promeditec

InSilicoTrials.com platform helps the scientific community define Good Simulation Practice

VPH 2016

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MISSION

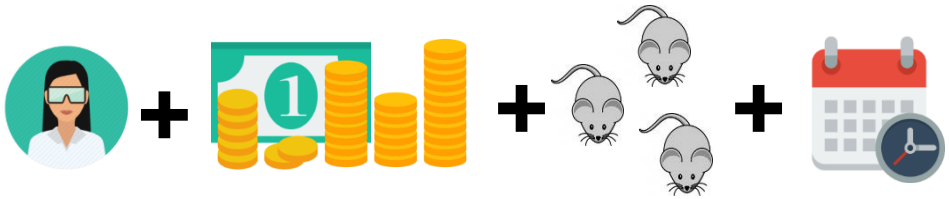
Promeditec was founded with the goal of proposing **innovative** *and* **efficient** *solutions in order to* **simplify** *the implementation and use of IT in the* **clinical research environment.**

THE CHALLENGE

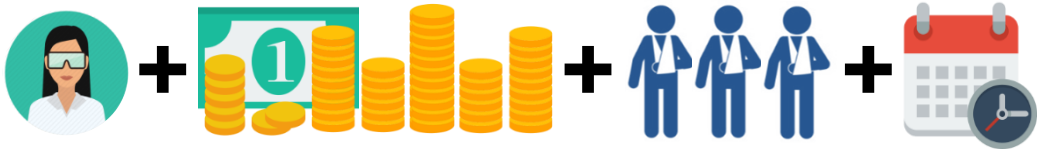
R&D and Traditional Clinical trials are expensive and give results after **long time**

R&D

Pre-clinical



Clinical



RESULTS

Although some medical device companies adopt modeling and simulation in the device design, **few or no patient-specific models** are used

In Silico Clinical Trials

"The use of individualised computer simulation in the development or regulatory evaluation of a medicinal product, medical device, or medical intervention."

In silico clinical trials: how computer simulation will transform the biomedical industry
Viceconti et al., 2016, Int J Clin Trials

REGULATORY TRENDS

From Senate Fiscal Year 2016 FDA Appropriations Report:
"**The FDA has advocated the use of such systems** (*simulations*) as an additional innovative research tool. Therefore, the **Committee urges FDA to engage with device and drug sponsors** to explore greater use, where appropriate, of **In Silico Trials** for advancing **new devices and drug therapy applications**."

https://www.congress.gov/114/crpt/srpt82/CRPT-114srpt82.pdf

FDA Medical Device Development Tools (MDDT)
Pilot program to assess and refine the **qualification process** for **tools used to develop and evaluate medical devices**

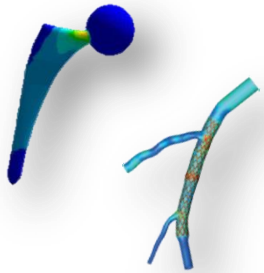
Medical Device Development Tools Draft Guidance
for Industry, Tool Developers, and Food and Drug Administration Staff, 2013, FDA

SIMULATIONS TODAY

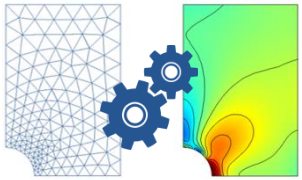
Computational Capacity

Limited computational capacity

Medical Devices

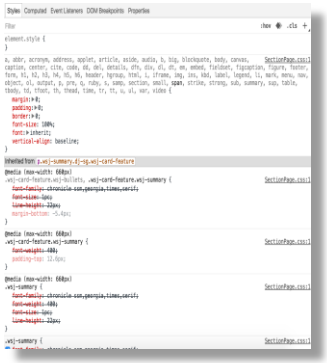


FEA Simulation



Engineering skills

Parameter sets



NO DRM
NO Validation
NO Sharing

Virtual Patients

Few cases

SIMULATION ADVANTAGES

	Cost	Time	Ability to vary parameters	Evaluation evolving harm	Simplifying assumptions	Relevance to Clinical Use	Evaluating disease state	Ability to interpret data and predict clinical use	Experimental control
Animal	moderate	moderate	Limited	Restricted	moderate	Species variability	Difficult	Limited	Relatively high
Bench	low	Short	Limited	Yes	Many and always	Limited	Simplified states	Limited	High
Human	Very high	Long	Not easy	No, unethical	Minimal	Direct	Yes	Not easy	low
Computer	Relatively low	Short to moderate	High	Yes*	Many and always	Variable	Yes*	Yes*	High

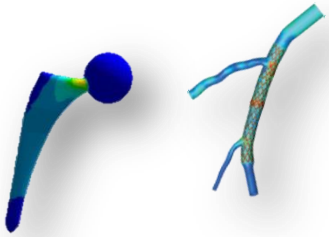
* Computational modeling and simulations in medical devices is the one method with the most potential for refinement and improvement because the other models have already matured.

