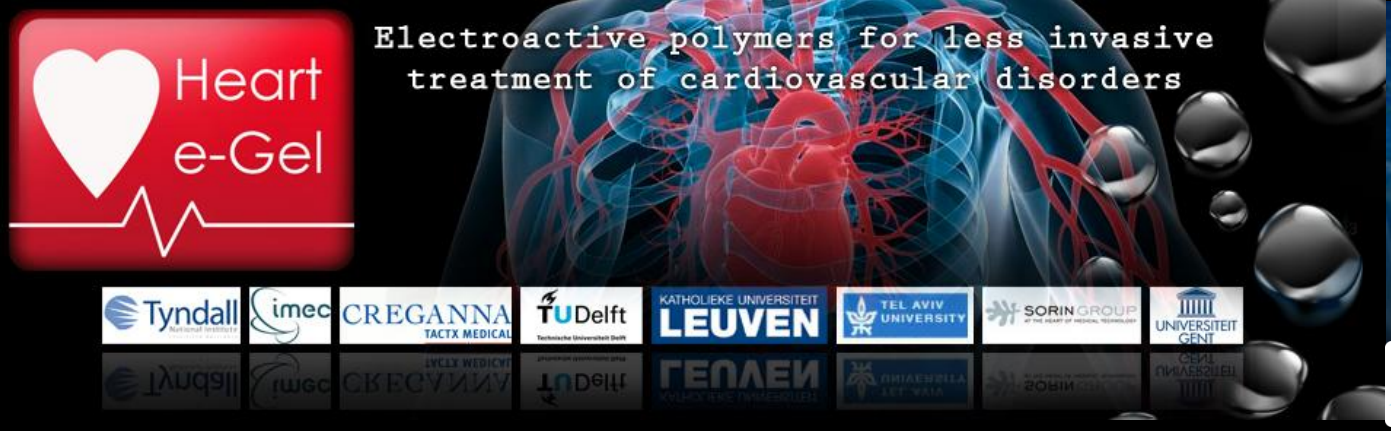


Heart-e-Gel project overview

"6th Concertation and Consultation Workshop of projects in Micro-Nano-Bio convergence Systems (MNBS)“
“Demokritos”, Athens, Greece
3-4 May 2012

Presented by Renzo DalMolin – Sorin Group

Heart-e-Gel is a project supported by the European Commission under the Framework 7 Microsystems objective ICT-2009.3.9

Project Objectives

The main **"objective"** of the Heart-e-Gel project is to utilize the material properties of an **Electro Active Hydrogel** (EAH) and develop novel **catheter-based cardiovascular treatment procedures** for controlled occluding, filling, or sealing off vessels or cavities.

- **EAH material objective:**

  Fabricate a biocompatible material, which complies with application specific swelling regimes, and is able to withstand long-term implanting in the bloodstream.

- **Delivery device objective:**

  To be able to transport the EAH implant to the desired vascular target location, electroactivate the implant with save current/voltage, assess the position and required level of swelling or anchoring and detach from the delivery device.

- **Testing objective**:

  - *In vitro* testing of "the hydrogel and the delivery device" in an artificial circulatory system using various blood-like solutions

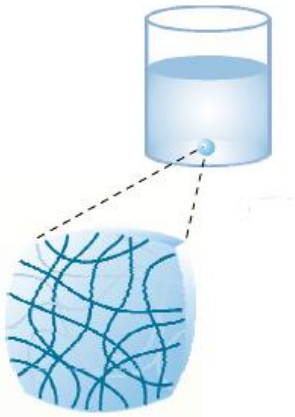
  - *in vivo* testing in small animals to validate the EAH occlusion and system integrity potential when subjected to real biological conditions.

Project Partners & roles

- **Tyndall National Institute, University College Cork, Ireland** – project coordinator & electrode integration
- **University of Ghent, Belgium –** EAH material development
- **Inter universitaire Micro-Electronica Centrum Vzw, IMEC, Leuven, Belgium** – electronics platform & system integration
- **Tel Aviv University, Israel** – electrode development & modelling
- **Catholic University Leuven, Belgium** – *in vitro* and *in vivo* testing
- **Technical University Delft, The Netherlands -** EAH material characterisation
- **Sorin CRM, Paris, France** - Exploitation & Dissemination

What is an electro-responsive hydrogel?

