

# Transverse, Intrafascicular Multichannel Electrode system for induction of sensation and treatment of phantom limb pain in amputees (TIME)

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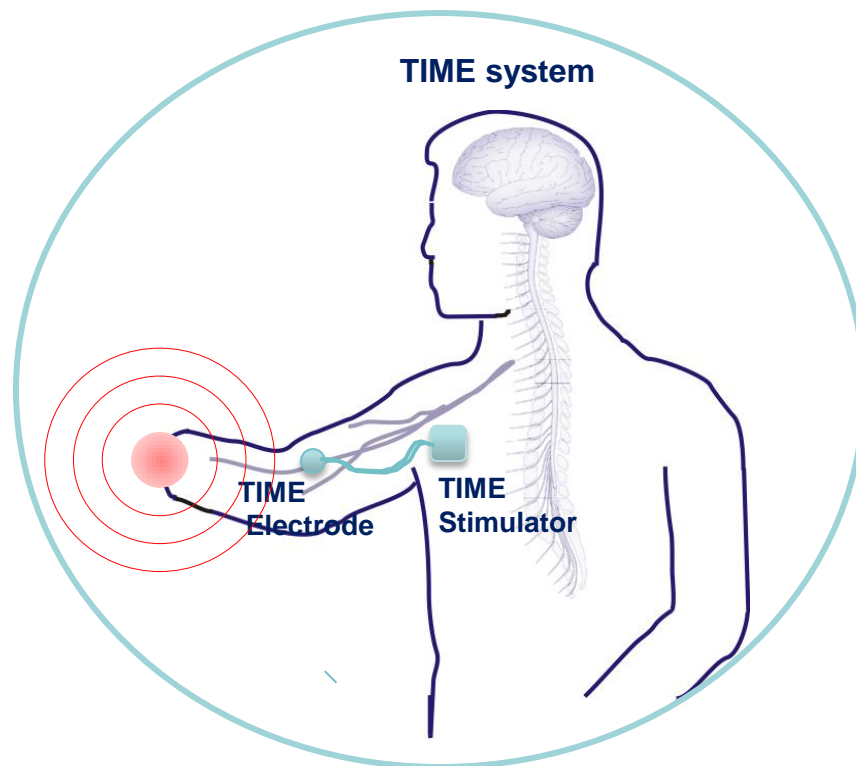
FP7 - ICT-2007.3.6 Micro/Nanosystems priority  
project number 224012



## Concept of project TIME

### *Phantom pain*

In 50-80% of amputees neuropathic pain develops in the lost limb, called **phantom limb pain**.



Our aim is to develop a Human Machine Interface (HMI) to manipulate phantom limb pain by applying electrical stimulation through implanted electrodes in the peripheral nerve

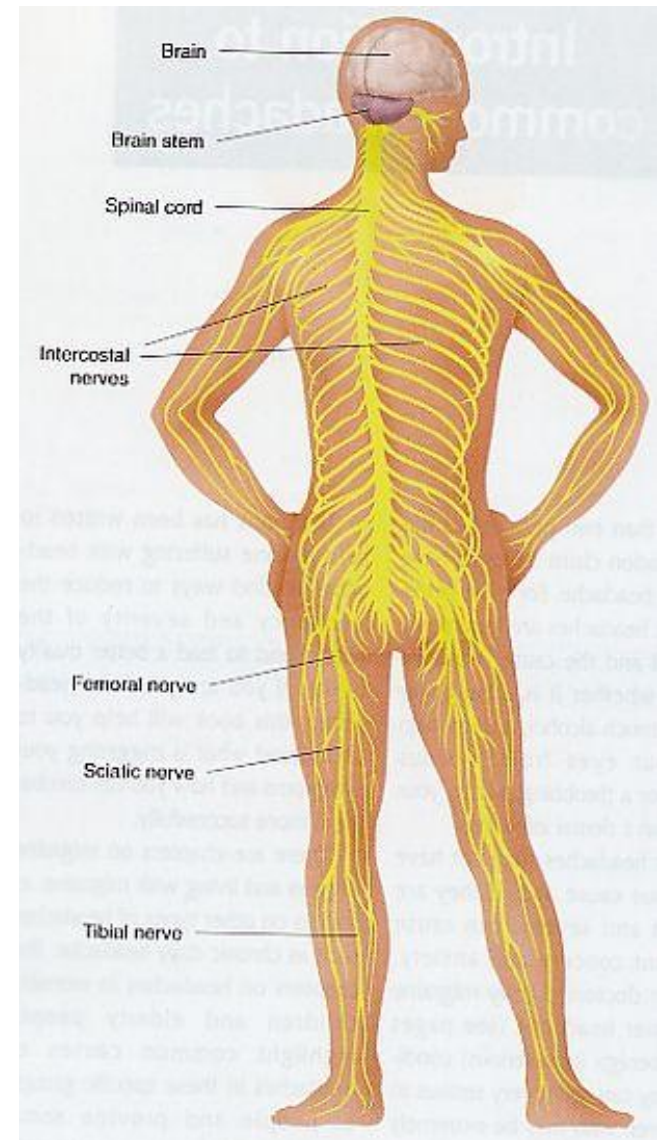
# Why does phantom limb pain occur? Neurological changes after amputation

## Central changes include

- Unmasking
- Sprouting
- General disinhibition
- Map remodelling
- Loss of neurons and neuronal function
- Denervation
- Alterations in neuronal and glial activity
- Sensory-motor and motor-sensory incongruence