Source: FDA

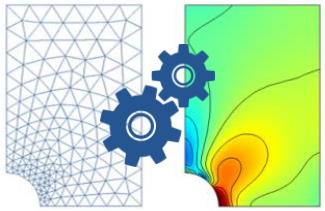
InSilicoTrials.com is a platform to **develop**, **evaluate** and **support the surgical planning** of medical devices

Many Virtual Patients

Medical Devices

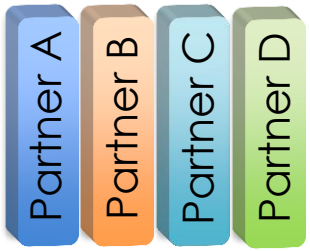


FEA Simulation



Digital Library

Partner's Modules



High Computational Capacity

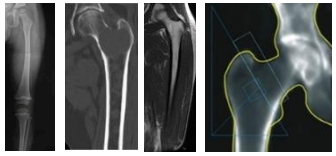
Public, Private Cloud and HPC

Background process for a simulation based on real clinical trial patient data

WEB-BASED GUI

CLINICAL TRIAL DATA

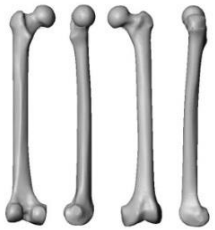
XR CT MRI DEXA



DE-IDENTIFICATION, VISUALIZATION AND SHARING

3D RECONSTRUCTION

AUTOMATIC SEGMENTATION

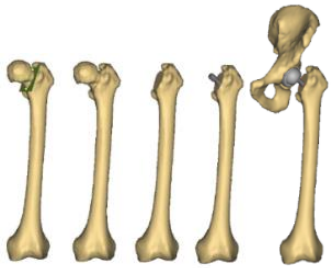


3D MODELS

PROSTHESES 3D MODELS DATABASE