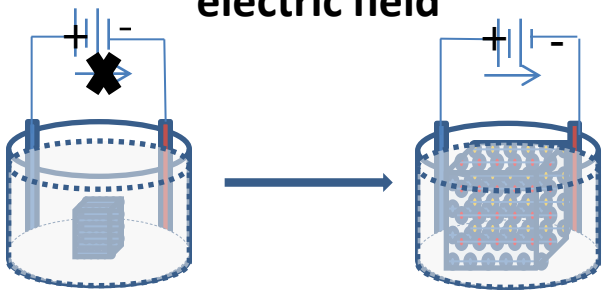
- A crosslinked water soluble 3D polymer which can undergo a volume phase transition (due to a change in environment) without dissolution
- The polymers that constitute these gels bear fixed ionic polar functional groups (with localised counter ions). The counter ions become transported to different parts of the gel when stimulated electrically.

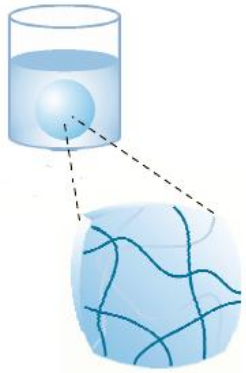


collapsed state

chain-chain interactions dominate

pH, salt concentration, Temperature, light, electric field





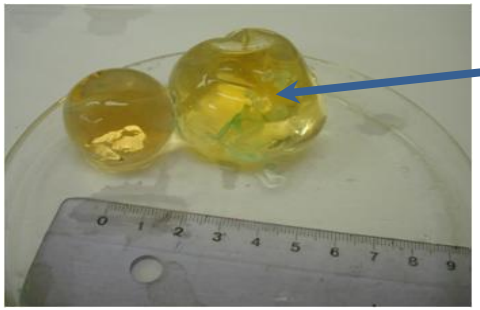
swollen state

chain-solvent interactions dominate

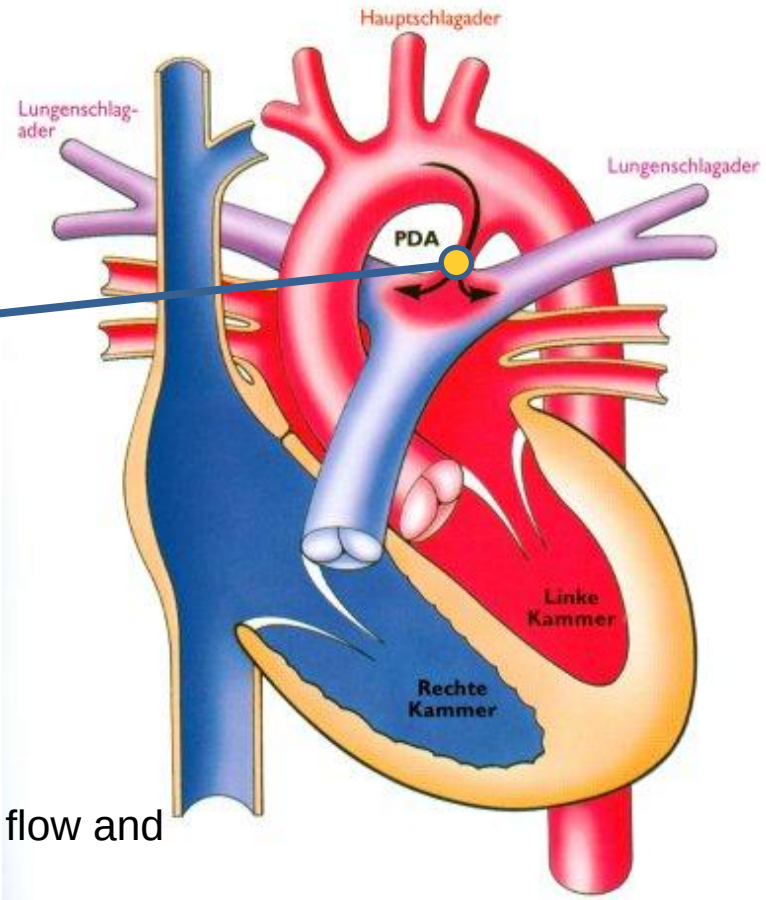
Ionic EAH gels require low voltage (≤ 1V), but they consume large current (10^2 mA)

How could the Electro-active Hydrogel be used?

