VPH Institute
Building the Virtual Physiological Human

An ecosystem for digital twins in healthcare

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DTH = community effort

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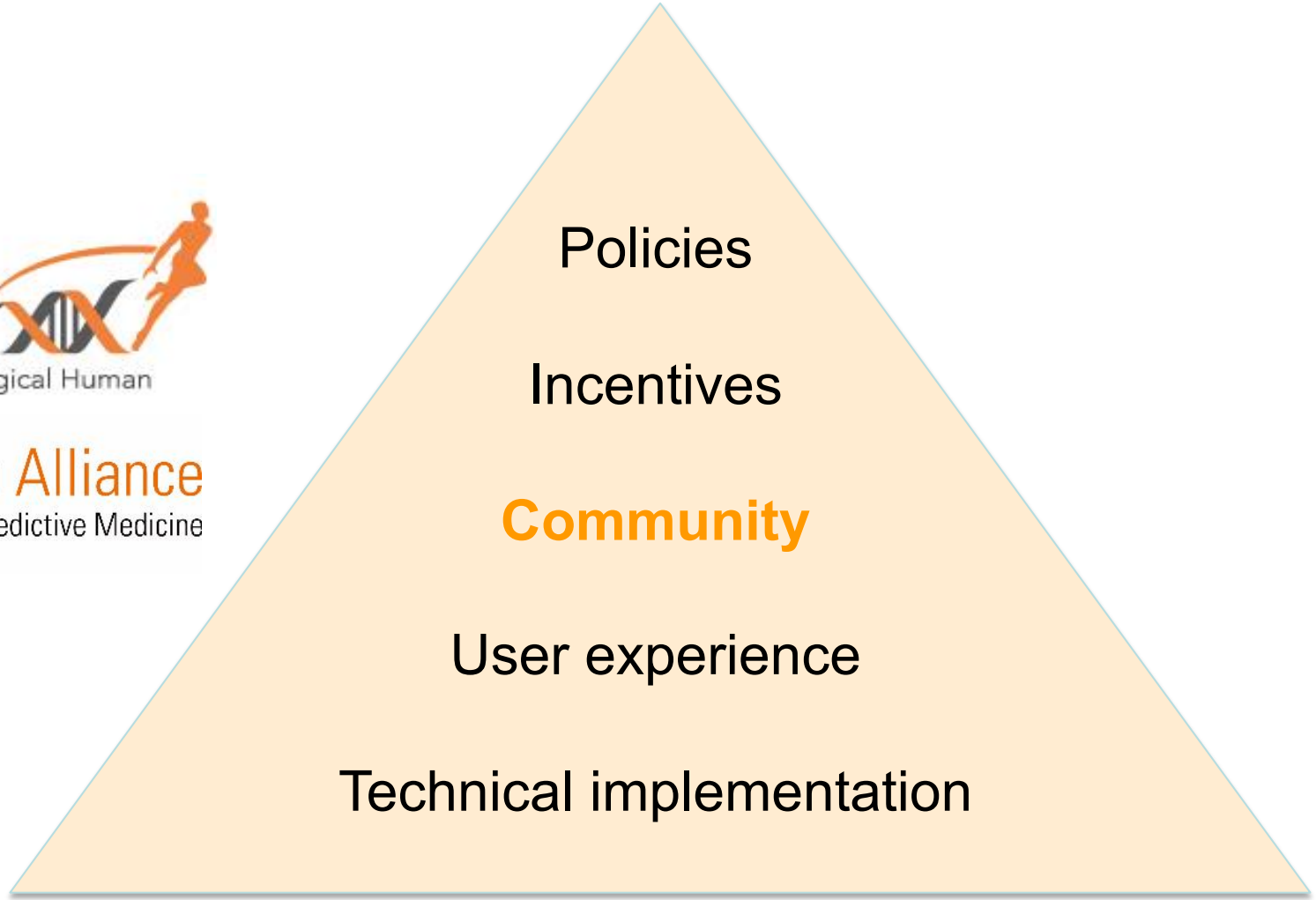
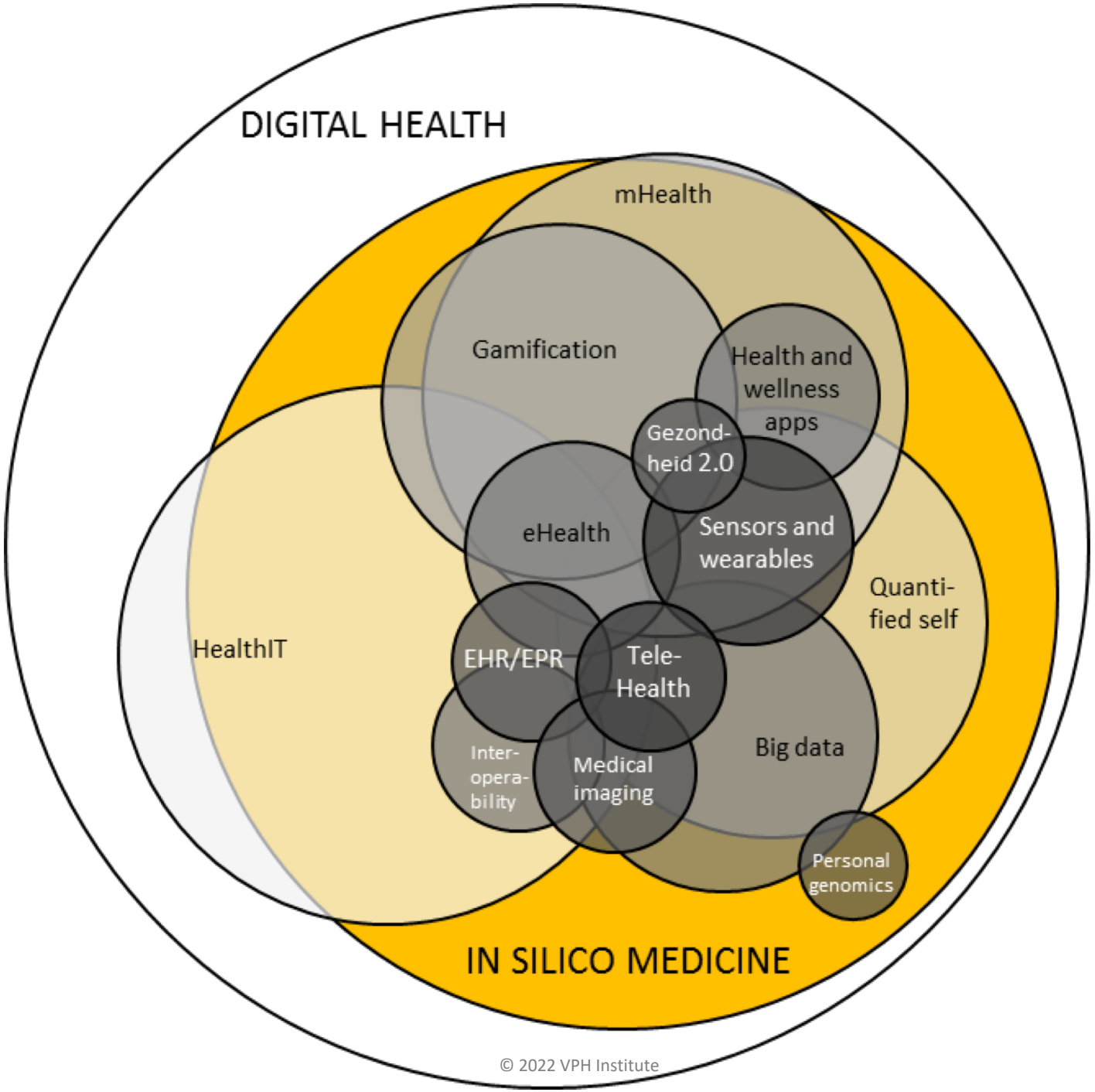
Avicenna Alliance
Association for Predictive Medicine





