal Defect (AVSD)	3 (10)
Atrial Septal Defect (ASD)	1 (3)
Right ventricular outflow tract (RVOT)	2 (7)
Other	2 (7)
ASD & VSD	1 (3)
VSD & RVOT	4 (13)
ASD, VSD & RVOT	1 (3)
VSD & Other	3 (10)
NYHA Functional Class	**N** (%)
Class I	20 (67)
Class II	7 (23)
Class III	2 (7)
Class IV	1 (3)
Primary Surgical Procedure	**N** (%)
Ventricular Septal Defect Repair (VSD)	14 (47)

Atrioventricular Septal Defect (AVSD)	3 (10)
Atrial Septal Defect (ASD)	1 (3)
ASD & VSD	2 (7)
VSD & RVOT	6 (20)
VSD & Other	2 (7)
Vascular Patch	1 (3)
Other	1 (3)
Follow-up	**N** (%)
Total number of implants	30
Patients loss due to non-graft-related mortality	5
Follow up at 6 months	21/25 (84)
Follow up at 12 months	18/25 (72)
Follow up >12 months	14/25 (56)

Conclusion:

In patients with congenital heart disease, followed for 12 months, CardioCel demonstrated safety, durable efficacy and favourable haemodynamic properties. Five deaths occurred during the study, however none of these were device related. No graft related morbidity or mortality was observed in the extension study out to 84 months, no graft-related adverse events were reported.

Stable haemodynamic data was obtained for all patients at 12-month follow-up echocardiography, in addition to 18-36 month follow up on 19 (76% of the surgery surviving population), with no adverse events reported, CardioCel exhibited favourable safety outcomes.

Discussion:

This study provides evidence that CardioCel can be used as a patch to repair several types of paediatric congenital heart anomalies including ASD, VSD, AVSD and also involved RVOT reconstruction, aortic arch repair, truncus repair and aortic root enlargement. However, this study does have some limitations in its design; it is a non-randomised, single-center study with small patient numbers and no control group.

However, the device continually demonstrated desirable characteristics throughout the study including thickness, flexibility and elasticity. Performance and safety outcomes were superior for septal defect repairs when compared to the more complicated indications. The complexity of the surgical repair was scored using the Aristotle complexity score. The 5 patients who died had a significantly higher score than those who survived [mean = 12.40 (1.70) for deceased patients, 7.02 (2.41) for surviving patients; P-value <0.0001 from t-test]. Fisher's test indicated that those with high complexity surgical repairs had significantly lower survival rates than those with low-complexity repairs (P-value = 0.0055; 58% survival in the high-complexity group and 100% survival in the low-complexity group). There were no further deaths reported for the remaining follow-up of the study as evidenced in the summary of the mid- to long- term follow-up study below. No clinically significant calcification was observed, and there was no graft-related morbidity or mortality. Overall, this study showed promising results for the repair of septal defects using CardioCel in indicated patients who would have had limited alternative treatment options.

iii) Summary of clinical data from other sources, if applicable:

Literature searches were conducted on 17-JAN-2024 following the strategy outlined in the literature search protocol and aimed to identify publications on the LeTEP Tissue Products. Careful screening and subsequent appraisal and analysis of the data were conducted by qualified professionals. A total of 97 references were identified based on the search limits and criteria in the Literature Review Protocol. After automatic removal of duplicates, 33 references were identified for further assessment. Of these, 18 were excluded. 12 were due to article type. 3 were single case reports, clinical trials. 2 were excluded due to reporting pooled data. Finally, 1 did not report safety or performance data for the device. After manually adding one reference, a total of 16 references were appraised as relevant to the device literature and included in the CER.

The table below provides a detailed overview of the clinical evidence retained on LeTEP Tissue Products

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
IV	#1 Bell D. et al. 2019 [79]	VSD and ASD closure: 183 patches (36%) AVSD repair: 38 patches (7.6%) PA reconstruction: 103 (20.5%) RVOT reconstruction: 74 (14.8%) Aortic valve/root/arch: (10.4%) Valve repair (aortic, mitral, tricuspid): 30 (6%) Intra-atrial baffle: 18 (3.6%)	377 patients/ 501 CardioCel patches Neonates: 62 (12.4%) Infants: 285 (56.9%) >1-yr:154 (30.7%)	Patch infection: Not reported (N/A) Patch dehiscence : n = 1 Patch calcification: n = 0 Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: Thrombosis n = 1 Amputation: Not reported (N/A)	Reintervention rate: 14 implants (2.8%) required 18 reinterventions (3.6%) Mortality: 11 deaths (2.9%), with one case related to CardioCel	CardioCel has good durability when used for the repair of congenital heart defects. It performs comparably in the systemic and pulmonary circulations in neonates, infants and older children. There was no significant difference in freedom from reintervention among neonates, infants, and older children. There was no statistically significant difference in the performance of CardioCel in the pulmonary circulation as compared with the systemic circulation.	Median: 31-mths, Range 1 to 60-mths

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
IV	#2 Bell D. et al. 2019 [80]	VSD: 69 patches (35%) Pulmonary artery: 34 9 (17.43%) ASD: 18 patches (9.2%) Transannular patches: 15 patches (7.69%) AVSD: 11 patches (5.6%) Aortic arch: 11 patches (5.6%) Intra-ventricular baffles: 8 (4.1%) Pulmonary artery conduit: 6 (3.0%) Pulmonary leaflet: 5 (2.56%) Transected MPA: 4 (2.0%) Repair of systemic veins: 3 (1.53%) Repair of AP window: 3 (1.53%) Repair supra- valvular stenosis: 3(1.53%) Intra-atrial baffle: 2 (1.0%) Other: 3 (1.53%)	135/195 CardioCel patches Neonates: 19 (13.6%) Infants: 77 (55%) >1-yr: 44 931.4%)	Patch infection: n = 0 Patch dehiscence: Not reported (N/A) Patch calcification: n = 0 Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: Thrombosis n = 1 Amputation: Not reported (N/A)	Reintervention rate: Eight patients (n = 135, 5.9%) required reintervention in 12 instances. In 6 of these patients, CardioCel implantation was the main indication for intervention. Mortality: No deaths were directly related to CardioCel.	At 24 months and beyond the follow-up, the performance of CardioCel remains acceptable with good haemodynamic performance. CardioCel can be used in all age groups and across a wide spectrum of congenital abnormalities in the systemic and pulmonary circulation. It has acceptable haemodynamic properties. It appears [to be] resistant to infection, and we did not identify any echocardiographic or radiological evidence of calcification at 24 months and beyond. Reinterventions were triggered by stenosis secondary to granulation tissue formation. In our overall experience over the past 5 years, the thicker granulation tissue formation on the rougher surface of the patch has not caused any additional significant haemodynami	Follow-up was 98.5% complete with 3 patients lost to follow-up (2 returned to Polynesian islands and 1 to Africa). There were 6 deaths (4.6%), but none directly related to CardioCel. The median duration of follow-up in the remaining 126 patients was 39 months (range 27–54 months).

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
						c narrowing beyond what has been described in this study. It is possible that the granulation tissue formation subsides with time. CardioCel performs comparably in systemic and pulmonary circulations.	
IV	#3 Nordmeyer S.et al. 2018 [81]	Aortic valve repair (valve cusp replacement or augmentation) Fifteen patients had a previous aortic valve surgery, and another 14 patients underwent previous transcatheter balloon aortic valvuloplasty previously.	N = 40 Median age: 9 (1.7 –34) years	Patch Infection: Not reported (N/A) Patch dehiscence: Not reported (N/A) Patch calcification: Not reported (N/A) Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: Not reported (N/A) Amputation: Not reported (N/A)	Reintervention rate: n = 8 (20%) Mortality: n = 1 (2.5%)	Our cohort was small and heterogenous with patients with congenital abnormal aortic valves who received AVR with leaflet extensions. Based on our experience, decellularized bovine pericardial patch material should be used with caution for reconstruction purposes of the aortic valve leaflets in patients with congenital aortic valve pathology.	Median follow-up: 22 (6–42) months.