## Peripheral changes include

- Structural changes in neurons and axons
- Ectopic impulses
- Ephaptic transmission
- Sympathetic-afferent coupling
- Alteration in channels and transduct molecules
- Selective loss of unmyelinated fibers



## Examples of phantom limb pain management

### **Neural blockades**

Epidural anaesthesia (*non-lasting effect*)

Regional anaesthesia (*non-lasting effect*)

### **Drug therapy**

- Ketamine, lidocaine, calcitonin (*non-lasting effect*)

### **Neurostimulation**

Transcutaneous electrical nerve stimulation (*variable results*)

Spinal cord stimulation (*variable results*)

Deep brain stimulation (*variable results*)

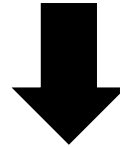
### **Other**

- Physical therapy – mirror box, use of prosthetic devices, virtual reality
- Acupuncture, Electroacupuncture
- Electroconvulsive therapy
- Psychological therapy – relaxation training, hypnosis
- Neurosurgical techniques
- Biofeedback

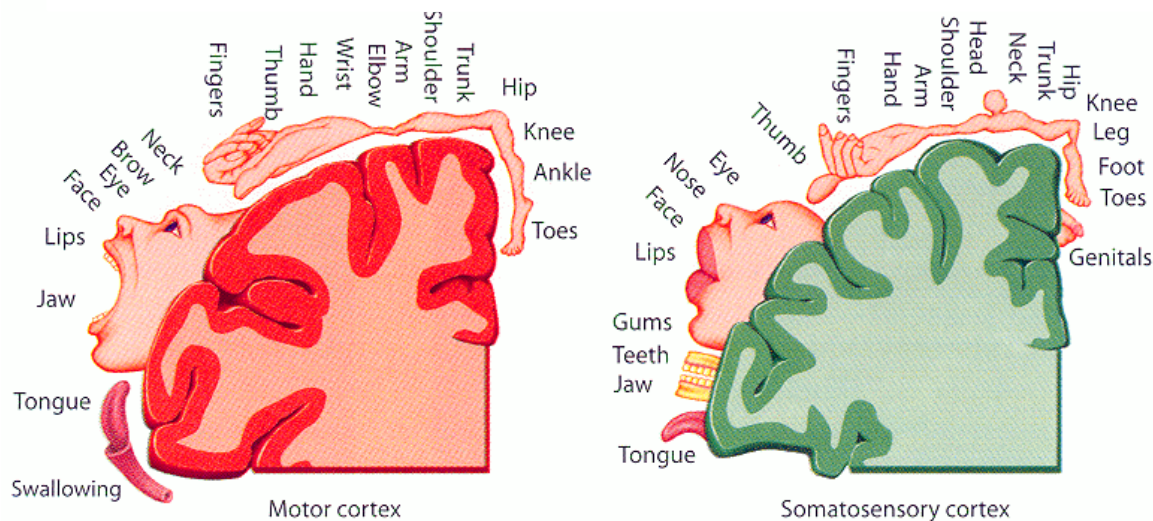
There are currently no effective, long-lasting treatments available for the treatment of phantom limb pain, which is a further cause of disability and loss of quality of life

## TIME hypothesis

There is evidence in the literature that the cortical organization (or mapping) changes following amputation



*Hypothesis: The transected nerve sends uncoordinated information to the brain – decoding of information in the brain is complicated by change in the motor/somatosensory mapping*

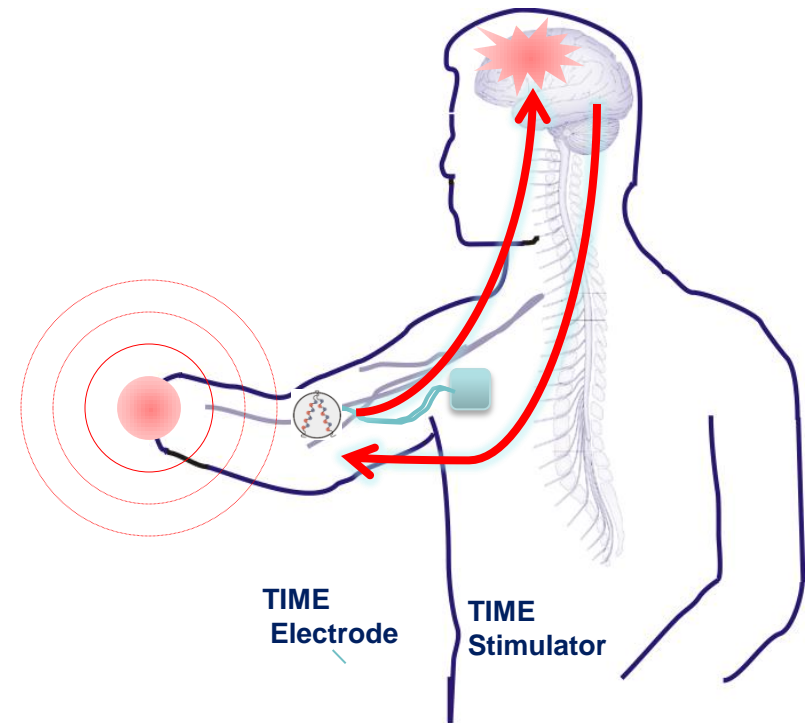
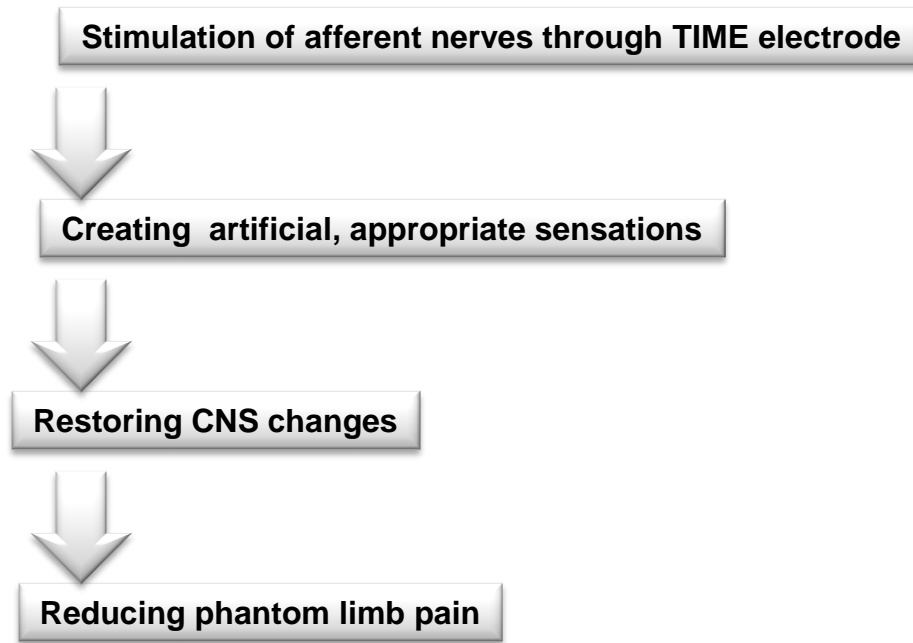