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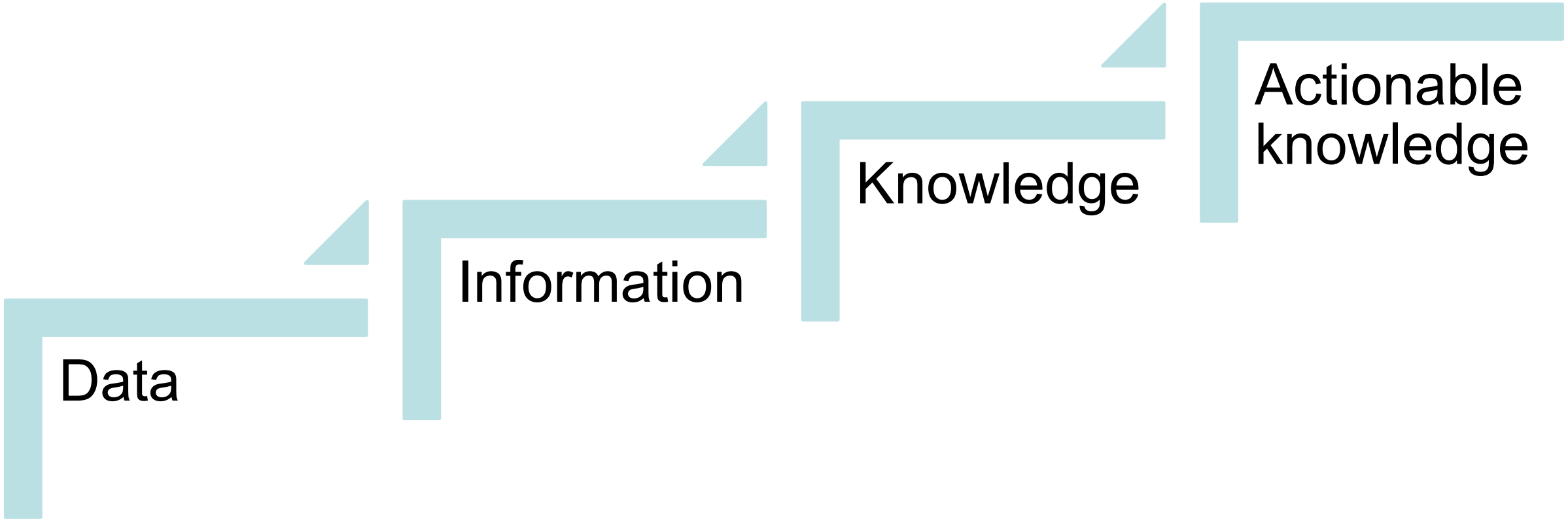
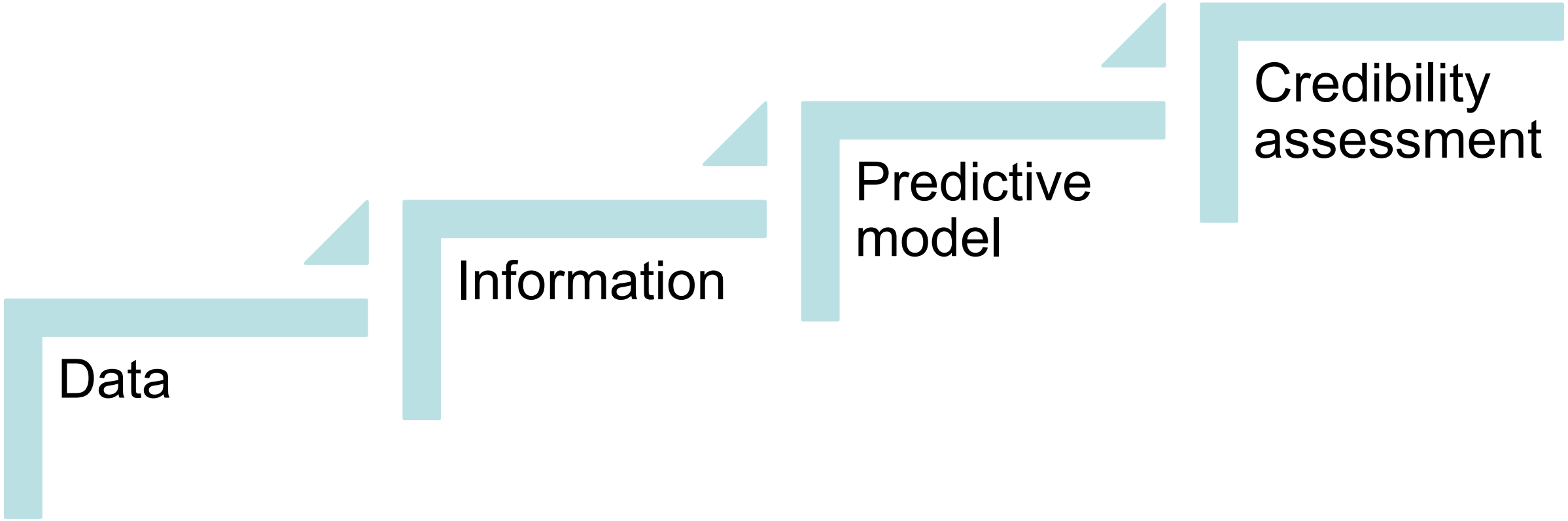
Adapted from NUVIUM