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
III`	#4 Patukale et al. 2023	Aortic root/sinus: CardioCel (n = 46) CardioCel Neo (n = 7) Aortic valve—leaflet extension: CardioCel (n = 33) CardioCel Neo (n = 27) Aortic valve—leaflet replacement: CardioCel (n = 5) CardioCel Neo (n = 5) Aortic valve—others: CardioCel (n = 12) CardioCel Neo (n = 3) Arch augmentation: CardioCel (n = 40) CardioCel Neo (n = 3) CardioCel 3D (n = 73) Ascending aorta: CardioCel (n = 39) CardioCel Neo (n = 4) CardioCel 3D (n = 7) ASD: CardioCel (n = 56) CardioCel Neo (n = 6) Atrial enlargement-LA: CardioCel (n = 4) CardioCel Neo (n = 2) Atrial enlargment-RA: CardioCel (n = 4) CardioCel Neo (n = 1) AVSD-single patch repair: CardioCel (n = 11) AVSD-2 patch repair-ASD component: CardioCel (n = 14) CardioCel Neo (n = 1) AVSD-2 patch repair-VSD component: CardioCel (n = 10) CardioCel Neo (n = 1) Branch pulmonary artery: CardioCel (n = 131) CardioCel Neo (n = 21) CardioCel 3D (n = 2) Inter-atrial Baffle: CardioCel (n = 24) Main pulmonary artery-	752 patients (n = 1184 patches) n = 752 (1184 patches). Out of total patches, CardioCel was implanted in n = 957 (81%), CardioCel Neo n = 142 (12%), and CardioCel 3D n = 85 (7%). Median age at implant was 12 months [interquartile range (IQR) 3.6–84]	Patch infection: (n = 0) Patch dehiscence: n = 1. Patient developed a deep sternal infection post-operation, leading to dehiscence of the CardioCel patch used in the right ventriculotomy, but no causative organism could be isolated from the CardioCel patch. Patch calcification: n = 2 (0.18%). One each for aortic and mitral valve repair Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: n = 2 (0.18%). One after arch augmentation and one used for pulmonary	Reintervention rate: Out of 1097 patches with complete follow-up data, n= 67 (6.1%) underwent reinterventions Mortality: n = 1. Was related to CardioCel.	CardioCel can be used for the repair of a variety of congenital heart defects. In our study, in patients receiving a CardioCel implant, reinterventions were higher when CardioCel was used to augment the pulmonary arteries in neonates and for aortic valve repair as compared to other sites.	The median follow-up time was 2.1 years (IQR 0.6-4.6)

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
		augmentation: CardioCel (n = 86) CardioCel (n = 8) Main pulmonary artery-transected stump: CardioCel (n = 14) Mitral valve-AML: CardioCel (n = 8) CardioCel Neo (n = 4) Mitral valve-others: CardioCel (n = 7) CardioCel Neo (n = 1) Mitral valve-PML: CardioCel (n = 11) CardioCel Neo (n = 6) Other: CardioCel (n = 57) CardioCel Neo (n = 7) CardioCel 3D (n = 2) Pulmonary valve-Monocusp: CardioCel (n = 7) Pulmonary valve-Sung repair: CardioCel (n = 10) CardioCel Neo (n = 1) Pulmonary Veins: CardioCel (n = 4) CardioCel Neo (n = 1) RVOT-RV-PA conduit hood: CardioCel (n = 27) CardioCel Neo (n = 3) RVOT patch-augmentation: CardioCel (n = 35) CardioCel Neo (n = 4) Systemic veins-IVC: CardioCel (n = 5) CardioCel Neo (n = 1) Systemic veins-SVC: CardioCel (n = 4) CardioCel Neo (n = 1) Transsannular patch: CardioCel (n = 68) CardioCel Neo (n = 7) Tricuspid valve-leaflet augmentation: CardioCel (n = 1) CardioCel Neo (n = 4) Tricuspid valve-others: CardioCel (n = 5)		valve repair Amputation: Not reported (N/A)			

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
		Ventriculotomy: CardioCel (n = 7) VSD: CardioCel (n = 160) CardioCel Neo (n = 13) CardioCel 3D (n = 1)					
IV	#5 Neethling et al. 2013	ASD: n = 1(3%) VSD: n = 14 (47%) AVSD: n = 3 (10%) RVOT: n = 2 (7%) ASD and VSD: n = 1 (3%) VSD and RVOT: n = 4 (13%) ASD, VSD and RVOT: n = 1 (3%) Vascular patch (aorta): n = 2 (7%) VSD and coarctation: n = 2 (7%)	CardioCel: N = 30	Patch infection: (n = 0) Patch dehiscence: Not reported (N/A) Patch calcification: n = 0 Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: n = 0 Amputation: Not reported (N/A)	Reintervention rate: n = 0 (30 day postoperative period) Mortality: Total of n = 5, n = 2 within 30 days. All 5 were determined as non-graft related	This study demonstrates the safety and efficacy of this engineered bovine pericardial patch as a cardiovascular substitute for surgical repair of both simple and more complex congenital cardiac defects.	Echocardiography assessment at 6 and 12 months and MRI findings in 10 randomly selected patients at 12 months. Echocardiographic data was available at 18-36 months for 19 patients.
III	#6 Neethling et al. 2020	ASD: n = 1 (3%) VSD: n = 14 (47%) AVSD: n = 3 (10%) RVOT: n = 2 (7%) ASD and VSD: n = 1 (3%) VSD and RVOT: n = 4 (13%) ASD, VSD and RVOT: n = 1 (3%) Vascular patch (aorta): n = 2 (7%) VSD and coarctation: n = 2 (7%)	CardioCel: N = 30 (34 patches) Median age was 18 months (17 days- 13.3 years)	Patch infection: n = 0 Patch dehiscence: n = 0 Patch calcification: n = 0 Patch retraction: Not specifically reported, but no structural issues like surface thickening	Reintervention rate: n = 0 Mortality: N = 2. Both non-graft related	The tissue-engineered ADAPT® bovine pericardial scaffold demonstrated excellent medium to long-term performance (up to 10 years) when used as a scaffold for repair of congenital cardiac defects in children.	Median of 7.2 years (25%: 3.6 years, 75%: 9.25 years), with a maximum follow-up of 10 years

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
				or leaks were detected in the implants. Stroke rate: Not reported (N/A) Thromboembolism: n = 0 Amputation: Not reported (N/A)		Durability, acellularity, biostability and non-calcifying potential of CardioCel® makes it a very attractive tissue for congenital cardiac repair procedures.	
IV	#7 Pavy C. et al. 2018 [82]	VSD: 54 (53%) ASD: 3 (3%) AVSD: 6 (6%) Vascular enlargement: 24 (23.7%) patients (ascending aorta, n = 4; aortic arch, n = 5 and pulmonary artery, n = 15) RVOT: 16 (15.8%) (infundibulum enlargement patch, n = 11 and transannular path, n = 5), Valvular reconstruction in 10 (9.9%) patients (aortic cusp extension/monocus p repair, n = 4; Ozaki procedure, n = 2; mitral valve plasty, n =3 and tricuspid plasty, n = 1) Venous anastomosis in 1 (1%) (Senning procedure).	N = 101 Number of patches not reported All patients were treated with CardioCel Mean age was 22 (±36.3) months (3 days - 18 years)	Patch infection: (n = 0) Patch dehiscence: Not reported (N/A) Patch calcification: n = 0 Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: Not reported (N/A) Amputation: Not reported (N/A)	Reinterventio n rate: n = 5 (4.9%) Mortality: n = 4 (3.9%)	Our 2-year experience showed a good handling characteristic of the material by the surgeons for implantation during the procedure, and no infections were related to it. The patch had a good behaviour in low-pressure areas without creating any stenosis because of calcification or thickness. However, we experienced early graft failure under high pressures because of a tremendous intimal reaction, which has not been previously reported for this type of patch.	Median follow-up period was 212 days (4-726)

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
						Our findings show that the patch becomes mainly stenotic in infants after enlarging the aortic arch, which we believe is a result of the mismatch between the elasticity of the native aorta and the CardioCel patch under systemic pressure. The blood flow creates shear stress against the aortic wall and can cause this intimal hypertrophy reaction leading to severe aortic stenosis. Our experience shows that the patch is well tolerated in the septal, valvular and pulmonary artery positions. However, we experienced graft failures in infants in the aortic position.	
IV	#8 Chivers S. C. et al. 2019 [49]	Aortic valve reconstruction (Ozaki procedure) Previous interventions: 5/6 (60%)	5 All used CardioCel patches/ 17.6 years (range: 11-29 years)	Patch infection: Not reported (N/A) Patch dehiscence: Not reported (N/A)	Reintervention rate: n = 2 Mortality: n = 0	Our experience demonstrates that the Ozaki procedure with CardioCel in paediatric and young adult patients should be approached with caution. Further research with	Mean follow-up: 29.6-mths (range: 22- 36-mths)