Example: Patent Ductus Arteriosus
The flow between high and low pressure vessels needs to be blocked.



EAH before & after swelling
Source: Tyndall NI



Der persistierende Ductus arteriosus (PDA)
http://www.tierkardiologie.lmu.de/besitzer/pda.html

Challenges:

- Is the EAH implant mechanically able to withstand flow and pressure conditions?
- How do you anchor the implant in the bio-tissue?
- Can long-term pulsatile fatigue resistance be obtained?

Relevant market situation and scope

- **Transcatheter Embolisation and Occlusion (TEO) procedures :**
  - **70 % : Peripheral Vascular (PV)**
  - **30 % : Interventional Neuro Radiology (INR) - Brain**

Restricted Europe	83,000	
USA	142,000	
TEO Procedures world	**~ 260,000**	**~ $ 260 millions**

- **Emerging cardiac growth indication: huge markets worth > ~$ 1 billion**

- **Heart-e-Gel position:**
  - **Initially targeting TEO PV Procedures => applications where coils or PV plugs are used ~ 50 % TEO market volume**
  - **Later on : targeting emerging cardiac applications**

TEO market segmentations

TEO Prodecures in Europe : France, Germany, Italy, UK (2012) 83 020

PV TEO procedures

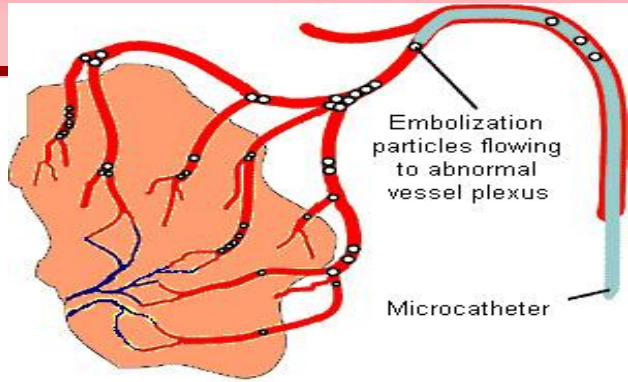
58 130

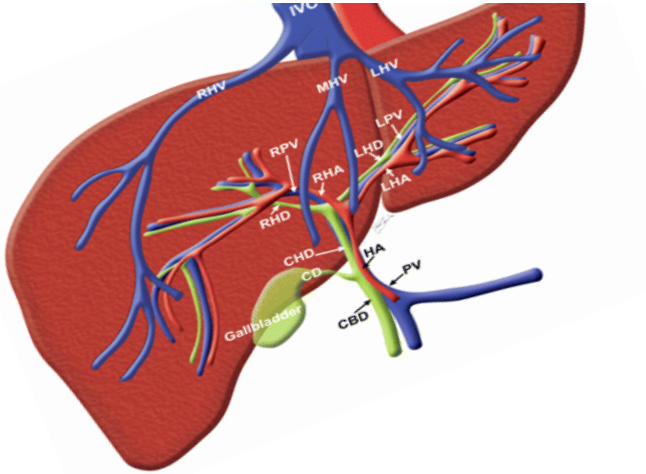
		annual growth
Tumor	18 680	13,40%
Varicocele	12 150	5,50%
Uterine Fibroid Embolization(UFE)	10 490	5,50%
Hemorrhage	6 870	1,30%
Aneurysme & Endoleak	5 980	5%
Vascular Anomaly	3960	3,40%