From data to action



From data to action



DT = wide spectrum of technologies

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Black box
Driven by data

Artificial Intelligence, machine learning

White box
Driven by knowledge

Physics-based models, Mechanistic models

- Turn data into actionable knowledge
- The problem determines the appropriate technology !

EDITH

the Human Digital Twin can be a distributed **digital infrastructure**, made of **data and model standards**, standard operative procedures (**SOPs**), and standardised application programming interfaces (**APIs**), that will allow our community to accrue all the predictive models it develops, and all experimental and clinical data employed in building and validating the model, into a **shared facility** for reuse and collaboration.

EDITH

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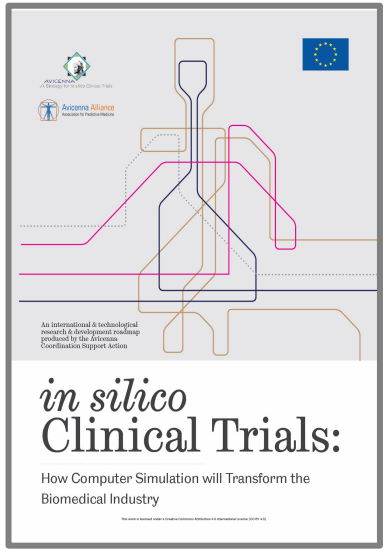
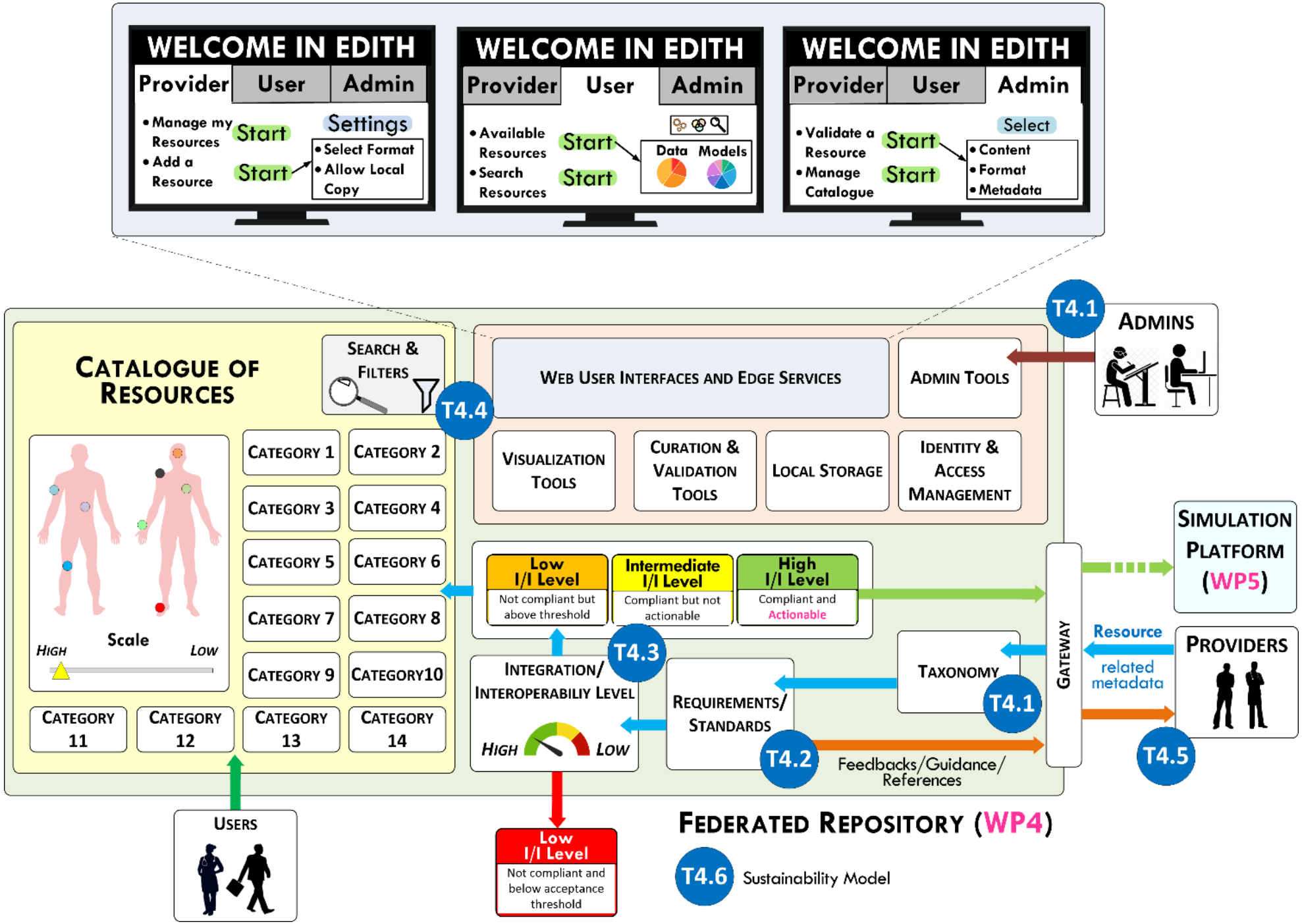
- Ecosystem
- Roadmap HDT
- Federated cloud-based repository
- Simulation platform

Roadmap towards HDT

- Personal Health Forecasting
  - for the patient/citizen; subject specific real-time simulations using data from wearable sensors
- The Digital Patient (CSA)
  - for the doctor; patient specific modelling for decision support
- In Silico Clinical Trials (CSA)
  - for the biomedical R&D; patient specific models to support industry value chain