### Plasticity

Changes in the strength of synaptic connections in response to either an environmental stimulus or an alteration in synaptic activity in a network.

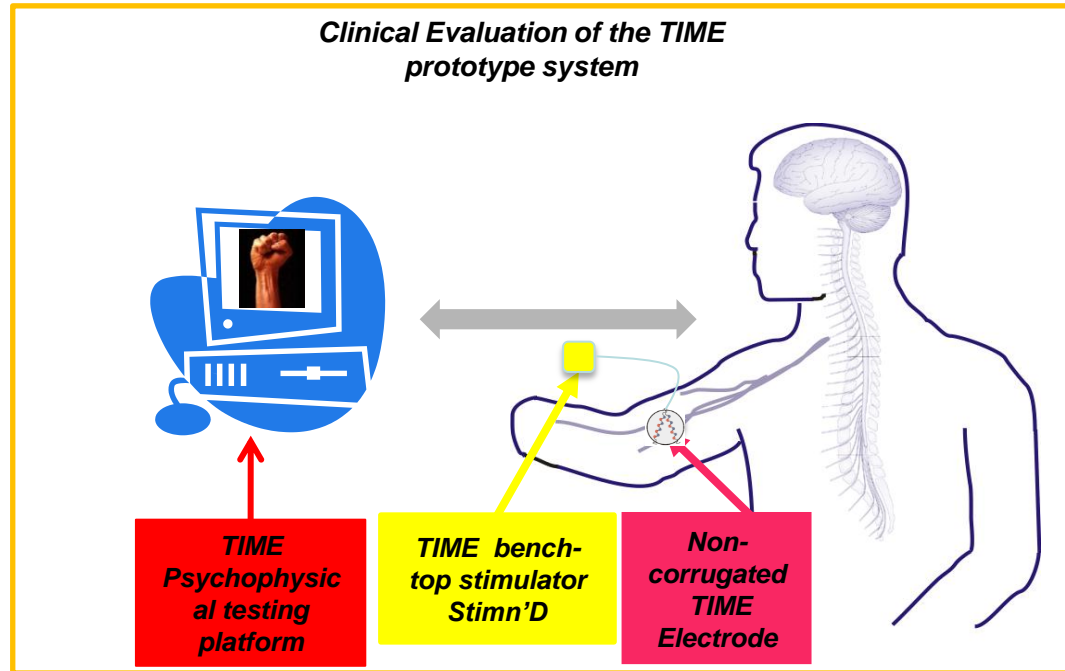
## TIME hypothesis

*By providing adequate patterns of stimulation to the transected afferent nerves central reorganization may be restored, and a normal processing of sensory signals recovered*