INR TEO procedures

24 890

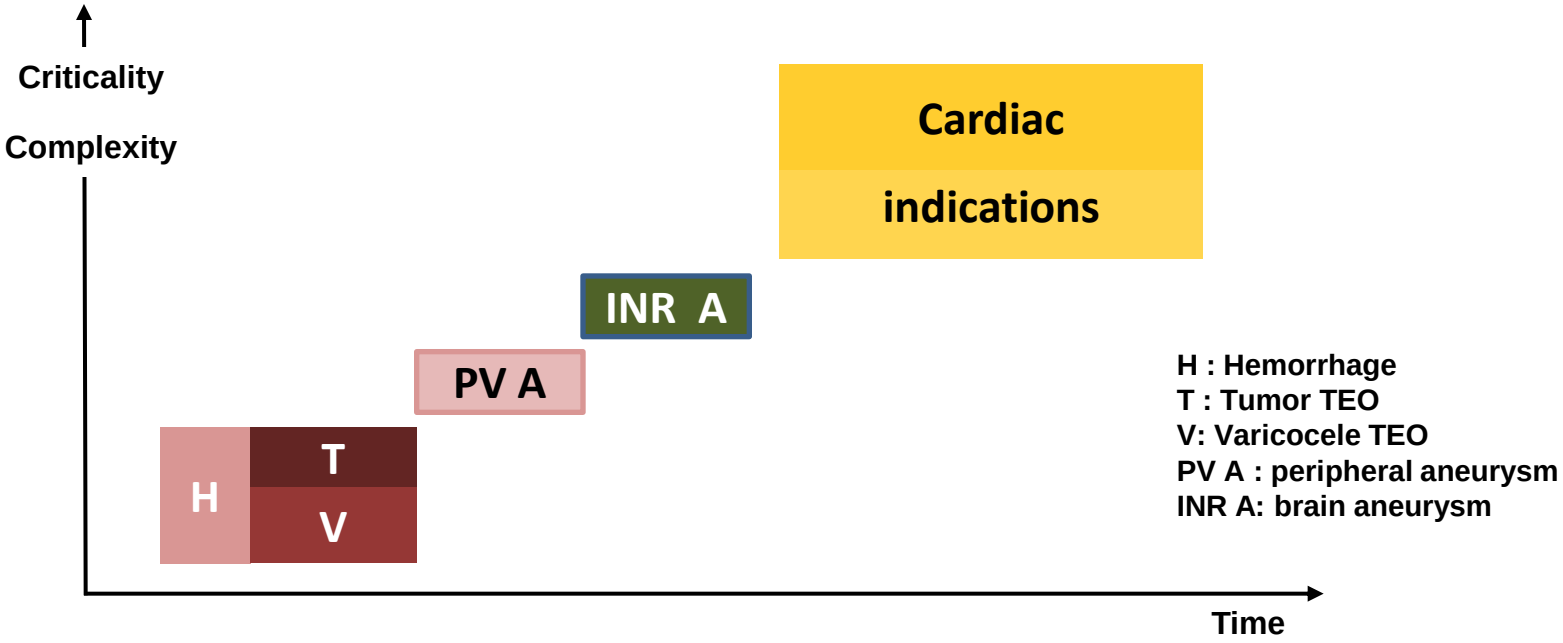
Aneurysm	17 110	6,10%
ArterioVenous Malformation (AVM)	5 280	3,80%
Parent Vessel Sacrifice	1 410	3,60%
Tumor	790	3,40%
Arteriovenous Fistula (AVF)	300	2,50%