WELCOME IN EDITH
Provider
User
Admin
• Manage my Resources
• Add a Resource
Start
Start
Settings
• Select Format
• Allow Local Copy
WELCOME IN EDITH
Provider
User
Admin
• Available Resources
• Search Resources
Start
Start
Data
Models
WELCOME IN EDITH
Provider
User
Admin
• Validate a Resource
• Manage Catalogue
Start
Start
Select
• Content
• Format
• Metadata
T4.1
ADMINS
CATALOGUE OF RESOURCES
SEARCH & FILTERS
T4.4
WEB USER INTERFACES AND EDGE SERVICES
ADMIN TOOLS
VISUALIZATION TOOLS
CURATION & VALIDATION TOOLS
LOCAL STORAGE
IDENTITY & ACCESS MANAGEMENT
CATEGORY 1
CATEGORY 2
CATEGORY 3
CATEGORY 4
CATEGORY 5
CATEGORY 6
CATEGORY 7
CATEGORY 8
CATEGORY 9
CATEGORY10
CATEGORY 11
CATEGORY 12
CATEGORY 13
CATEGORY 14
HIGH
Scale
LOW
Low I/I Level
Not compliant but above threshold
Intermediate I/I Level
Compliant but not actionable
High I/I Level
Compliant and Actionable
SIMULATION PLATFORM (WP5)
GATEWAY
Resource related metadata
PROVIDERS
T4.3
INTEGRATION/ INTEROPERABILIY LEVEL
HIGH
LOW
REQUIREMENTS/ STANDARDS
TAXONOMY
T4.1
T4.2
Feedbacks/Guidance/ References
T4.5
USERS
Low I/I Level
Not compliant and below acceptance threshold
FEDERATED REPOSITORY (WP4)
T4.6
Sustainability Model

Simulation platform

- Cfr presentation Yannis Ioannidis

Ecosystem

Regulators

Policy makers

HPC

In silico medicine

AI

Repositories

Users

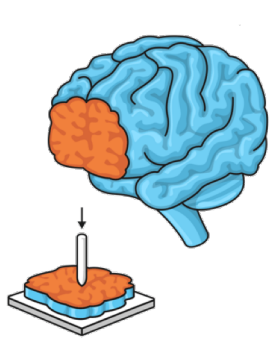
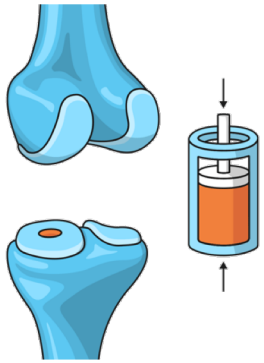
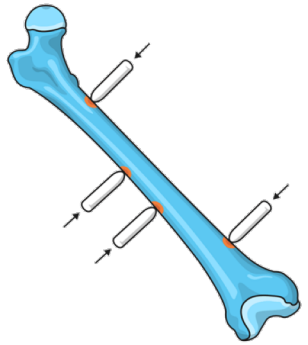
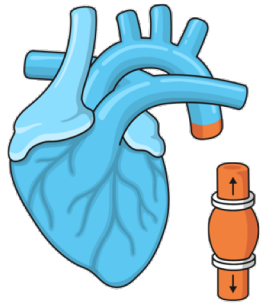
Wearables

Health data

Infrastructures

Barriers to adoption of in silico medicine

- New technologies
- **Validation collections (data)**
- Policies
- Regulatory pathways
- Scalable services
- Commercial services
- Better informed stakeholders
- Properly trained workforce
- Sustainability

C4Bio

Community Challenge towards Consensus on Characterization of Biological tissue

Nele Famaey
KU Leuven

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Avicenna Alliance
Association for Predictive Medicine

FIBER

AIM

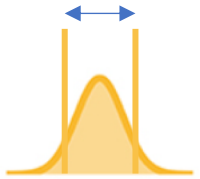
Achieve community consensus regarding the testing protocols for material characterization of biological tissue

and disseminate this consensus to the relevant standards bodies (i.a. ISO & ASME).