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
				Patch calcification: n = 1 Patch retraction: Not reported (N/A) Stroke rate: n = 1 Thromboembolism: n = 1 Amputation: Not reported (N/A)		larger groups of paediatric patients, comparison of different graft materials, and longer follow-up is required to ascertain long-term success in children.	
IV	#9 Tomšič A. et al. 2018 [83]	Mitral valve augmentation/reconstruction Large patches were used for Anterior mitral valve leaflet (AMVL) augmentation or reconstruction: 11 patients (36%) Smaller patches were used to reconstruct A1 or A2 segment defects of the AMVL: 13 patients (43%) In another 2 patients, reconstruction of the anterolateral commissure was performed, whereas in the last 2 patients, multiple CardioCel patches were used to repair both leaflets.	30/ All treated using CardioCel patches Mean age 57.2 ± 14.3- yrs	Patch infection: Two cases of operated valve infective endocarditis were reported, however, in one case, infection at the level of patch repair was not observed Patch dehiscence: In one case of the two cases of operated valve infective endocarditis, both echocardiographic and intraoperative observations indicated ring dehiscence. Patch calcificatio	Reintervention rate: n = 1 Mortality: Two (7%) early postoperative deaths occured (non-graft related). At follow-up, 3 additional deaths occured (2 due to infective endocarditis, 1 non-cardiac related)	This is the first study to explore the results of MV repair with the CardioCel pericardial patch in adult patients with good early valve repair performance demonstrated, thus implying good patch biocompatibility and resistance to early degeneration. On echocardiographic follow-up, a slight increase in patch thickness was observed (0.2 mm, not significant). This could be related to a controlled process of patch endothelialization and collagen layer formation that was previously observed in	Mean follow-up of 1.7 ± 0.9 years

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
				n: Not reported (N/A) Patch retraction: No significant differences in patch thickness were observed between predischarge and follow-up, suggesting no significant patch shrinkage or retraction Stroke rate: Not reported (N/A) Thromboembolism: Not reported (N/A) Amputation: Not reported (N/A)		juvenile sheep models where CardioCel was used for valve repair. However, two patients experienced operated valve IE. In 1 patient this occurred within 2 months after operation, with the infection limited to the yet unendothelialized prosthetic ring. The other patient did not undergo reoperation, and an infection of the implanted patch could not be excluded.	
IV	#10 Wiggins L.M. et al. 2020 [48]	Aortic valve leaflet reconstruction Neo-tricuspidalization (Ozaki procedure): 40 patients (69%) Single leaflet Reconstruction: 18 patients (31%) Twelve patients (21%) had concomitant procedures performed at the time of aortic valve surgery.	N = 58 CardioCel 32 (55%) vs Autologous pericardium 26 (45%) Median age of 14.8 years (IQR 10.6-16.8)	Patch infection: Not reported (N/A) Patch dehiscence: Not reported (N/A) Patch calcification: Of the six that required late operation, structural valve degeneration (decreased	Reintervention rate: n = 1 early reoperation due to a technical failure (i.e., neo-tricuspidalization with partial right neo-cusp detachment). N = 6 (10%) required late reoperation. Mortality: There was 1 mortality in a patient with a history of prior heart transplant for	We have demonstrated better performance of autologous pericardium compared to bovine pericardium with lower gradient across the aortic valve at final follow-up. However, we did not observe a significant difference in terms of material used for a composite outcome measure of	Median echocardiographic follow-up: 14.1-mths

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
				mobility and calcification of bovine pericardial leaflet) was observed in 1 patient. Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: Not reported (N/A) Amputation: Not reported (N/A)	dilated cardiomyopathy and severely impaired left ventricle function, 5.6 months after discharge following aortic valve reconstruction surgery.	AR, endocarditis, or reoperation rate. Aortic leaflet reconstruction provides acceptable short-term hemodynamic outcomes and proves the utility of this technique as an adjunctive strategy for surgical treatment of aortic valve disease in children and young adults. In addition, aortic leaflet replacement techniques may offer utility in paediatric patients with anatomy unsuitable for aortic valve replacement.	
Level IV	#11 Cua C. et al. 2021 [84]	Cylinder mitral valve replacement (cMVC) compared to mitral valve replacement (MVR)	N = 5 (100%) Age at surgery: 4.3 ± 4.2 years (median 2.2, .8–10.3 years)	Patch infection: Not reported (N/A) Patch dehiscence: Not reported (N/A) Patch calcification: Not reported (N/A) Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A)	Reintervention rate: Not reported (N/A) Mortality: Not reported (N/A)	Echocardiographic indices of left ventricular function improved over time in patients undergoing cMVC. There were no significant differences between cMVC and MVR patients in echocardiographic values.	Time interval from hospital discharge echocardiogram to the most recent echocardiogram was 1.2 ± 0.7 years (median 1.0 year, 0.6 - 2.0 years)

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
				Thromboembolism: Not reported (N/A) Amputation: Not reported (N/A)			
Level III	#12 Van Beynum I. et al. 2021 [85]	Aortic arch reconstruction	CardioCel: 10 (10/36; 27.8%) Homograft: 26 (26/36; 72.2%) Median age: 2 weeks (2-32)	Patch infection: Not reported (N/A) Patch dehiscence: Not reported (N/A) Patch calcification: Not reported (N/A) Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: Not reported (N/A) Amputation: Not reported (N/A)	Reintervention rate: n = 7 (70%) for restenosis. A second reintervention was performed in n = 5 patients. A third intervention was performed in n = 1 patient. A fourth intervention was performed in n = 1 patient. Mortality: No late mortalities reported	Considering that coarctation resection was more frequently (80%) performed in the CardioCel group than in the homograft group (23%), we found it worrisome that the restenosis rate was significantly higher in the CardioCel group. We conclude that choice of patch material is likely to be an important determinant for the risk of restenosis needing reintervention following reconstruction of the aortic arch in neonates and infants and the number of reinterventions needed to treat them. Based on our own observations and in accordance with the findings of previous studies by other investigators, we favor the use of homograft	Reinterventions within the first postoperative year

Reference (Level of Evidence)	Study Number/First Author/Year	Procedure/Aetiology	## of Subjects related to CardioCel / ## of Patches/Age	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
						patch material for aortic arch augmentation in neonates and infants, and we no longer use CardioCel patch material for this application.	

Published Systematic Papers:

Reference (Level of Evidence)	Study Number/First Author/Year	Indication	Methods	Safety Results	Performance Results	Conclusions from Authors
Level IV	Patukale A. et al. 2023 [86]	Systematic review of CardioCel in cardiac surgery	13 human studies included for review	16 deaths (11%), however, no death was related to aortic arch obstruction	Repair of hypoplastic/interrupted aortic arch by transection above and below ductal insertion, excision of ductal tissue, and standardized patch augmentation provided good mid-term durability. Freedom from intervention at five years was over 90%.	We conclude that CardioCel is a strong, flexible tissue substitute with good handling characteristics and a low incidence of thrombosis, aneurysm formation, infection, or structural degeneration. It can be used for a variety of intracardiac and extracardiac repairs of congenital heart defects in all age groups with good durability at mid-term follow-up. However, the use of CardioCel in certain positions requires caution. Information on the long-term performance of CardioCel is lacking.

Summary of Published Studies of Explanted CardioCel (Total of 2 studies)

Reference (Level of Evidence)	Study Number/First Author/Year	## of explants/ Age	Procedure	Safety Results	Performance Results	Conclusions from Authors	Follow-up Time
Level IV	#1 Deutsch O. et al. 2020 [87]	N = 9 explants (obtained during reoperation) Time to explantation : Mean 242 (3-1247) days Age: 28 ± 21 years	Cardiac valve repair	Patch infection: Not reported (N/A) Patch dehiscence: Not reported (N/A) Patch calcification: n = 2 Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: n = 1. The patient died of pulmonary embolism 13 days after atrioventricular valve repair. However, the article did not explicitly state that the CardioCel patch implant was the direct cause of the pulmonary embolism Amputation: Not reported (N/A)	Mortality: No interoperative deaths and n = 2 postoperative deaths. However, none of the deaths were directly attributed to the CardioCel patch implant.	Our data suggest that the CardioCel patch is initially tolerated in most cases. However, we also experienced graft failures with a distinct histopathological pattern.	Mean follow-up time of 374 ± 254 days
Level IV	#2 Nordmeyer S. et al. 2019 [88]	12 explants (11 explanted surgically, 1 autopsy). Mean time to explant: 27 mths Mean age was 6.75 years	Aortic valve repair	Patch infection: Inflammation was found in all explanted specimens, but it was not correlated with patch implantation time Patch dehiscence: Not reported (N/A) Patch calcification: In 10 of 12 specimens, there was evidence of significant calcification affecting the patch material and to some	Mortality: Not reported (N/A)	In our cohort, all CardioCel patches used for aortic valve repair in patients with congenital heart disease demonstrated appositional growth of fibroblasts and extracellular matrix components, and calcification after an implant time of at least 23 months.	Not applicable

				extent surrounding tissue components Patch retraction: Not reported (N/A) Stroke rate: Not reported (N/A) Thromboembolism: Not reported (N/A) Amputation: Not reported (N/A)			

• Clinically relevant information based on clinical data obtained from the implementation of the manufacturer's PMCF and PMS plans, such as: Conducted PMCF investigation(s);

Interim Clinical Investigation Report – Post-Market Registry in Europe for the Use of CardioCel®, CardioCel® Neo and CardioCel® 3D

This is a European post-market, multi-centre, open-label registry designed to collect prospective safety and performance data on the use of CardioCel implant devices in patients with cardiovascular disorders and in accordance with local standards of care.