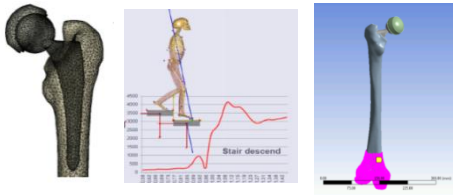
VIRTUAL SURGERY, MODEL ASSEMBLY

DEFINE SURGERY



MESH, LOADS AND CONSTRAINTS

DEFINE SIMULATION SETTINGS: PARAMETERS, BOUNDARY CONDITIONS, PATIENT PARAMETERS AND SURGERY

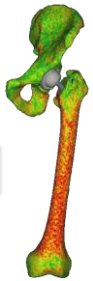


MESH REALISTIC LOADS CONSTRAINTS

SIMULATIONS

RUN SIMULATION USING ANSYS ENGINE AND SPECIFIC PARTNERS' MODULES

ANSYS

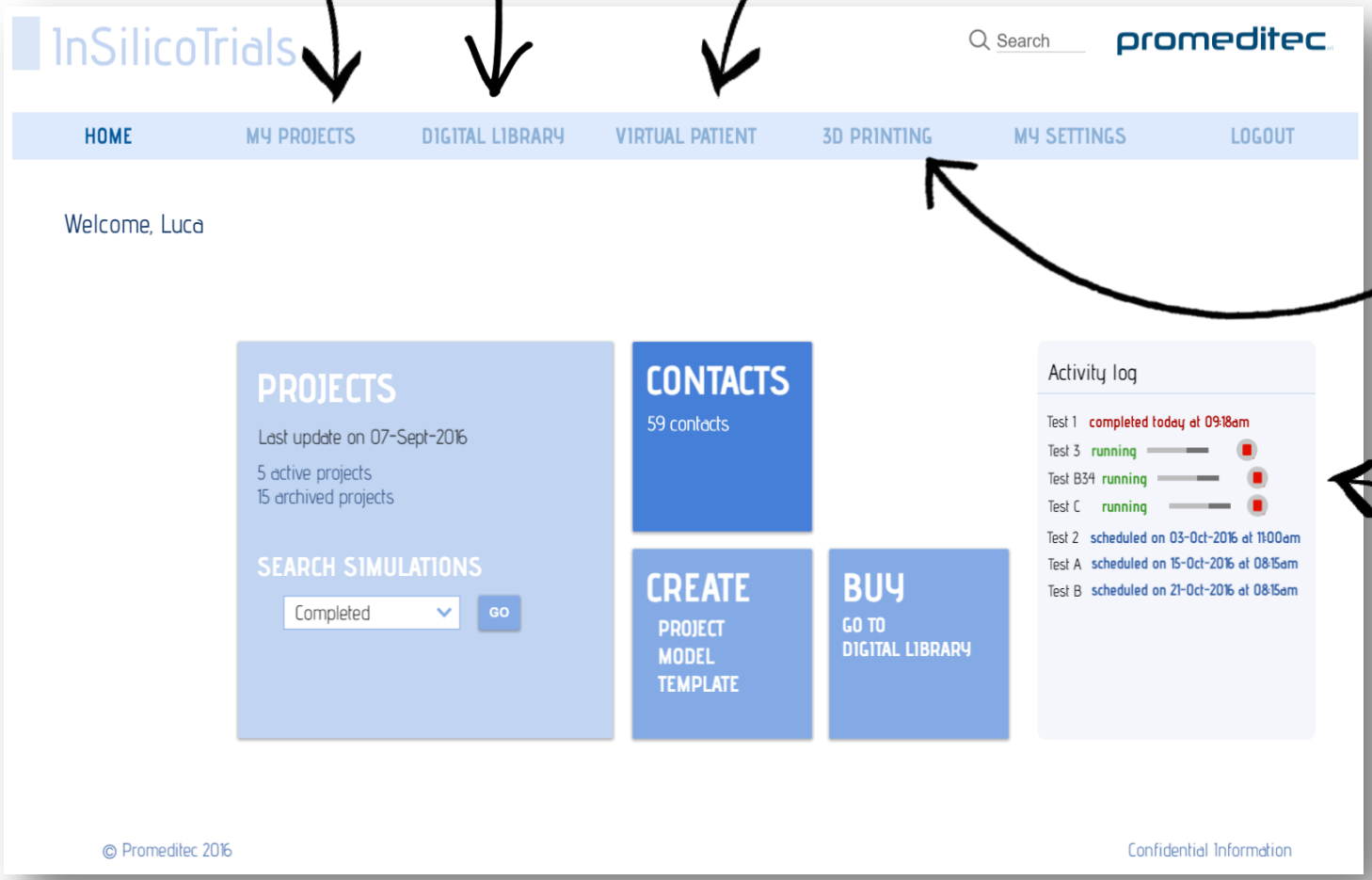


InSilicoTrials.com

Store, share and buy 3D models or **simulation** based on **publications**

Create and share projects with **colleagues**

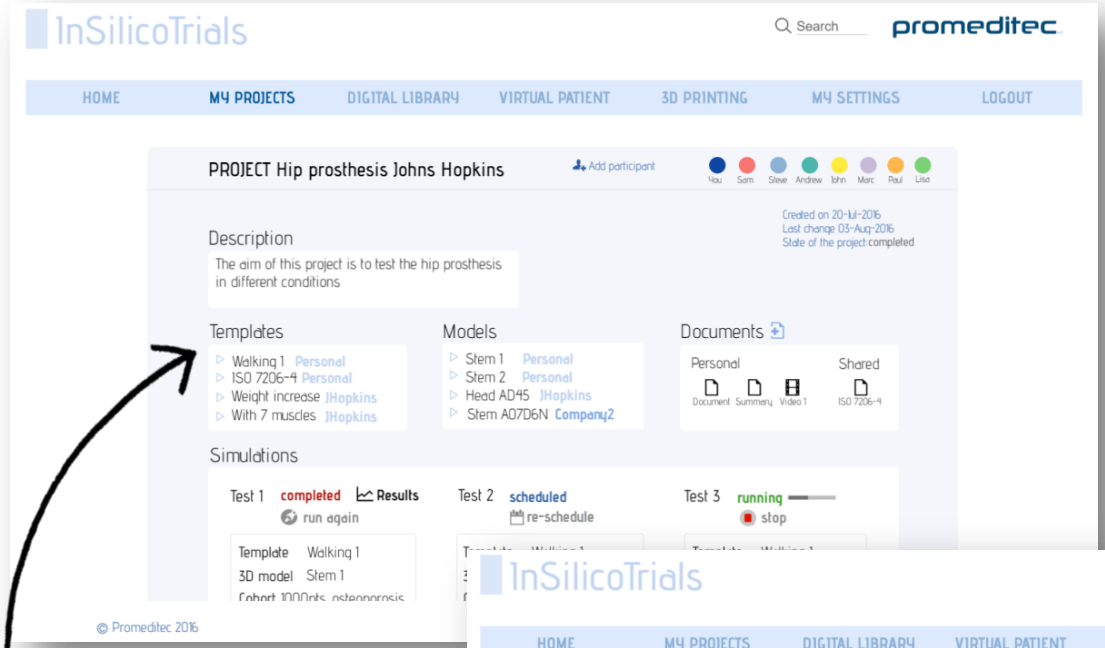
Choose a **cohort** selecting the virtual patients from the database, or make the **3D reconstruction** of your **own patients**