Market and road map

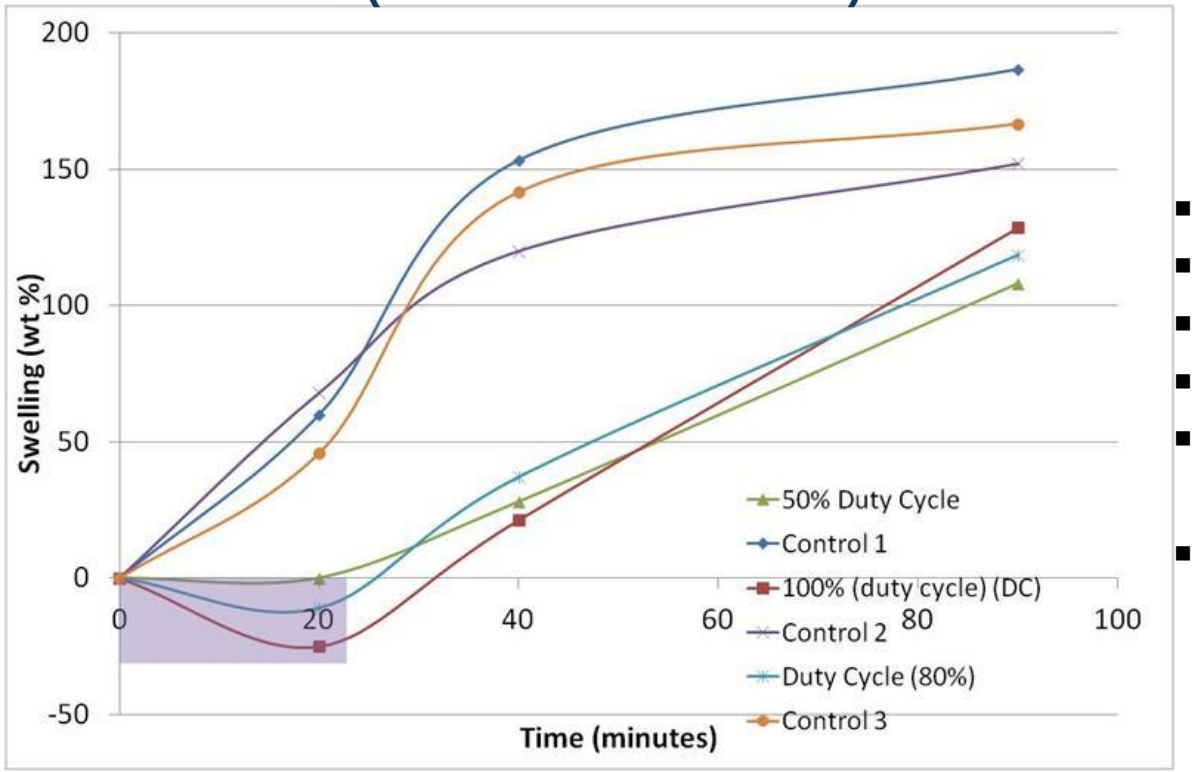
- **Function :**
  - **Arterial or venous occlusion**
  - **Aneurysm Embolization, mainly in brain**
  - **Cardiac indications**
- **Size/location/access**
- **Criticality of the procedures**



H-e-G Technical Achievements 2011/2012 (1)

Novel EAH showed promising swelling results

Pulsed DC bias (10V/100Hz for 20 min.) used for electroactivation in blood substitute.



- Samples Ø7mm/ 4mm high
- 50% DC=0% swelling
- 80% DC= 11% shrinkage
- 100% DC= 25% shrinkage
- Controls all swelled around 50-75% during biasing time
- All Biased gels swelled after biasing stopped

Results:

1) Regulatory pulsed DC bias, shrinks gel, but after this out-swells the non-pulsed samples