Objectives: To investigate the safety and performance of the CardioCel implant device in 57 patients with heart or blood vessel defects that were present since birth or acquired. Indications included intracardiac and septal defects, valve and annulus repair, great vessel reconstruction, peripheral vascular reconstruction, suture line buttressing.

Methods: Of the 57 patients included in this study, the report only describes the results of 49 patients, who were implanted with a CardioCel device during a 2-year follow-up period. The mean age of the patients was 2.03 ± 4.76 years (range 0.01 – 25.00 years). The age categories of the patients included 3 neonates, 38 infants, 6 children, 1 adolescent, and 1 adult. Device model use per indication was as follows: Model ECO202 was used in 50% of subjects being treated for intracardiac defect (1/2), 2.5% for septal defect (1/40), and 12.5% for great vessel reconstruction (1/8). For device model ECO404N, 50% of subjects being treated for intracardiac defects (1/2), 35% for septal defects (14/40), 50% for great vessel reconstruction (4/8), and 25% for other (i.e. pulmonary artery reconstruction post PA banding) (1/4) received this device. For device model ECO404, 55% of subjects being treated for septal defects (22/40), 50% for valve and annulus repair (1/2), and 50% for other (i.e. hemi mustard baffle, valvular and muscular sub valvular pulmonary stenosis – repair of muscular VSD and valvular PS (trans-annular patch) and creation of small ASD) received this device (2/4). For device model ECO508, 5% of subjects being treated for septal defects (2/40), 50% for valve and annulus repair (1/2), 12.5% for great vessel reconstruction (1/8), 100% for suture line buttressing (1/1), and 50% for other (i.e., hemi mustard baffle, RVPA conduit hood) (2/4) received this device. For device mode ECO508N, 2.5% of subjects being treated for septal defects (1/40) and 12.5% for great vessel reconstruction (1/8) received this device. Finally, for device ECO406A, 12.5% of subjects being treated for great vessel reconstruction (1/8) received this device. Of the subjects being treated for septal defect (40/49; 81.6%), 6.1% (3/49) were atrial septal defect, 77.6% (38/49) were ventricular septal defect, and 2.0% (1/49) were atrioventricular septal defect. Of the subjects being treated for valve

and annulus repair (2/49; 4.1%), 4.1% (2/49) were pulmonary valve and 2.0% (1/49) were tricuspid valve.

Several outcome measures were recorded to determine the safety and performance of the CardioCel device and its use in different cardiac and blood vessel related defects. The primary performance endpoint was incidence of graft related reintervention at 30 days post procedure and the primary safety endpoint was incidence of patch related morbidity at 30 days post procedure. The secondary endpoints for performance included incidence of graft related reintervention at 1- and 2-years post procedure. For safety this included incidence and nature of device related safety events, including but not limited to patch dehiscence, patch calcification, patch retraction, and unanticipated and rare events.

Results: The main performance outcome parameter showed that no reoperation was needed 30 days after the initial implant procedure. Additionally, reoperation was also not needed at the 1- and 2-year follow-up timepoints. For specific cardiac and blood vessel defects, it was also determined that there were no reports of backward blood flow or blood vessel narrowing following treatment with the CardioCel device. Only one unexpected medical problem occurred, the CardioCel device did not attach properly to the treated area, however, this problem was resolved, and the patient was treated as needed.

Conclusions: Overall, the performance and safety of the CardioCel device was acceptable within the clinical expectations and within the limits reported by scientific literature. This interim report has shown that the CardioCel device performs well and that it can be safely used in invasive heart procedures. More data is needed for the remaining heart and blood vessel treatment applications. No new or unexpected risks have been identified for the CardioCel device in this interim report. These outcomes suggest that the device is safe and performs as intended.

Interim Clinical Investigation Report – Post-Market Registry in Europe and US for the Use of VascuCel™

This is a European and US post-market, multi-centre, open-label registry designed to collect prospective safety and performance data on the use of VascuCel in patients who require great vessel reconstruction, peripheral vascular reconstruction, or suture line buttressing, and in accordance with local standards of care.

Objectives

The objective of this registry is to collect prospective safety and performance data on the on-label use of VascuCel™ in patients who require great vessel reconstruction, peripheral vascular reconstruction, or suture line buttressing up to 2 years following implantation.

Population

Patients were considered eligible for the VascuCel™ registry if they required great vessel reconstruction, peripheral vascular reconstruction, or suture line buttressing and have signed informed consent.

The VascuCel™ registry aims to collect data with a minimum of 50 patients per major indication. Major indications included great vessel reconstruction and peripheral vascular reconstruction. Suture line buttressing is not considered a major indication as the procedure does not consistently use tissue patches for repair. Therefore, this data is only included if there are eligible patients; no minimum number is set for this specific indication.

At the moment of this interim analysis, a total of 30 patients were enrolled at 3 investigational centers in 2 countries. Centre 1 (Varese University Hospital, Italy) enrolled 15 patients, center 3 (University of North Carolina, US) 3 patients and center 5 (Kootenai Health, US) 12 patients. For this interim clinical study report, great vessel reconstruction has been omitted from the analysis, since no patients with this indication were enrolled. Twenty-eight (28) of the 30 enrolled patients were treated for peripheral vessel reconstruction, one (1) for suture line buttressing and one (1) had a combined indication for peripheral vessel reconstruction and suture line buttressing. The peripheral vascular reconstruction indication included treatment of carotid artery disease during

carotid endarterectomy (15/28, 53.6%), aneurysms during femoral artery repairs (9/28, 32.1%), vessel repair during arteriovenous access revisions (1/28, 3.6%), and other vessels or unknown (3/28, 10.7%).

For peripheral vessel reconstruction, the EV2080 model was used in six of the 28 patients (21.4%), each in the lower limb, and the EV0880 model was used in 22 of the 28 patients (78.6%) for the carotid (16/28; 57.1%), lower limb (5/28; 17.9%), and other (i.e. radial artery) (1/28; 3.6%). For the lower limb, locations included the common femoral artery, femoral artery, and iliofemoral artery. For suture line buttressing, the EV2080 and EV0880 models were each used in one of the two patients (50%), with the former being used in the lower limb (1/2; 50%) and the latter being the carotid (1/2; 50%).

Design and Methods

Data was prospectively collected at the day of procedure, post-operatively at 30 days, and at 1- and 2-years follow-up by the sites on registry-specific electronic case report forms (eCRFs). The primary, secondary and exploratory endpoints assessed the device's short- and long-term safety and performance through measures and images obtained via the facility's standard of care at the respective registry site.

Primary endpoints

- Performance: Incidence of graft-related reintervention at 30 days post-procedure
- Safety: Incidence of patch-related morbidity at 30 days post-procedure

Secondary endpoints

- Performance: Incidence of graft-related reintervention at 1- and 2-years post-procedure
- Performance per indication
    - Great vessel reconstruction[1]: Rates of restenosis at 30 days and 1- and 2-years follow-up
    - Peripheral vascular reconstruction: Rates of measurement of the dynamic flow by facility standard of care ≥110-175 cm/sec[2] for peripheral vascular locations at 30-days and 1- and 2-years post procedure
- Safety: Incidence and nature of device related safety events, including but not limited to
    - Patch dehiscence
    - Patch calcification
    - Patch retraction
    - Unanticipated events

Exploratory endpoints[3]

- Patch histology
- User satisfaction with the devices' handling and performance

Results

Patient disposition and demographics

This first annual interim clinical investigation report (CIR) reports on the short-term safety and performance data of the VascuCel™ registry. Twenty-eight (28) of the 30 enrolled patients were treated

[1] For this interim clinical study report, great vessel reconstruction has been omitted from the analysis, since no patients with this indication are enrolled yet.

[2] The accepted peak velocity depends on the implant location. The accepted peak velocity for ascending aorta is: 175 cm/sec; distal aorta and iliac vessel: 150 cm/sec and proximal carotid, branchial and superficial femoral arteries: 110 cm/sec.