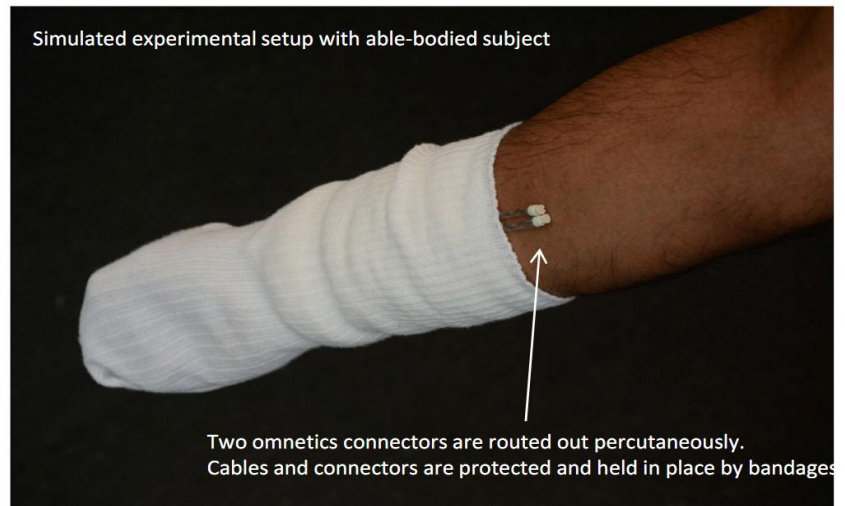
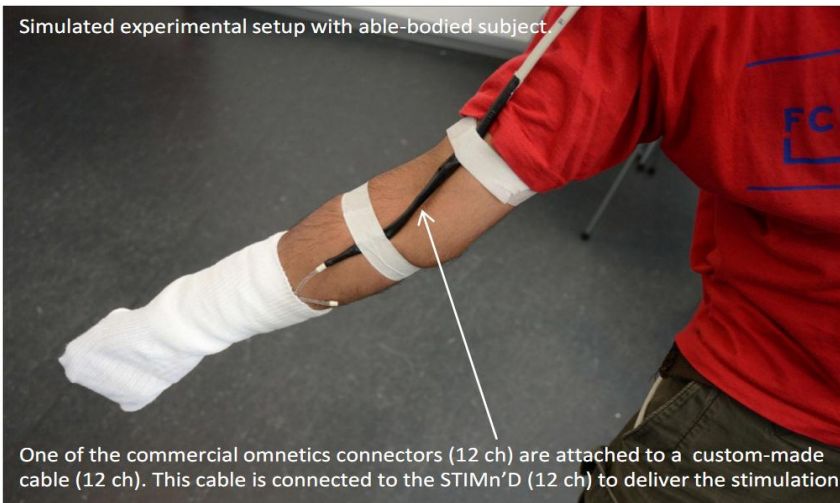
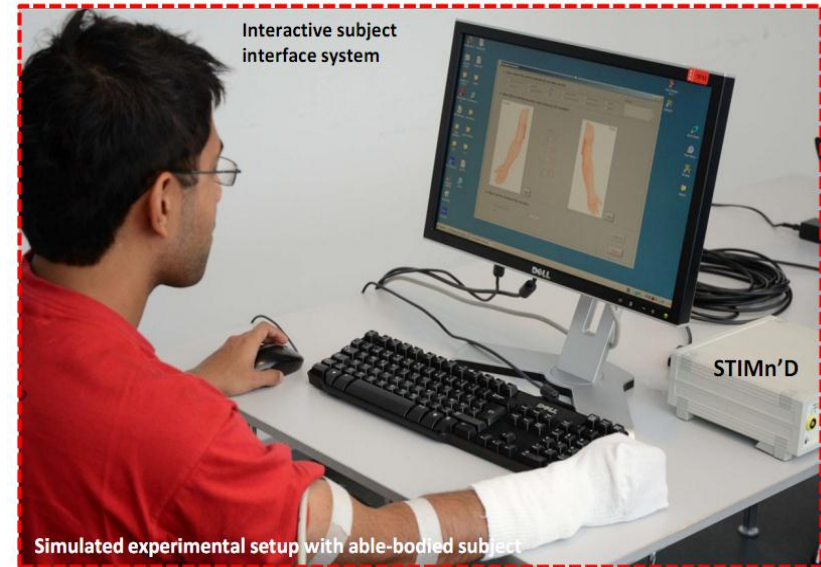