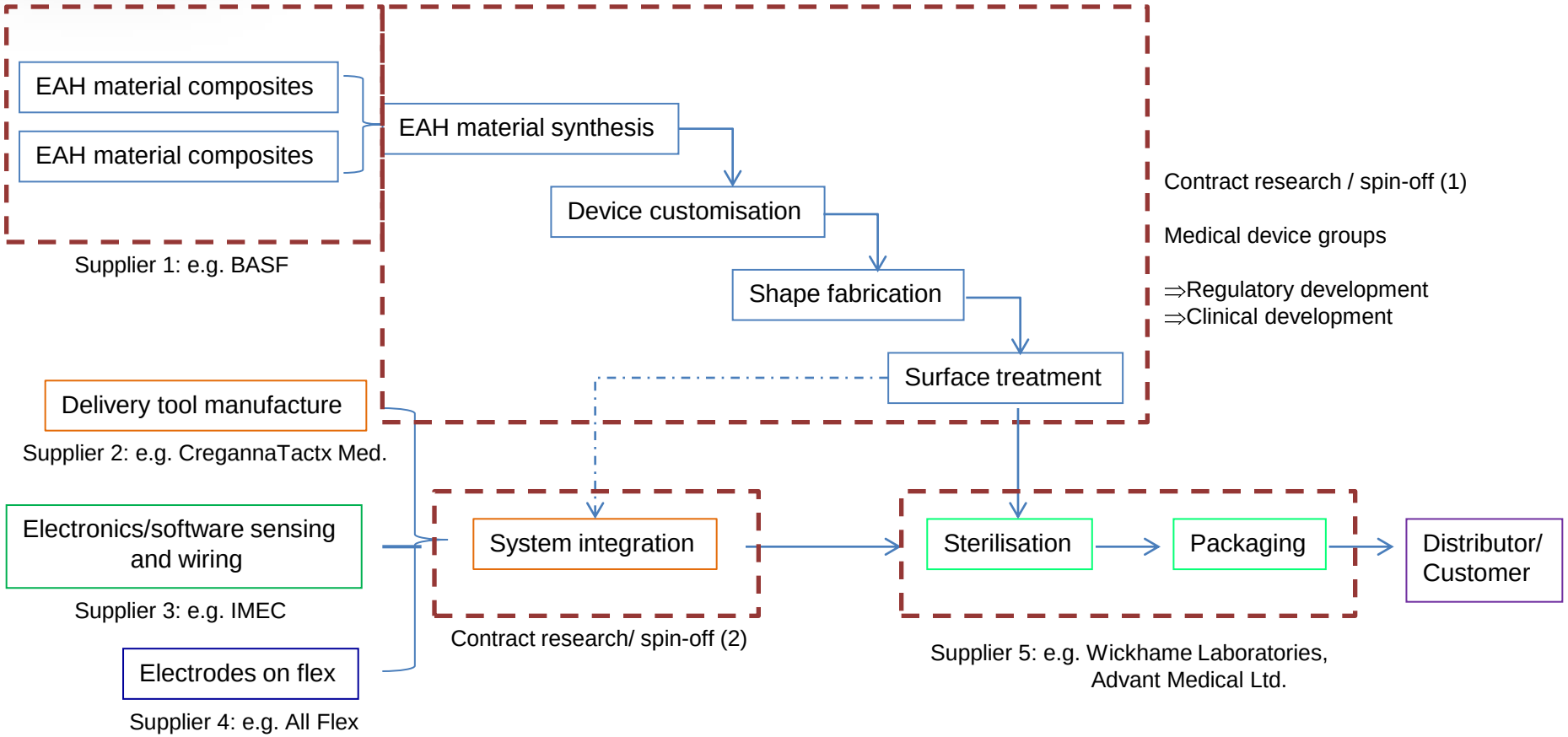
2) Initial tests showed that the novel H-e-G EAH is biocompatibility

H-e-G Technical Achievements 2011/2012 (2)

- **A first generation electronic control platform (hardware and software) was built with following features:**
  - **capable of DC electroactivation with output of 5V/ 100mA**
  - **handheld unit with interactive display**
  - **fully programmable, and USB/PC compatible**
  - **customised waveform and impedance measurement programs under development**

- **Electrode prototypes were fabricated and showed the following:**
  - **solid Platinum electrodes better than gold or metal coated ones**
  - **embedded electrodes don't function well as fluid makes no direct contact with them**
  - **not clear yet if swelling mechanism is electrical field or pH driven**