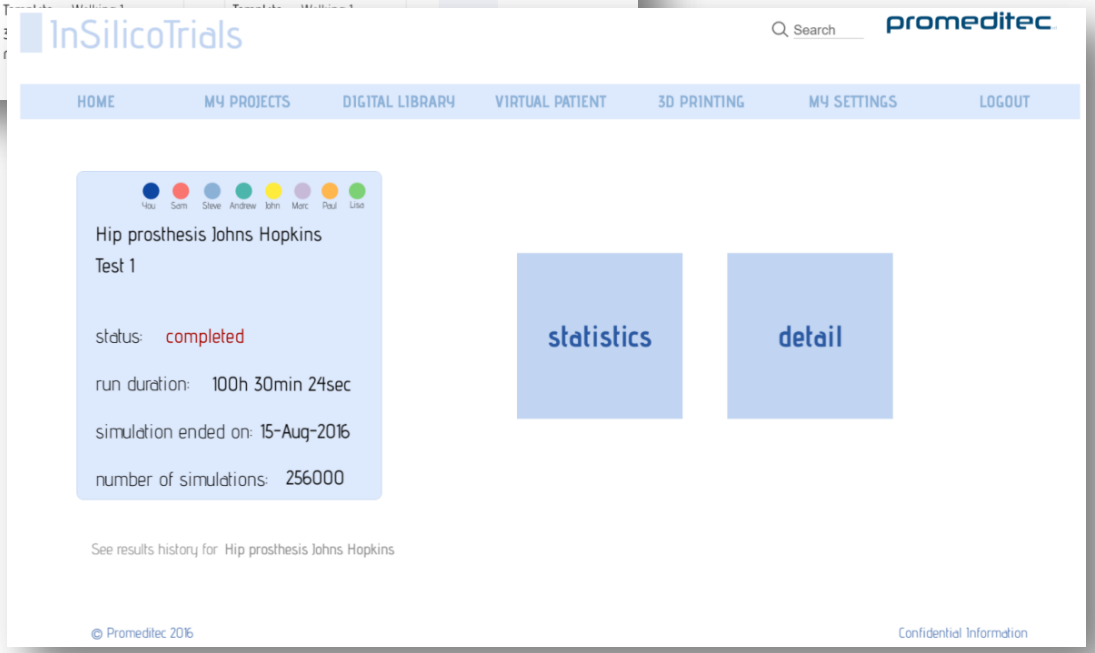
Modify and test new designs **before 3D printing –spell check feature**

Monitor your activities

InSilicoTrials.com



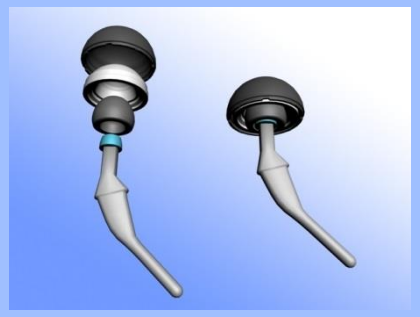
Project management with **templates** and **models** used and simulation activity state



Use **templates** created by **experts**

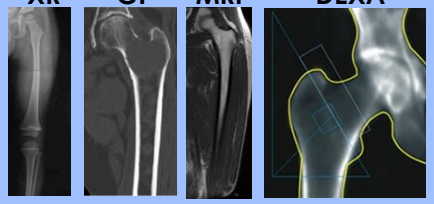
Results view with **statistical** and **detailed reports**