*Consortium strategic decisions on clinical trials*

## TIME prototype system chosen for evaluation in human volunteer



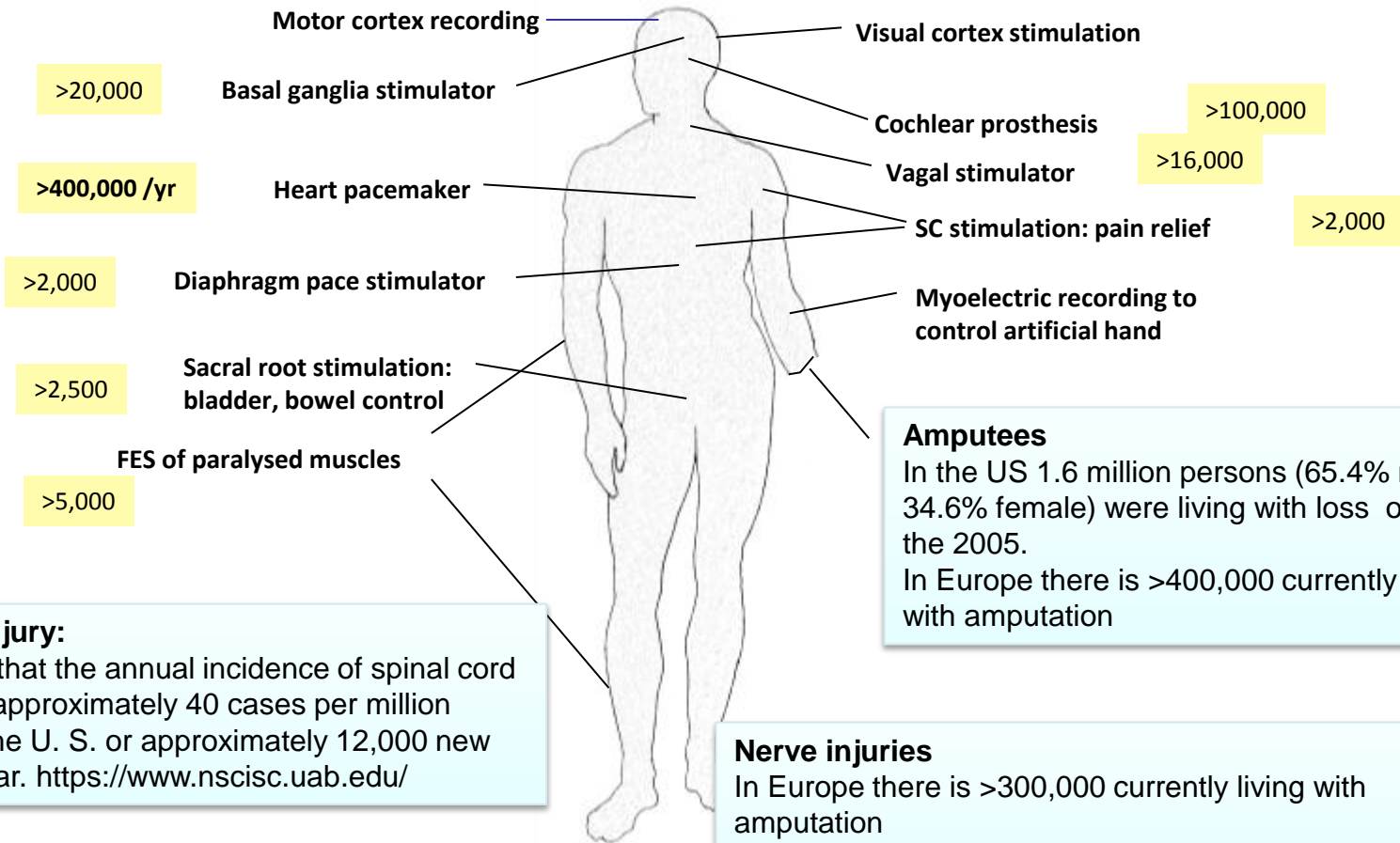






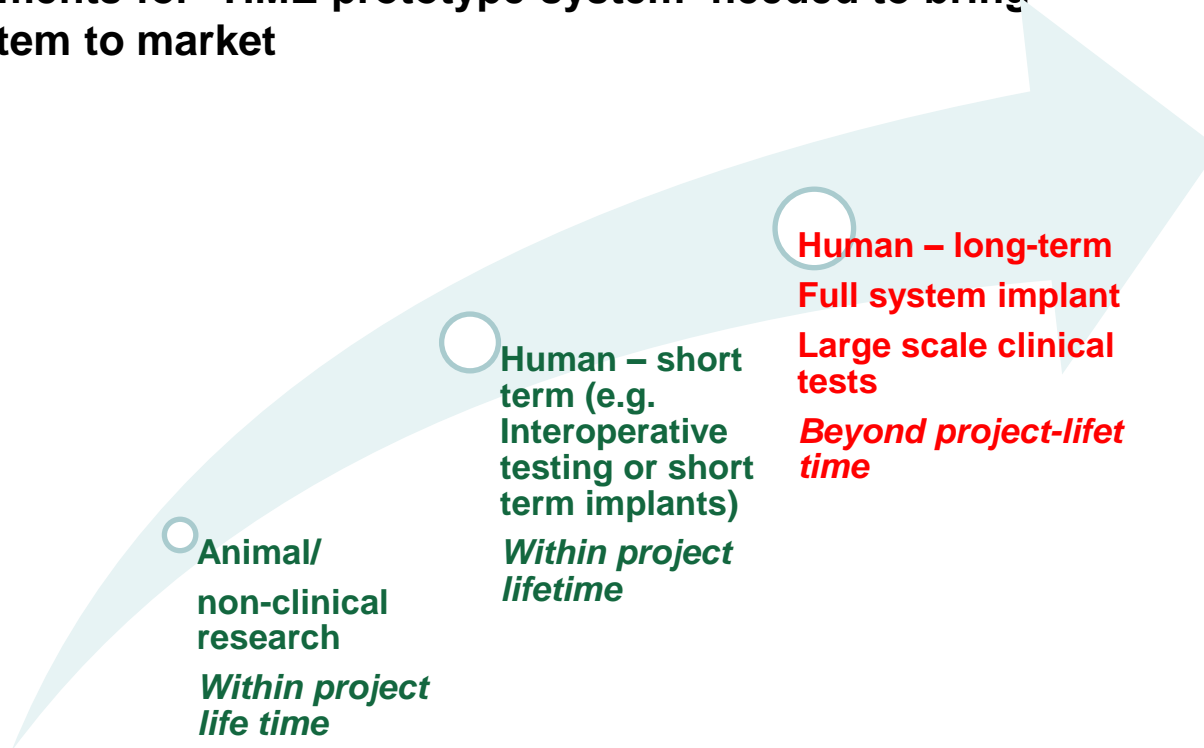
# Market potentials for the 'TIME prototype system'

## Patient population in Europe /US



Numbers in black: Number of patients with implanted neuroprosthetic devices

## Tech developments for 'TIME prototype system' needed to bring complete system to market

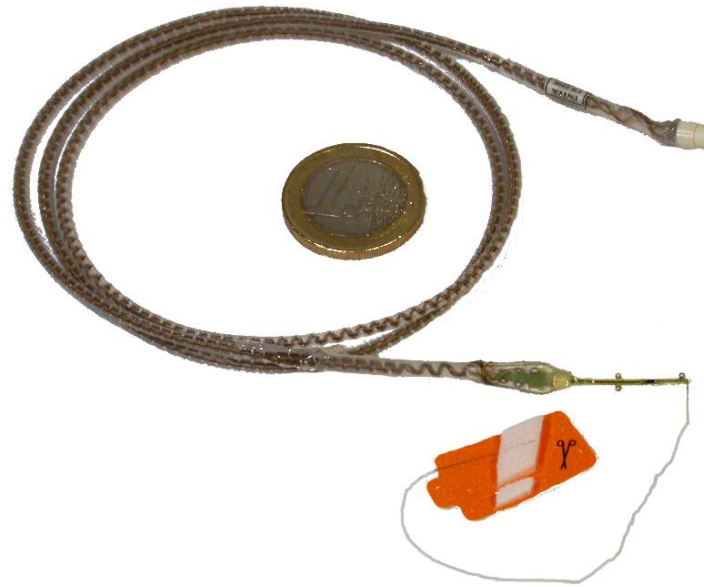


- **From R&D to the clinic:** further clinical testing, putting technology to the market
- **Design of patient-specific syste:** Fitting & manufacturing of optimal electrode, choice of effective stimulation paradigm
- **Robotic support for a safer and less invasive electrode implantation**
- **Signal transmission:** Wireless transmission of large amount of data ( or implantable, micro-scale computing power
- **Power:** Providing long-term power (yrs) or selfpowered systems
- **Biocompatibility and robustness:** life-long system