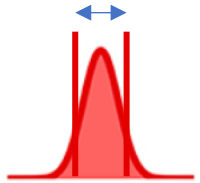
Initial focus: mechanical properties

Test campaign: 4 steps

1. **Quantify the variability** among different research groups: testing using participants' own methodology



3. **Evaluate standardized approach** by retesting using consensus methodology



2. **Standardize the approach** by defining consensus methodology between participants

4. **Make the outcome publicly available** in a white paper with results & consensus methodology

Barriers to adoption of in silico medicine

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- **Policies**
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US policy makers

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Calendar No. 177

115TH CONGRESS *1st Session* | SENATE | REPORT 115–131

AGRICULTURE, RURAL DEVELOPMENT, FOOD AND DRUG ADMINISTRATION, AND RELATED AGENCIES APPROPRIATIONS BILL, 2018

JULY 20, 2017—Ordered to be printed

Mr. HOEVEN, from the Committee on Appropriations, submitted the following

REPORT

In Silico Clinical Trials.—In Silico clinical trials use computer models and simulations to develop and assess devices and drugs, including their potential risk to the public, before being tested in live clinical trials. Advanced computer modeling can also be used to predict how a drug or device will behave when deployed in the general population, thereby protecting the public from the unintended consequences of side effects and drug interactions. In Silico trials protect public health, advance personalized treatment, and can be executed quickly and for a fraction of the cost of a full scale live trial. By understanding the impact a drug or device will have on the human body immediately and over time, as well as within different populations, millions of dollars in development costs can be saved. A mere ten percent improvement in predicting failures before a clinical trial could save $100,000,000 in development costs per drug. As such, the Committee directs the FDA to expand its use of in silico clinical models through a pilot project aimed at creation of a full human in silico model able to test drugs and devices across the entire body, including long-term effects and among distinct populations. If necessary to enact this project, the FDA shall issue a unified guidance to allow the model to be used to test both drugs and devices. The Committee requests a written report outlining the FDA's plans for development of the model within 120 days of enactment of this act.

"… the committee directs the FDA to expand its use of in silico models …"

The European Commission

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Communication on building a European Health Union

- *"The rapidly evolving technological environment **and digital solutions (AI, High Performance Computing, computational models and simulation system)** provides an opportunity to update surveillance systems, integrating data from new and different sources, and to create sensitive systems that detect early signals"*
- *"In order to facilitate the work and the exchange of information under this Regulation, provision should be made for the establishment and management of IT infrastructures and synergies with other existing IT systems or systems under development, including the EUDAMED IT platform for medical devices. That work should also be facilitated by, where appropriate, **emerging digital technologies such as computational models and simulations for clinical trials**, as well as data… "*

European Commission

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- New technologies
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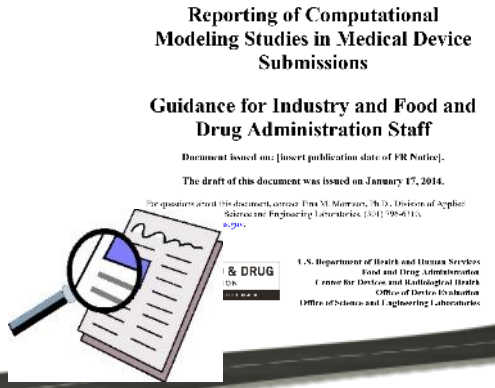
U.S. FOOD & DRUG ADMINISTRATION

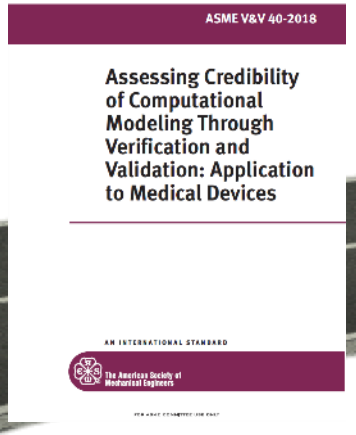

Reporting of Computational Modeling Studies in Medical Device Submissions

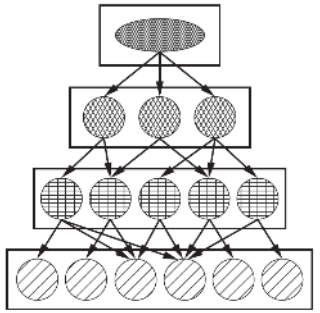
Guidance for Industry and Food and Drug Administration Staff