[3] No data on exploratory endpoints are available yet for this interim clinical study report.

for peripheral vessel reconstruction, 1 for suture line buttressing and 1 had a combined indication for those two. All 30 patients completed the baseline visit (visit before device implantation), 29 had the device implanted, 13 completed short-term follow-up (any follow-up visit that occurs within 0 to 30 days after implantation), and 6 completed mid-term follow-up (any follow-up visit that occurs from 30 days to 1 year after the implantation). In this interim analysis, no patient completed long-term follow-up (any follow-up visit that occurs from 1 year up to 2 years after implantation). The mean age of the enrolled patients was 71.3 ± 9.25 years (range: 47-84 years), and 65.5% (19 of the 29 patients) was male.

Primary endpoints
Regardless the indication, no patch-related morbidity <30 days from the procedure was observed in patients with the device implanted (0/29; 0%). One graft-related reintervention within 30 days from the procedure was reported in a patient with peripheral vascular reconstruction (1/28; 3.6%; surgical indication - aneurysms during femoral artery repairs; surgical wound infection, see below - adverse events section) in the lower limb (1/11; 9.1%), but not in patients with a suture line buttressing indication (0/2; 0%). The acceptance criteria for these two endpoints were both set at ≤10%, indicating that the primary endpoints on performance and safety were met for this interim analysis. However, statistical assessment after inclusion of the total sample size needs to be performed to draw final conclusions.

Secondary endpoints
Increased dynamic blood flow can be present during, e.g., aneurysm, stenosis, and AV fistula. These pathological conditions can cause turbulence, which can ultimately lead to the development of thrombosis. The dynamic flow of the only patient that was measured was not elevated (≥110-175 cm/sec) for peripheral vascular locations, indicating that the flow velocity at the anatomical location of the implant was normal and no turbulence was present, minimizing the risk for thrombosis in this patient. Additionally, one peripheral vascular reconstruction patient experienced graft-related reintervention between 30-days and 1-year post-procedure (1/21; 4.8%; surgical indication - aneurysms during femoral artery repairs; lower limb implant location; patch dehiscence; see below - adverse events) in the lower limb (1/8; 12.5%), while no suture line buttressing patient experienced this (0/1; 0%). The acceptance criteria for these two endpoints were both set at ≤10%, indicating that both the general and peripheral vessel indication-specific secondary performance endpoints were met in this interim analysis. However, statistical assessment after inclusion of the total sample size needs to be performed to draw final conclusions, especially since the dynamic flow rate was only measured in one patient.

Regardless of indication, no unanticipated events were reported or patch calcification or retraction was observed in patients with the device implanted (0/29; 0%). In suture line buttressing patients, no patch dehiscence was observed at any time point (0/2; 0%), while in peripheral vessel reconstruction patients, patch dehiscence was not observed at the intra-operative ultrasound and short-term follow-up (<30 days). At the mid-term follow-up visit (any follow-up visit that occurs from 30 days to 1 year after the implantation), however, patch dehiscence was observed in one peripheral vessel reconstruction patient (1/28; 3.6%; surgical indication - aneurysms during femoral artery repairs; lower limb implant location) in the lower limb (1/11; 9.1%) and this was considered an SAE (see below - adverse events). Since the acceptance criteria for these endpoints were set at ≤3% (unanticipated events), or ≤10% (patch calcification, retraction, or dehiscence), the secondary safety endpoints were met. However, statistical assessment after inclusion of the total sample size needs to be performed to draw final conclusions.

Exploratory endpoints
No patch histology was performed for this interim clinical study report. Additionally, no results from user satisfaction questionnaires are present.

Adverse events and device deficiencies
There were no deaths reported in this interim study analyses. There were three (3) device- and/or procedure-related AEs reported during the clinical study until database lock on 11 October 2023 for the first annual

clinical study report. Those three (3) AEs were reported in two (2) patients who received the VascuCel™ device for the indication of peripheral vessel reconstruction. Of these three (3) AEs, two (2) were related to a lower limb implant (surgical indication was aneurysms during femoral artery repairs) and one (1) was related to a carotid implant (surgical indication was carotid artery disease during carotid endarterectomy). No patient with a suture line buttressing indication experienced any device- and/or procedure-related AE.

The first AE occurred in a patient that presented with a surgical wound infection 15 days after the procedure of the lower limb (surgical indication was aneurysms during femoral artery repairs). This AE was anticipated and causally related to the procedure, but not to the device. The wound infection was treated with wound revision and resolved with sequelae, as this mild AE presumably led to the development of an SAE of patch dehiscence that occurred 77 days after the index procedure of the lower limb. This SAE comprised a superinfection that developed into patch dehiscence and disruption of the suture. This SAE was considered a device deficiency, causally related to the device and procedure. If not intercepted and/or treated, this SAE might have led to massive lethal bleeding from the groin. Reintervention occurred by a patch explant and iliac-profunda femoris artery bypass, and the SAE was resolved after 12 days.

The last AE occurred at the index procedure in a peripheral vascular reconstruction patient (surgical indication was carotid artery disease during carotid endarterectomy) and was considered as causally related to the procedure but not to the device, anticipated, and of moderate severity. The patient experienced about 300 mL intraoperative blood loss and was treated with a blood transfusion, after which this AE resolved in one day.

Taken together, for this interim clinical study report, there were three (3) anticipated device and/or procedure-related AEs reported in two (2) of the 28 peripheral vascular reconstruction patients (1 patch dehiscence [1/28; 3.57%], 2 'other' [2/28; 7.14%]), and no AEs in the two (2) suture line buttressing patients (0/2; 0%). Of these three events, two were in the lower limb (1/11; 9.09%) and one was in the carotid (1/16; 6.25%). The incidence of mild, moderate and severe device and/or procedure related AEs was 3.57% (1/28) for all severities in patients with a peripheral vascular reconstruction indication. The incidence of procedure-related AEs was 7.14% (2/28), while the incidence of the device-related AEs[4] was 3.57% (1/28) in patients with a peripheral vascular reconstruction indication.

Long-term follow-up data

Ad hoc data extraction was performed on 20 August 2024 to gather long-term follow-up data (i.e., any follow-up data from 1 year up to 2 years after implantation) that was entered after the database lock. A total of six patients had data captured >1 year after implantation, i.e., falling in the long-term follow-up time window of 1 year up to 2 years after implantation. The indications included aneurysms during femoral artery repairs (n=1, lower limb implant location) and treatment of carotid artery disease during carotid endarterectomy (n=5, carotid implant location). None of these six patients experienced a device or procedure related AEs or required a graft related intervention at the long-term follow-up visit. In addition, no device deficiencies were reported at the long-term follow-up visit. Table below provides an overview of the long-term follow-up data for all six patients.

Table: Long-Term Follow-Up Data Post-Market Registry VascuCel

Subject ID	Indication	Location of Implant	Implantation Date	Long-Term Follow-Up Visit Date*	Device or Procedure related AEs	Device Deficiencies	Graft-related reinterventions
1004	Aneurysms during femoral artery repairs	Lower limb	20-JUN-2023	22-JUL-2024	No	No	No
1005	Treatment of carotid artery disease during carotid endarterectomy	Carotid	21-JUN-2023	22-JUN-2024	No	No	No
1006	Treatment of carotid artery disease during	Carotid	27-JUN-2023	19-JUL-2024	No	No	No

[4] This entailed the SAE of patch dehiscence, which was related to both the device and procedure. However, if an event is related to both device and procedure, it is only reported among the device related events.

	carotid endarterectomy						
5001	Treatment of carotid artery disease during carotid endarterectomy	Carotid	14-JUL-2023	24-JUL-2024	No	No	No
5003	Treatment of carotid artery disease during carotid endarterectomy	Carotid	19-JUL-2023	24-JUL-2024	No	No	No
5004	Treatment of carotid artery disease during carotid endarterectomy	Carotid	19-JUL-2023	24-JUL-2024	No	No	No
*, the long-term follow-up visit is considered any follow-up visit that occurs from 1 year up to 2 years after implantation.							

- **Analysis of clinical data from medical device registries. Any known limitations such as incomplete follow-up should be disclosed:** NA, two ongoing PMCF studies that are not complete yet.

iv) An overall summary of the clinical performance and safety

Based on the clinical data evaluated in this CER, the LeTEP Tissue Products are in conformity with requirements on clinical performance (MDR GSPR 1 and TGMDR EP3):

Clinical data evaluated for LeTEP Tissue Products have demonstrated that the LeTEP Tissue Products achieve their expected performance during three crucial timepoints; intra-operatively, peri-operatively and post-operatively up to 10-years follow-up. The performance outcomes reported for CardioCel CardioVascular patch and VascuCel vascular patch compared similarly with data from benchmark devices, as described in the State-of-the-Art section. All pre-determined criteria were met by CardioCel and VascuCel vascular patch. Clinical studies held by LeMaitre showed that that the LeTEP Tissue Products are soft, pliable, handles well during suturing and are sufficient in terms of surface area being supplied. For VascuCel, the overall suture line bleeding was felt by surgical staff to be significantly reduced compared to prosthetic patches. Compared to other cardiac patches the recoarctation rate for CardioCel cardiovascular patch is lower and has durable efficacy and favourable haemodynamic properties. CardioCel cardiovascular patch seemed to allow good leaflet reconstruction, with the additional potential of minimal calcification and conversion to host-compatible leaflets over time.