Consortium strategic decisions on clinical trials

## TIME prototype system chosen for evaluation in human volunteer: Non-corrugated TIME-3H Electrode

Features	TIME-3H
	Human
# electrodes	18
indifferent	No
ground dimensions	1 x 0.25mm <sup>2</sup>
pitch	400 µm
width	350 µm
width in mid line	120 µm
Ø active sites	80 µm
electrode coating	IrOx
charge injection capacity	3.8 mC/cm <sup>2</sup> (190nC)
track width & pitch	15 µm
cable	Helical, flexible
Stabilization	Anchor holes 90 deg bend
connector	Omnetics
Implant method	Commercial ethicon needle



Motivation for the choice of non-corrugated TIME-3H electrodes:

- Major tests performed - integration of knowledge from in-vivo, in-vitro and modelling work
- Design change in yr 2 (use of IrOx as active material) required repetition of the biocompatibility testing
- Omnetics connector has been used in chronic animal experiments and is robust, small and light weight (commercial connector)

Consortium strategic decisions on clinical trials

## TIME prototype system chosen for evaluation in human volunteer: Bench-top STIM'nD stimulator



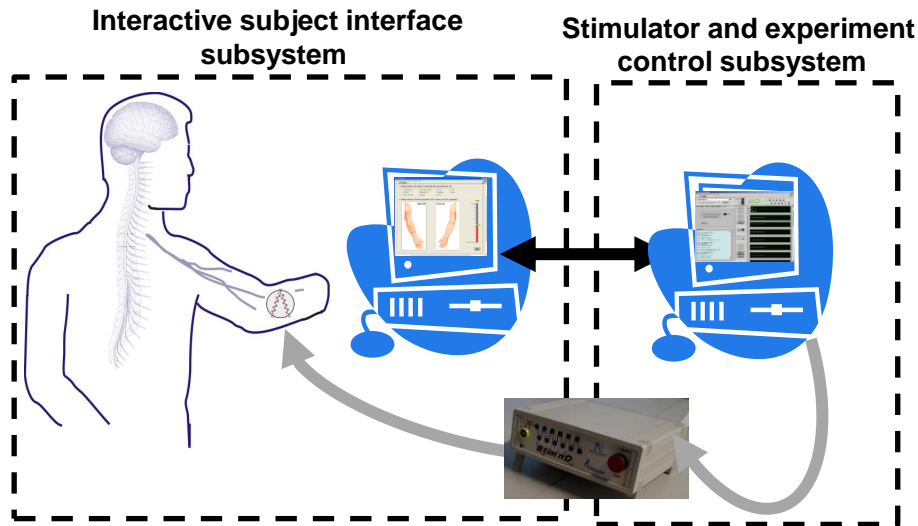
Features	STIMn'D
# independent configurable channels	12
Max current amplitude	5 mA (step size: 5 uA)
Pulse duration	1-511 $\mu$ s (step size: 1us)
Pulse waveform	Arbitrary
Control mode	SENIS manager Or SEC manager (Psychophysical testing platform)
Configuration	Each channel can be configured as anode or cathode or shunt to VHt

### Motivation for the choice of STIM'nD:

- offers the same stimulation functionalities as the minaturized version
- offers the same safety level as the minaturized version
- has been tested in animal experiements and together with the psychophysical testing platform