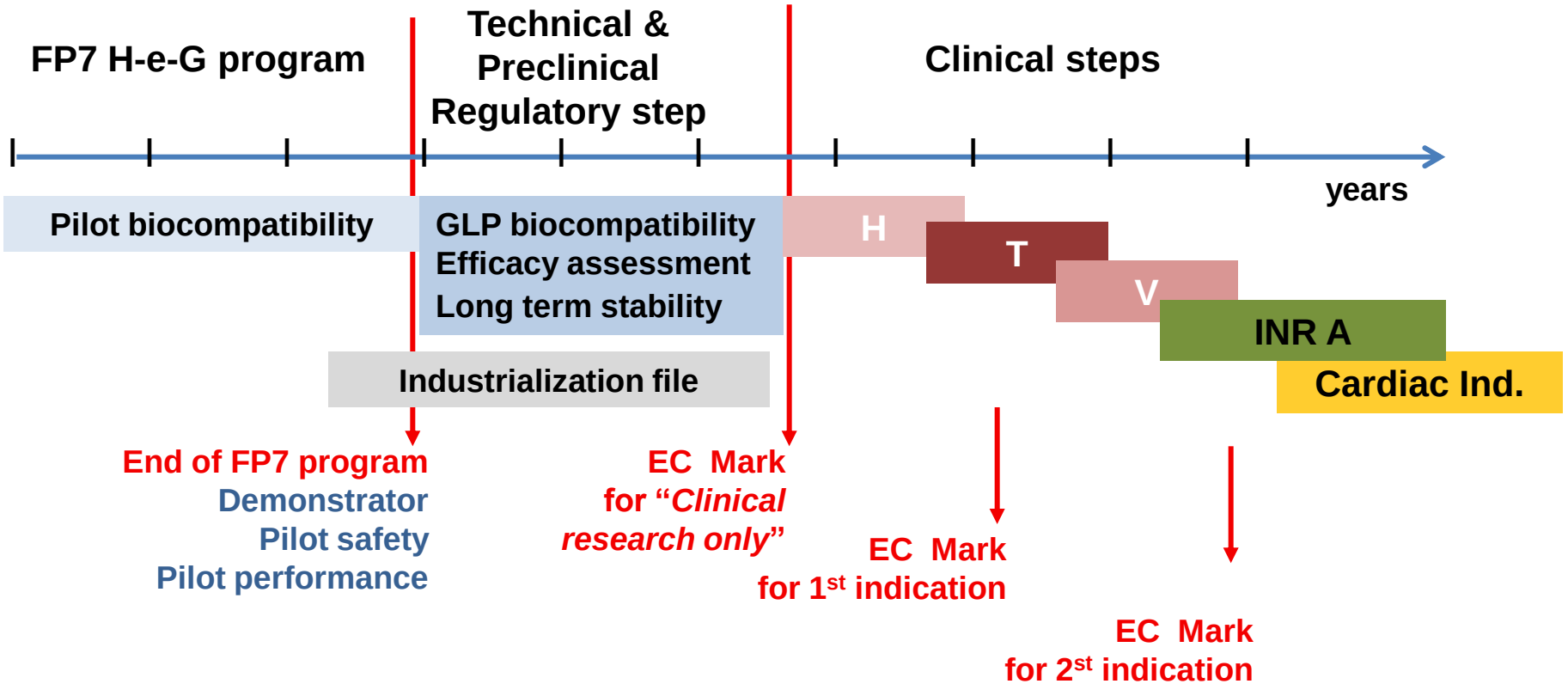
Supply Chain strategy & Example companies



Development Plan : From H-e-G to market entry

- **Device classification**: Class 3 in Europe ; PMA process in US

- **Overall plan development**:



Exploitation - Access to the Market

- **Organisations that could be potentially interested:**
  - **Medical devices companies: TEO market =/= cardiac indications**
    - **worldwide access to the market**
    - **Cardiovascular oriented ; increase of the cardiovascular product line**
  - **Start-up ?**
- **Minimum prerequisites**
  - **IP protection**
  - **Pre-clinical Proof of Concept :**
    - **Occlusion performance and long term stability (rational + pilot study results)**
  - **Biocompatibility: strong rational + pilot studies**
  - **Controlled production: reproducibility, control means, costing**
  - **Validated development plan; time to market**
  - **Business plan including milestones**

Intellectual Property

A provisional patent was filed on 15 March 2012 in the US based on an integrated system comprising of an EAH, a delivery device and an electroactivation platform.

Patent No. 61/611380

Heart e-Gel

Thank You!

Annex : Existing devices

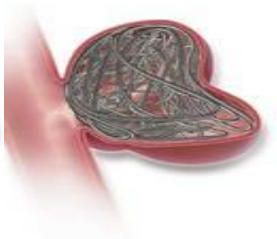
Transcatheter Embolization and Occlusion devices

PVA

Micropheres

Embolisation coils

pushable, detachable,
expandable hydrogel polymer coated or not



Plug devices (Amplatzer)

Embolic glue/liquid (Onyx)

Gelfoam, Drug eluting beads, Rabioembolization