The 16 articles from the literature describing clinical performance reported satisfactory handling characteristics with acceptable haemodynamic properties, good biocompatibility, and resistance to early patch degeneration. CardioCel cardiovascular patch showed good leaflet coaptation and is well tolerated in septal, valvar and pulmonary positions. In contrast to Tomšič et al. (2018), Nordmeyer et al. (2018) reported that the freedom of aortic valve dysfunction decreases over time when Cardiocel cardiovascular patch was used for leaflet reconstruction of the aortic valve.

Overall, the preclinical testing, clinical studies held by the manufacturer, PMS data and scientific literature demonstrate that LeTEP Tissue Products perform as intended by LeMaitre. The performance characteristics are consistent with the state of the art.

Safety Outcomes per indication

Indication	Device	N Studies	Events	Total	Rate (%)	Lower CI	Upper CI
Patch Infection							
Intra-Cardiac Defects	CardioCel cardiovascular patch	4	0	296	0.49	0	1.28
Septal Defects	CardioCel cardiovascular patch	4	0	296	0.49	0	1.28

Valve and Annulus Repair	CardioCel cardiovascular patch	4	0	267	0.46	0	1.26
Great Vessel Reconstruction	CardioCel cardiovascular patch	4	0	273	0.46	0	1.26
Peripheral Vascular Reconstruction	VascuCel vascular patch	1	1	28	3.57	0	10.45
Patch Dehiscence							
Intra-Cardiac Defects	CardioCel cardiovascular patch	4	3	860	0.29	0	0.65
Septal Defects	CardioCel cardiovascular patch	4	3	860	0.29	0	0.65
Valve and Annulus Repair	CardioCel cardiovascular patch	4	3	831	0.28	0	0.64
Great Vessel Reconstruction	CardioCel cardiovascular patch	4	3	837	0.28	0	0.64
Peripheral Vascular Reconstruction	VascuCel vascular patch	1	0	28	1.72	0	6.46
Patch Calcification							
Intra-Cardiac Defects	CardioCel cardiovascular patch	5	0	797	0.14	0	0.4
Septal Defects	CardioCel cardiovascular patch	5	0	797	0.14	0	0.4
Valve and Annulus Repair	CardioCel cardiovascular patch	5	0	768	0.14	0	0.4
Great Vessel Reconstruction	CardioCel cardiovascular patch	5	0	774	0.14	0	0.4
Peripheral Vascular Reconstruction	VascuCel vascular patch	1	0	28	1.72	0	6.46
Patch Retraction							
Intra-Cardiac Defects	CardioCel cardiovascular patch	1	0	30	1.61	0	6.05
Septal Defects	CardioCel cardiovascular patch	1	0	30	1.61	0	6.05
Valve and Annulus Repair	CardioCel cardiovascular patch	1	0	1	25	0	85.01
Great Vessel Reconstruction	CardioCel cardiovascular patch	1	0	7	6.25	0	23.02
Peripheral Vascular Reconstruction	VascuCel vascular patch	1	0	28	1.72	0	6.46
Thromboembolism							
Intra-Cardiac Defects	CardioCel cardiovascular patch	3	1	195	0.89	0	2.21
Septal Defects	CardioCel cardiovascular patch	3	1	195	0.89	0	2.21
Valve and Annulus Repair	CardioCel cardiovascular patch	3	1	166	0.84	0	2.21
Great Vessel Reconstruction	CardioCel cardiovascular patch	3	1	172	0.86	0	2.23
Peripheral Vascular Reconstruction	VascuCel vascular patch	1	0	28	1.72	0	6.46

Performance outcomes per indication

Indication	Device	N Studies	Events	Total	Rate (%)	Lower CI	Upper CI
Reintervention Rate							
Intra-Cardiac Defects	CardioCel cardiovascular patch	4	2	662	0.25	0	0.63
Septal Defects	CardioCel cardiovascular patch	4	2	662	0.25	0	0.63
Valve and Annulus Repair	CardioCel cardiovascular patch	4	2	662	0.25	0	0.63
Great Vessel Reconstruction	CardioCel cardiovascular patch	5	2	644	0.25	0	0.63
Peripheral Vascular Reconstruction	VascuCel vascular patch	1	1	28	3.57	0	10.45
Mortality							
Intra-Cardiac Defects	CardioCel cardiovascular patch	6	1	901	0.29	0	0.65
Septal Defects	CardioCel cardiovascular patch	6	1	901	0.29	0	0.65
Valve and Annulus Repair	CardioCel cardiovascular patch	7	1	902	0.29	0	0.65
Great Vessel Reconstruction	CardioCel cardiovascular patch	7	1	889	0.29	0	0.64
Peripheral Vascular Reconstruction	VascuCel vascular patch	1	0	28	1.72	0	6.46

The below parameters were considered relevant to determine the acceptability of the benefit/risk profile within the Clinical Evaluation.

The quantifiable acceptance criteria for the safety objectives are:

- Minors (<18 years old)
  - Patch infection (≤30 days post-surgery): 0.4% (95% CI 0 – 0.91%)
  - Patch dehiscence (≤30 days post-surgery): 0.0 (95% CI 0 – 3.48%)
  - Patch calcification (≤30 days post-surgery): 0.0 (95% CI 0 – 0.4%)
  - Thromboembolism (≤30 days post-surgery): 0.0 (95% CI 0 – 0.35%)
- Adults (≥18 years old)
  - Patch infection (≤30 days post-surgery): 0.21% (95% CI 0 – 0.49%)
  - Thromboembolism (≤30 days post-surgery): 1.42% (95% CI 0 -3.04%)

The quantifiable acceptance criteria for the performance objectives are:

- Minors (<18 years old)
  - Reintervention rate (≤30 days post-surgery): 1.69% (95% CI 0.59 – 2.78%)
  - Reintervention rate (>30 days post-surgery): 1.57 (95% CI 1.57 – 2.58%)
  - Mortality with outlier data (≤30 days post-surgery): 4.7 (95% CI 0 – 12.07%)
  - Mortality without outlier data (≤30 days post-surgery): 0 (95% CI 0 – 3.48%)
- Adults (≥18 years old)
  - Reintervention rate (≤30 days post-surgery): 1.43% (95% CI 0.51 – 2.36%)
  - Reintervention rate with outlier data (>30 days post-surgery): 16.13% (95% CI 0 – 44.13%)
  - Reintervention rate without outlier data (>30 days post-surgery): 1.54% (95% CI 0 – 3.24%)
  - Mortality (≤30 days post-surgery): 0.44% (95% CI 0 – 0.79%)

The benefits of using CardioCel cardiovascular patch and VascuCel vascular patch include permanence, regeneration and durability once implanted into human tissue, requiring fewer re-interventions. Both CardioCel cardiovascular patch and VascuCel vascular patch are biocompatible and incorporate into recipient tissue with associated cell and microvascular ingrowth without sensitisation, irritancy or allergenicity. The intended clinical benefit of LeTEP Tissue Products was achieved, because all the above acceptance criteria were met under conditions consistent with the intended purpose and within the intended patient population for the LeTEP Tissue Products. Acceptance criteria were also calculated per indication for use (see **Section** Error! Reference source not found. and **Section** Error! Reference source not found. **in the CER** for details) an d were all met for the LeTEP Tissue Products.

The current Clinical Evaluation confirmed the benefits of LeTEP Tissue Products and ensured its safety through the review and appraisal of clinical data, and Risk Management documentation provided by LeMaitre.

The benefits of using LeTEP Tissue Products compared to other similar cardiovascular patches, such as other cardiovascular patches manufactured using bovine pericardium, have been discussed in the State-of-the Art review. The use of cardiovascular patches manufactured from bovine pericardium remains a popular and commonly used option and is considered a state-of-the art treatment.

The following clinical benefits were described through the literature review:

- Increased survival rates
- Improved quality of life:
    - General improvement in overall health/wellness
    - Improvement in exercise tolerance
- Prevention/reduction of further surgery in later life

Through this Clinical Evaluation, the clinical benefits identified from the literature on LeTEP Tissue Products are in line with the objectives established as state of the art for Bioprosthetic Pericardial Patches.

No specific adverse events or device malfunctions were reported in the clinical data generated on LeTEP Tissue Products.