Consortium strategic decisions on clinical trials

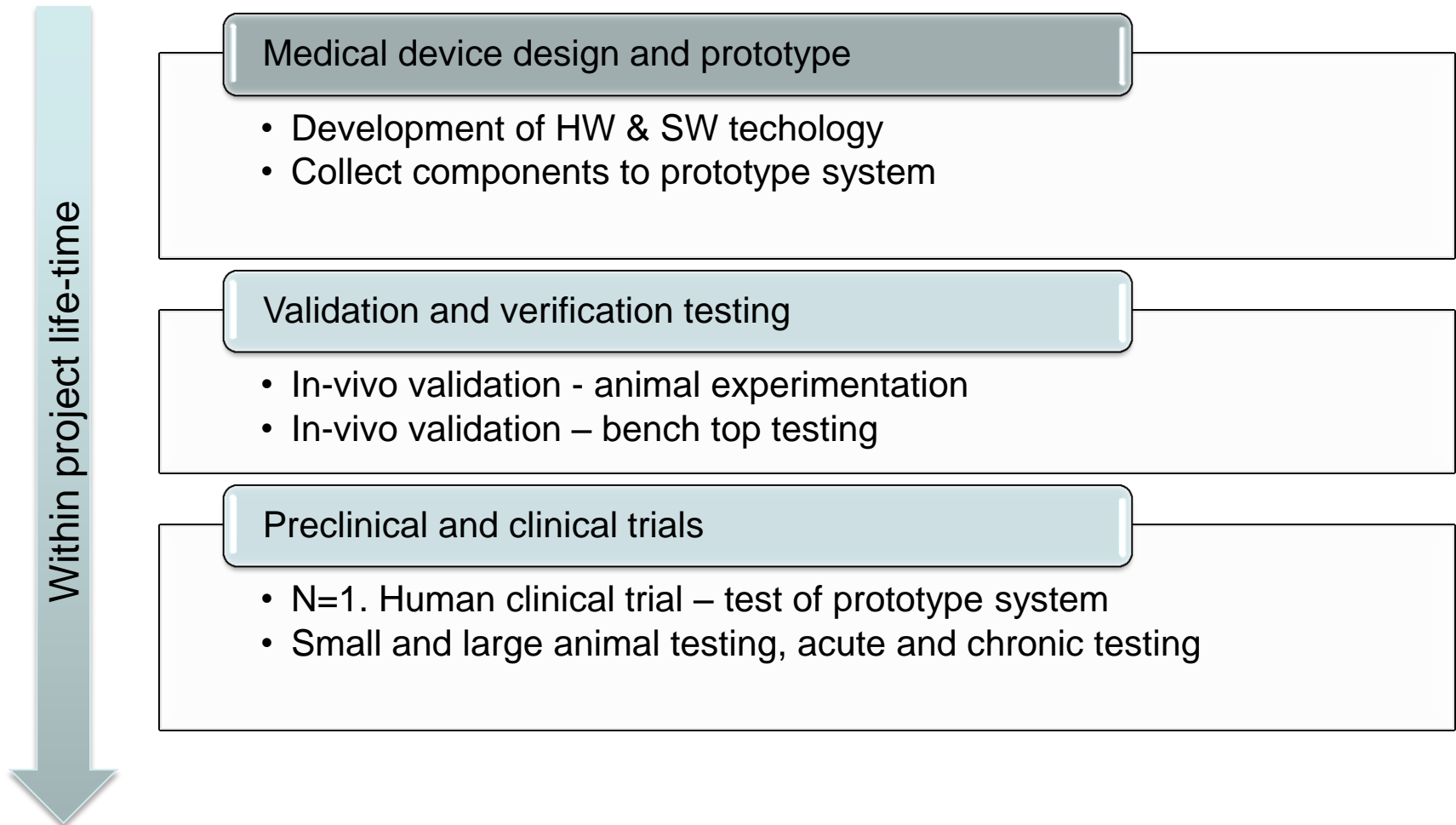
## TIME prototype system chosen for evaluation in human volunteer: Psychophysical testing platform



Features	Psychophysical testing platform
<b>ISI subsystem</b>	Measure perception threshold Measure sensation location, type and strength
<b>SEC subsystem</b>	Setup stimulation sequence Deliver stimulation Collect and save pt response
<b># independent configurable channels</b>	12
<b>Max current amplitude</b>	5 mA (step size: 5 uA)
<b>Pulse duration</b>	1-511 $\mu$ s (step size: 1us)
<b>Pulse waveform</b>	Square-wave, mono or bi-hasic
<b>Configuration</b>	Each channel can be configured as anode or cathode

The TIME psychophysical testing platform will be used to control delivery of electrical stimulation and collection of the pt response.

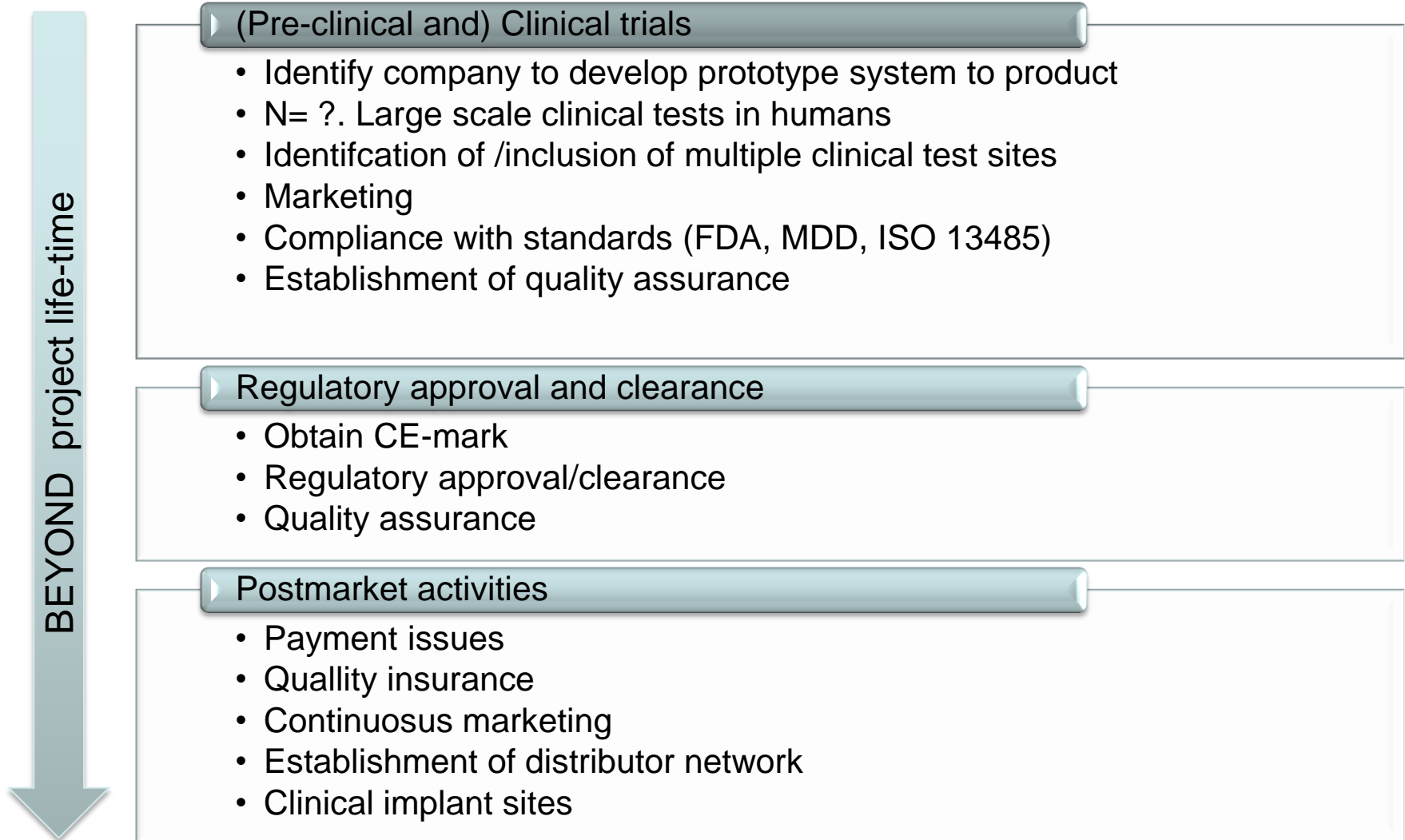
## The medical device life cycle / the supply chain