EXAMPLE OF USE CASES



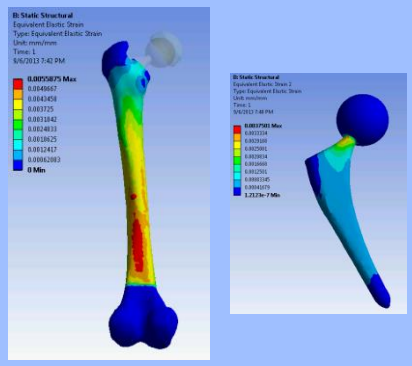
PROSTHESIS MODEL

XR CT MRI DEXA



CLINICAL IMAGES

InSilicoTrials.com



A) DEVICE DEVELOPMENT OR VALIDATION

WORST BEST

B) SECOND OPINION FOR DEVICE SELECTION

A) Test of device on a population, **B)** Test of different surgical options on a single patient

InSilicoTrials.com USER BENEFITS

- **Full process** (from DICOM to simulation results) or **single modules** (e.g. 3D reconstruction, virtual surgery, etc)
- Democratization of simulations: no high-level knowledge required
- Creation of a centralized data repository
- Private sessions between colleagues with easy sharing features
- Private cloud with no download feature to protect data and models IP

MEDICAL DEVICES COMPANIES

- Acceleration of R&D process
- Access to scientifically valuable knowledge

SIMULATION SERVICE PROVIDERS

- Deliver services leveraging the platform features
- Integration of proprietary modules on a comprehensive process from images to results

BENEFITS FOR TRADITIONAL CLINICAL TRIAL SPONSORS

- **Candidate prioritization**
- Prepare a **better protocol**
- Add info in **results evaluation by regulatory bodies**
- Support **HTA discussion**
- Compare simulation results with **RWE**

Clinical Trial
A research study in which **one or more human subjects** are prospectively **assigned to one or more interventions** (which may include placebo or other control) **to evaluate the effects** of those interventions on health-related biomedical or behavioral outcomes.

NIH Clinical Trial Definition

Good clinical practice (**GCP**) is an **international quality standard** that is provided by ICH*, an international body that defines standards, which **governments can transpose into regulations for clinical trials** involving human subjects.
A similar guideline for clinical trials of medical devices is the **international standard ISO 14155**, that is valid in the European Union as a harmonized standard.

*International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use

What about In Silico Trials?

As GCP is defining how to conduct a Clinical Trial **why don't we start** to think about **GSP - Good Simulation Practice** to conduct In Silico Trials?

GSP Good Simulation Practice

Available regulations:

- **FDA 21CFR part 812** 'Investigational Device Exemptions'
- **ISO 14155:2011** 'Clinical investigation of medical devices for human subjects - - Good clinical practice' (last version harmonized with GCP and adapted for device studies)
- **ASME V&V40** 'Verification and validation in computational modeling of medical devices' – not yet published