In conclusion, considering the results presented in this Clinical Evaluation, and the state of the art established in the medical field of LeTEP Tissue Products, it is demonstrated that any risks that might be associated with the use of LeTEP Tissue Products are acceptable when weighted against the benefits to the patient. In conclusion, the benefit/risk profile is considered acceptable for LeTEP Tissue Products when used as intended in its target population.

Conclusions

In summary, although less-invasive treatment options are available and are commonly used to repair many cardiac diseases and defects, for many patients open heart surgical procedures are the treatment of choice. This choice is made by the physician(s) and the patient (or their guardian) based on consideration of anatomy, age, complications and other cardiac malformations. Current clinical guidelines recommend the use of cardiovascular patches for a wide range of indications. In many cases there is no specific recommendation for the type of patch material.

The pros and cons of all available cardiovascular patch materials have been discussed above. The benefits of cardiovascular patches manufactured using bovine pericardium for the repair of cardiac septal disorders have also been discussed, along with the potential complications.

The LeTEP Tissue Products been available for use for more than a decade and have demonstrated all characteristics required from a cardiovascular patch. It is plentiful in supply, requires little pre-use preparation and perform well relative to similar patches in regard to complications commonly associated with patches manufactured from bovine pericardial tissue, such as calcification,

antigenicity and lack of ability to remodel, regenerate and integrate with the recipient's body. These benefits are due to the unique processes to which LeTEP Tissue Products undergo during the tissue engineering process. Relative to benchmark devices, the LeTEP Tissue Products perform similarly in terms of performance, specifically, incidence of reoperation and survival rate.

v) Ongoing or planned post-market clinical follow-up

The manufacturer conducts ongoing post-market surveillance (PMS) of the subject device according to the following procedure, SOP28-001. Post-Market Clinical Follow-up (PMCF) activities are planned for the subject device. A multi-stepped approach will be used to substantiate the performance claims of the device and ensure that the risk/benefit remains positive. LeMaitre has planned/sponsored a Post-Market Clinical Follow-Up (PMCF) plan. The aims of the PMCF activities are to proactively collect clinical safety and performance data on the CardioCel Bioscaffold Patch and VascuCel Bioscaffold Patch, including 1) a systematic literature review to capture all published clinical information on the CardioCel and VascuCel Bioscaffold Patch and similar devices, 2) a PMCF study that aims to assess the safety and performance of the CardioCel and VascuCel Bioscaffold Patch up to one year post implantation, 3) an end user survey that aims to collect heneral user feedback to determine possible systematic misuses or off-label use of the CardioCel and VascuCel Bioscaffold Patch, 4) an open ended registry study to collect data on the safety and performance of the CardioCel and VascuCel Bioscaffold Patch throughout the intended lifetime of the device. For details regarding this PMCF plan, refer to Section 8.1 [Ref PMCF037].

6.0 Possible diagnostic or therapeutic alternatives:

Indication for Use		Alternative Treatments	Performance and Safety Outcomes	References
Intracardiac and Septal Defects	Atrial Septal Defect	Transcatheter closure (TC)	Reduced complication rates, shorter hospital stays, and lower overall mortality In elderly patients, improved functional capacity and cardiac parameters Device embolization Higher incidence of residual shunts, compared to surgical closure	Abaci 2013, Baroutidou 2023
		Anterolateral minithoracotomy (ALMT)	Both techniques demonstrated equivalent safety and efficacy ALMT showed faster functional recovery and superior cosmetic outcomes	Lei 2021
		Median sternotomy (MS)		
		Multiple device closure (MDC)	MDC is as safe and effective as SDC, with no significant differences in overall complication rates, arrhythmia incidence, or residual shunt rates	Jabbar 2023
		Single device closure (SDC)		
	Ventricular Septal Defect	Perventricular device closure (PDC)	High success rates and proving to be safe and effective for perimembranous VSDs (pmVSD) Reducing the likelihood of significant complications	Li 2020, Yu 2022, Huang 2020

Indication for Use		Alternative Treatments	Performance and Safety Outcomes	References
			compared to Conventional Surgical Repair (CSR) Shorter hospital stay, similar rates of major and minor complications compared to CSR, and a lower incidence of residual shunts High success rates were found for doubly committed subarterial VSDs (dcsVSDs) Compared to CSR, it poses a higher risk of aortic regurgitation	
		Transcatheter closure	Outperforms mini-invasive closure and open-heart surgical repair in terms of operative time, major complications, and length of ICU and hospital stay for pmVSDs in children	Yi 2018
		Percutaneous device closure Surgical closure	Comparable to surgical closure, significantly reducing the need for blood transfusion and shortening hospital stay	Saurav 2015
		Transthoracic device closure	Compared to conventional open-heart surgery, it was associated with reductions in the duration of the procedure, ICU stay, hospital stay, the number of transfusions, and the incidence of post-operative arrhythmia Compared to conventional open-heart surgery, it was associated with a higher risk of intra-operative residual shunts and lower success rate This disadvantage was not observed in randomized clinical trials	Zhou 2017
	Atrioventricular Septal Defect	Primary repair Staged repair	In AVSD with ToF, no significant difference was found in survival and reintervention rates with respect to the left atrioventricular valve (LAVV) between primary repair and staged repair`	Lenko 2018
		Modified single patch Two patch repair	Single patch required less cardiopulmonary bypass time and cross-clamp time Single patch superior to two patch repair in terms of aortic cross-clamp time and cardiopulmonary bypass time in patients with complete atrioventricular septal defects	Loomba 2019, Wu 2020

Indication for Use	Alternative Treatments	Performance and Safety Outcomes	References
		No significant impact on various postoperative outcomes, both techniques are effective	
Valve and Annulus Repair	Transannular patch repair with or without monocusp valve reconstruction	Monocusp group showed advantages in decreasing the length of ICU stay and reducing the degree of perioperative pulmonary regurgitation (PR) in TOF patients compared to without monocusp No significant difference in perioperative mortality between the monocusp and non-monocusp groups	Wei 2022
	Mitral valve repair or replacement	Both MV repair and replacement are worthwhile surgical approaches for treating ischemic MR and that the choice between the two should be viewed as part of a surgical armamentarium, with the best technique chosen based on the individual patient and the surgeon's expertise.	Di Mauro 2022
Great Vessel Reconstruction	Interposition arteriovenous bundle graft	Low rate of perfusion-related complications. 95.7% success rate, suggesting this technique is effective in bridging vascular gaps with minimal donor morbidity.	Kim 2022
	Autologous vein patch	PTFE patches appeared to have fewer complications than Dacron grafts in terms of perioperative stroke and transient ischaemic attack (TIA) rates, as well as early and late arterial re-stenosis and occlusion. Bovine pericardial patches might reduce the risk of perioperative fatal stroke, death, and infection compared to other synthetic patches. Bovine pericardium or PTFE seems to be associated with a lower rate of short-term and late outcomes following carotid endarterectomy Possibility that pseudoaneurysm formation may be more common in patients who receive vein patches compared to those that receive synthetic patches. No significant difference in the occurrence of perioperative and long-term ipsilateral stroke	Orrapin 2021, Lazarides 2021
	Synthetic patch (including polytetrafluoroethylene, dacron, polyurethane, polyester)		
	Bovine pericardium		

Indication for Use	Alternative Treatments	Performance and Safety Outcomes	References
		between patients who received vein patch materials and those who received synthetic patch materials	
Peripheral Vascular Reconstruction	Absorbable Permeable Membrane (APM) reinforcement	APM has a significantly lower rate of staple-line leaks compared to oversewing, use of sealants, nonabsorbable bovine pericardial strips, or no reinforcement.	Gagner 2020
	Oversewing (suture)		
	Nonabsorbable bovine pericardial strips		
	Tissue sealant or fibrin glue		
	Supermicrosurgery	Overall flap success rate was 96.6% (95%CI 95.2%-98.1%), with a cumulative rate of partial flap loss of 3.84% (95%CI 1.8%-5.9%) and an overall vascular complication rate resulting in complete or partial flap loss of 5.93% (95%CI 3.5%-8.3%)	Escandón 2022

7.0 Suggested profile and training for users

The CardioCel Patch and VascuCel Patch are surgical tools intended for use by experienced vascular surgeons trained in the procedures for which they are intended.