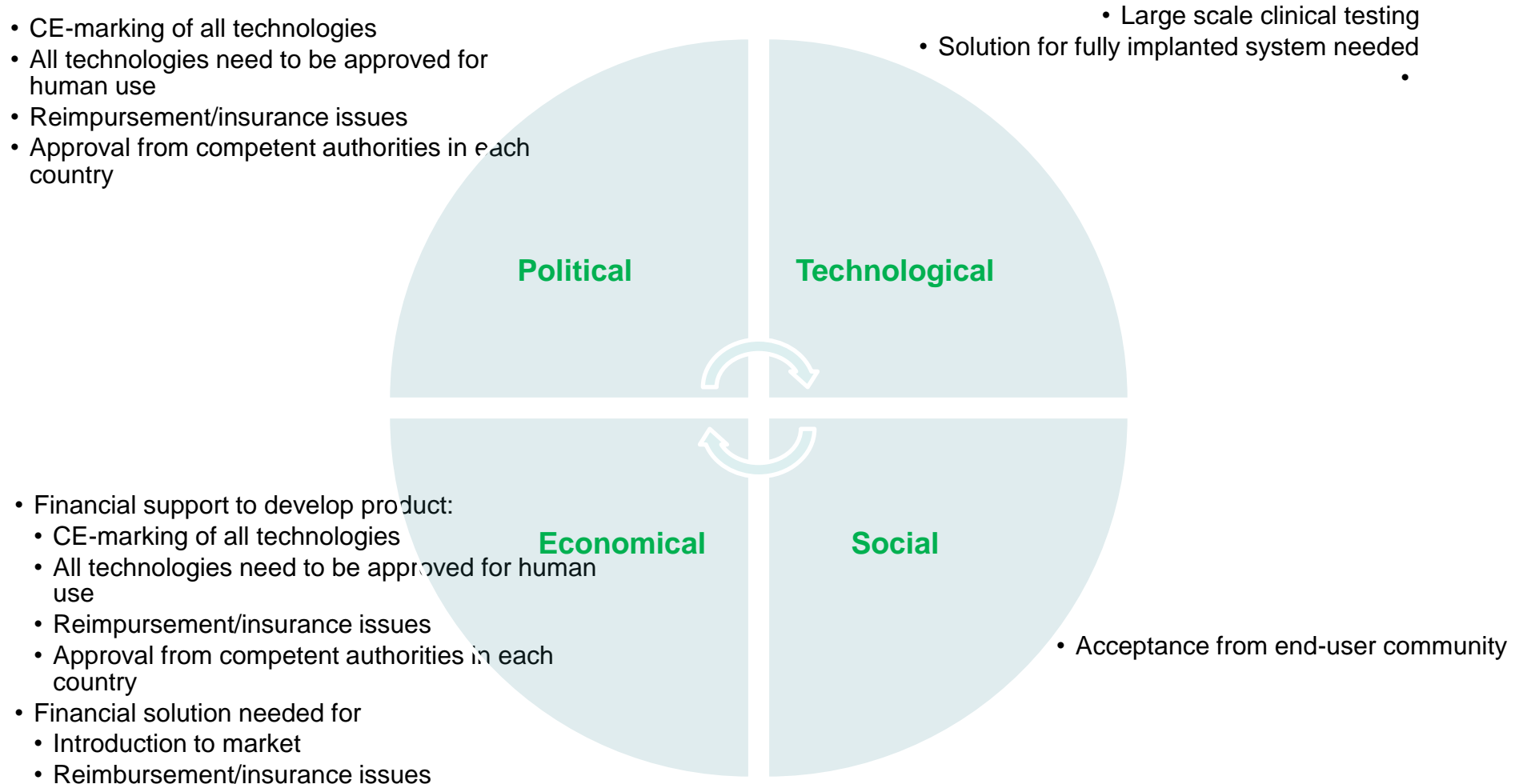
Exploitation strategy/analysis – bringing the TIME prototype system to market

## The medical device life cycle / the supply chain



Exploitation strategy/analysis – brining the TIME prototype system to market

## PEST analysis: Where are the bottle-necks?





# TIME

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