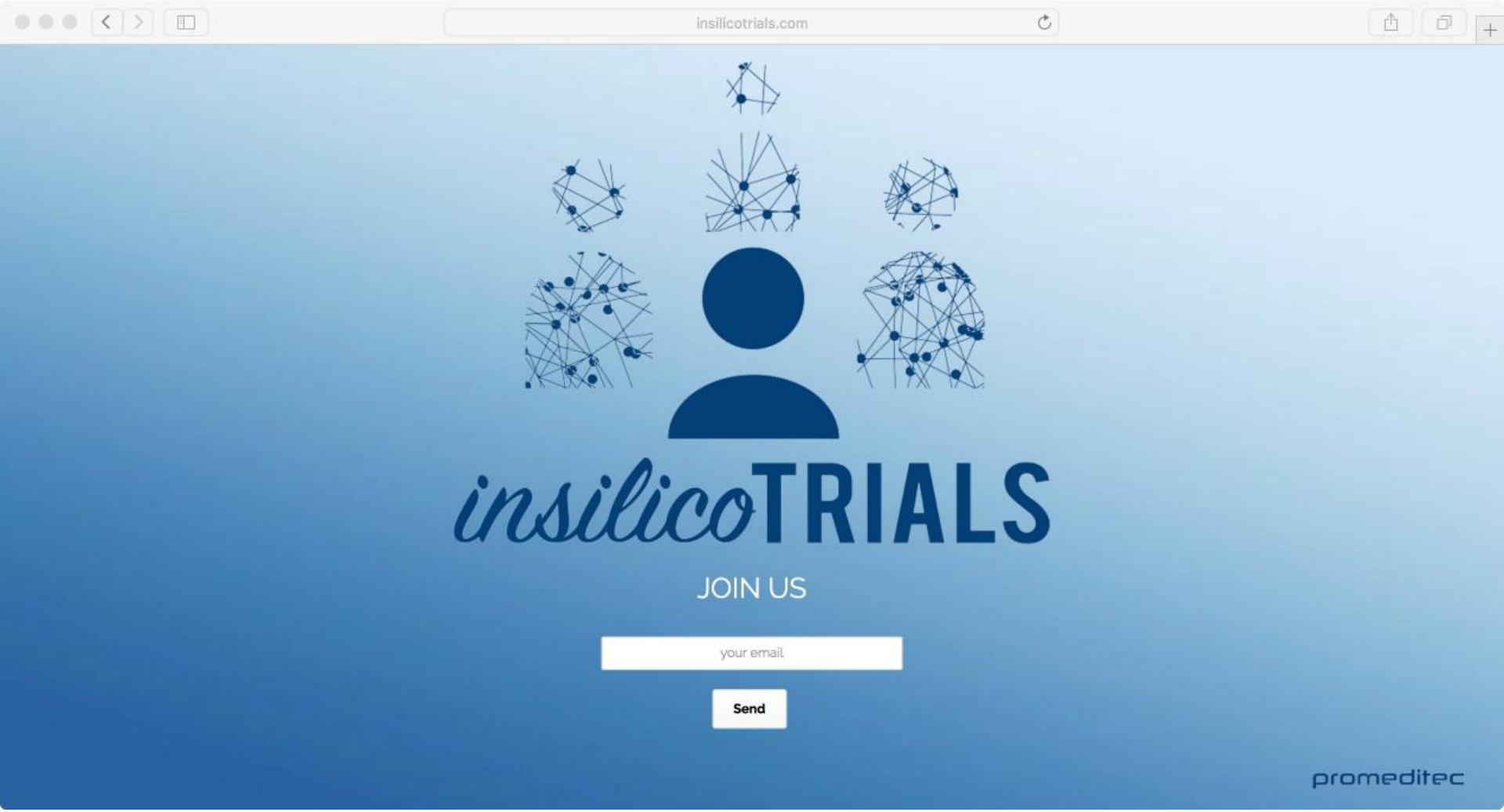
GSP could help to:

- Assure Scientific validity and reproducibility of In Silico tests
- Avoid fake results thanks to traceability of source data
- Formalize study objectives, endpoints
- Define logic for archiving, Data sharing, Peer review
- Regulate relationship between Investigator and Sponsor

Example of points regulated for traditional clinical trials interesting for the definition of GSP	Comments and open questions on GSP
IRB Review and Approval	Do we need IRB? Who should it be? What would the approval mean?
Clinical Trial Protocol and **documents for the conduct of a trial**	Are you using a protocol or other documents?
Data handling, Record keeping, Record Access E.g. correspondence with other investigators, sponsor or FDA; records of receipt, use or disposition of device, protocol and documents showing dates of and reasons for deviation from protocol, etc.	How can data (patient's imaging and clinical data, models, simulations) be organized, archived and published in a standardized way? Do you keep track of records related to the study? Do you have an access policy to your records?
Investigational plan The investigational plan shall include, in the following order: a) *Purpose,* b) *Protocol,* c) *Risk analysis,* d) *Description of device,* e) *Monitoring procedures,* g) *Consent materials,* h) *IRB information,* i) *Other institutions, j) Additional records and reports.*	How should a document including all parts of an In Silico Trial be structured? (Imaging, Model creation, Mesh, Boundary Conditions, Solver Settings, Results...) Do we need to perform also other activities of a traditional trial(e.g. monitoring, consent materials)?
Confidentiality of data and information	How can clinical data and models be properly secured and anonymized/encrypted/etc.?
Trial Design, Trial Management	Is there a standard way to design an In Silico trial?
Financial aspects of the trial documented and reviewed by IRB	Should we include this? What if IRB does not exist?
Statistics	How statistics should be documented? How can statistical methods be evaluated?

How will InSilicoTrials.com help in the process towards the definition of GSP?

- Data Archiving in validated environment
- Data Sharing with colleagues and researcher
- IT Secured Peer Review for scientific and industrial R&D purposes
- Keep tracing of source data
- Simulations and results versioning
- Definition of study endpoint
- IT Security and source data anonymization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