8.0 Reference to any harmonized standards and CS applied

Standard Title	**Standard Reference: Revision Year**
Sterilization of medical devices. Requirements for medical devices to be designated "STERILE". Part 2: Requirements for aseptically processed medical devices	EN 556-2:2015
Medical devices Information to be supplied by the manufacturer	ISO 20417:2021
Cardiovascular implants and extracorporeal systems – Vascular prostheses -- Tubular vascular grafts and vascular patches	ISO 7198:2016
Biological evaluation of medical devices – Part 1: Evaluation and testing	ISO 10993-1:2018
Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity	ISO 10993-3:2014
Biological evaluation of medical devices – Part 4: Selection of tests for interactions with blood	EN ISO 10993-4:2017
Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity	ISO 10993-5:2009
Biological evaluation of medical devices – Part 6: Tests for local effects after implantation	EN ISO 10993-6:2016
Biological evaluation of medical devices – Part 10: Tests for irritation and delayed-type hypersensitivity	ISO 10993-10:2013
Biological evaluation of medical devices – Part 11: Tests for systemic toxicity	ISO 10993-11:2018
Biological evaluation of medical devices Part 17: Establishment of allowable limits for leachable substances	EN ISO 10993-17:2009
Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems	ISO 11607-1:2020

Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing and assembly processes	ISO 11607-2:2020
Sterilization of medical devices – Microbiological methods – Part 1: Determination of a population of microorganisms on products	ISO 11737-1:2018
Tests of sterility performed in the definition, validation and maintenance of a sterilization process	ISO 11737-2:2020
Medical devices – Quality management systems – Requirements for regulatory purposes	EN ISO 13485:2016/ A11 2022
Sterilization of health care products – Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives – Requirements for characterization, development, validation and routine control of a sterilization process for medical devices	ISO 14160:2020
Clinical investigation of medical devices for human subjects — Good clinical practice	ISO 14155:2020
Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness	ISO 14644-1:2015
Medical devices – Application of risk management to medical devices	EN ISO 14971:2019
Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied —Part 1: General requirements	EN ISO 15223-1:2021
Medical devices utilizing animal tissues and their derivatives – Part 1: Application of risk management	ISO 22442-1:2020
Medical devices utilizing animal tissues and their derivatives – Part 2: Controls on sourcing, collection and handling	ISO 22442-2:2020
Medical devices utilizing animal tissues and their derivatives – Part 3: Validation of the elimination and/or inactivation of viruses and TSE agents	EN ISO 22442-3:2007

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9.0 Revision History

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
Not submitted	27/06/2023	Initial release	☐ Yes Validation language: English (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB) ☐ No
A	30/05/2024	Updates per NB feedback, removed suture line buttressing, updated patient population	☒ Yes Validation language: English (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB) ☐ No

10. Patient information

A summary of the safety and clinical performance of the device, intended for patients, is given below.

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. Your healthcare provider has a more extensive summary of safety and clinical performance.

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an implant card or the instructions for use to provide information on the safe use of the device.

1. Device general information

a. Device trade name

i. CardioCel Patch (Cardiac) and VascuCel Patch (Vascular)

b. Producer; name and address

i. LeMaitre Vascular, Inc. 63 Second Avenue, Burlington, MA 01803

c. Basic UDI-DI

i. CardioCel 08406631CardioCelUW
ii. VascuCel 08406631VascuCelGM

d. Year when the device was first CE-marked

i. CE mark in 2013 for CardioCel and 2019 for VascuCel

2. Intended use of the device

a. Intended purpose

i. The Cardiac patch is intended for use as a patch in cardiac and vascular defects. The patch material is a permanent implant used to repair damaged arteries or cardiac tissue.
ii. The Vascular patch is intended for use as a patch in peripheral vascular repair. The patch material is a permanent implant used to repair damaged arteries

b. Indications and intended patient groups

i. The cardiac patch used in the repair of heart and blood vessels.
ii. The vascular patch is indicated for use as a patch material in the treatment of blocked arteries and weakened artery repair.
iii. Patient groups:
The intended target population for the Cardiac Patch is patients of any gender, age, or ethnicity in need of a permanent implant to repair heart deformities. There is no data for the use of this device on pregnant women.
The intended target population for the Vascular Patch are patients of any gender, age or ethnicity in need of vascular repair. There is no data for the use of this device on pregnant women and children. It is the surgeon's discretion on whether to use it on this population.

c. **Do not use for:** persons with known allergy to cows

3. **Device description**
   a. **Device description and material/substances in contact with patient tissues**
      i. The Patches are made of heart fluid sacs from cows that are prepared using the LeTEP Tissue Processing Technology. The devices are sterile, off-white, moist, pre-cut, flat sheets of acellular collagen, presented sterile in a solution and sealed in a container that does not allow air or moisture in. The Patches are supplied in a range of sizes.
   b. **Information about medicinal substances in the device, if any**
      i. n/a
   c. **Description of how the device is achieving its intended mode of action**
      i. Per regulations, the Patch achieves its effect through non-medicinal means. It achieves this goal as a physical barrier device as its mode of action.
   d. **Description of accessories, if any**
      i. n/a
4. **Risks and warnings**

Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

Potential device-related adverse events	Severity	Occurrence	RPN
When an artery that was opened becomes narrowed again (Restenosis)	7	2	14
a life-threatening inflammation of the inner lining of the heart's chambers and valves (Infective endocarditis)	8	2	16
Buildup of excess calcium (Calcification)	8	2	16
Ruptured red blood cells (Haemolysis)	7	2	14
Blood clots in veins (Thromboembolism)	7	2	14
Inflammation	6	1	6
Decline (degeneration) of the implants	7	2	14
Formation of clinically significant fibrous tissue	8	2	16
Infection	8	2	16
Blood clotting in vein (Thrombosis)	7	2	14
Graft becomes dilated (Dilatation)	7	1	7
Heart Attack (Myocardial infarction)	9	2	18
Bleeding	8	2	16
Stroke	9	1	16
Death	10	1	10

Potential procedure-related adverse events	Severity	Occurrence	RPN
Narrowing of tubular structures (Stenosis)	7	4	28
Flow obstruction	7	4	28
When your heart can't pump well because the pouch around it thickens (Pericardial adhesions)	8	2	16
Injured blood vessel wall that leads to leaking (Pseudoaneurysm formation)	8	1	8
Patch rupture	10	1	10

- **How potential risks have been controlled or managed**
  - Analysis has concluded that the benefits outweigh any residual risks and that the risk has been reduced as far as possible
- **Remaining risks and undesirable effects**
  - Please refer to the device IFU or your healthcare provider.
- **Warnings and precautions**

1. Your new device is a foreign body and therefore needs close monitoring and careful observation. It may take 6-8 weeks for full recovery.
2. After placement, the implant area may be swollen and tender for up to a week.
3. Watch for any new redness or tenderness.
4. Watch for any opening in the incision(s).
5. Watch for numbness, tingling or pain.

NOTE: If you experience any symptoms described in 3, 4 or 5 above please contact your provider.

6. Do not puncture or manipulate the patch.
7. If the patch was implanted in your leg, swelling in the extremity is expected because of increased blood flow. Elevate or move the extremity according to your provider's instructions.
8. It is preferable to have the surgical site covered for the first week to protect skin and incision(s). (Follow your provider's instructions.)
9. Keep bandages or wound covering on as per your provider's instructions.
10. If you have adhesive surgical tape or strips across your incision(s), wear loose clothing that does not rub against your incision(s). The adhesive surgical tape or strips will curl up and fall off on their own after a week.
11. You may shower or get the incision(s) wet, once your provider says you can. DO NOT soak, scrub, or have the shower beat directly on the incision(s).
12. DO NOT soak in the bathtub, a hot tub, or a swimming pool. Ask your provider when you can start doing these activities again.
13. Your provider will tell you how often to change your wound covering and when you may stop using one. Keep your incision(s) dry. If your incision(s) goes to your groin, keep a dry gauze pad over it to keep it dry.
14. Clean your incision(s) with soap and water every day once your provider says you can. Look carefully for any changes. Gently pat it dry.
15. DO NOT put any lotion, cream, or herbal remedy on your incision(s) without first discussing with your provider.
16. Consult your provider for instructions on taking any prescription or over-the-counter medications after surgery.

Summary of clinical evaluation and post-market clinical follow-up

a. **Clinical background of the device**

The Patches are class III and are all available on the US market and have been CE-marked and marketed in Europe since 2013 for CardioCel and 2019 for VascuCel. The Patches do not use new technology. Device types have been used for several years in the medical field of cardiovascular and vascular surgery. There were no clinically relevant changes to the device since US clearance and CE-marking

b. **The clinical evidence for the CE-marking**

The device was first approved for CE mark in 2013 for CardioCel and 2019 for VascuCel. Studies were conducted to ensure the grafts were safe and effective. See the IFU for further details.

c. Safety

There are ongoing clinical trials on this graft that will be used to confirm the safety and performance throughout the expected lifetime of the device through the proactive and continuous collection of data.

d. **Possible alternatives**

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

e. **Suggested training for users**

This device is intended to be used by surgeons. Considering how complex this surgery is, it is left to the surgeon to proper surgery and graft type as well as the therapy to adopt before, during