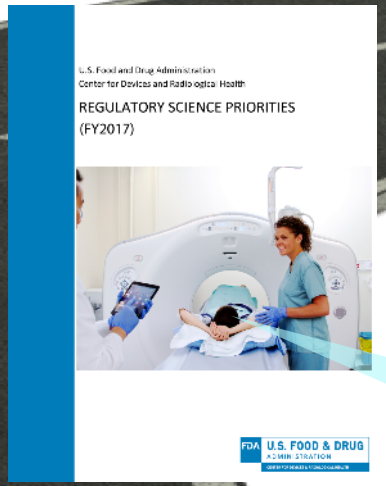
Document issued on: [insert publication date of FR Notice].

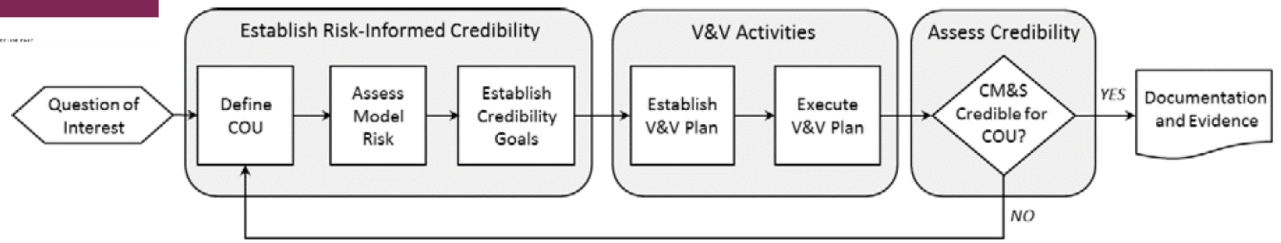
The draft of this document was issued on January 17, 2014.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Office of Science and Engineering Laboratories









"Develop computational modeling technologies to support regulatory decision-making"

Courtesy Avicenna Alliance

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Citation: CPT Pharmacometrics Syst. Pharmacol. (2020) 9, 195–197; doi:10.1002/psp4.12504

COMMENTARY

Verifying and Validating Quantitative S Pharmacology and *In Silico* Models in Current Needs, Gaps, and Challenges

Flora T. Musuamba[1,2,3,*], Roberta Bursi[4], Efthymios Manolis[1,5], Kristin Karlsson[1,6], A Jean-Pierre Boissel[7], Raphaëlle Lesage[8], Cécile Crozatier[9], Emmanuelle M. Voisin[9], Rossana Alessandrello[11] and Liesbet Geris[8,12]

The added value of *in silico* models (including quantitative systems pharmacology models) for drug development is now unanimously recognized. It is, therefore, important that the standards used are commonly acknowledged

case, the inco
low standards
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CPT: Pharmacometrics & Systems Pharmacology

ARTICLE | Open Access

Scientific and regulatory evaluation of mechanistic *in silico* drug and disease models in drug development: building model credibility

Flora T. Musuamba, Ine Skottheim Rusten, Raphaëlle Lesage, Giulia Russo, Roberta Bursi, Luca Emili, Gaby Wangorsch, Efthymios Manolis, Kristin E. Karlsson, Alexander Kulesza, Eulalie Courcelles, Jean-Pierre Boissel, Cécile F. Rousseau, Emmanuelle M. Voisin, Rossana Alessandrello, Nuno Curado, Enrico Dall'ara, Blanca Rodriguez, Francesco Pappalardo, Liesbet Geris ... See fewer authors

First published: 08 June 2021 | https://doi.org/10.1002/psp4.12669

Barriers to adoption of in silico medicine

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- New technologies
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- Policies
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- Scalable services
- **Commercial services**
- Better informed stakeholders
- Properly trained workforce
- Sustainability

Business model

- EDITH aims to determine how to regulate, incentivise, and support the DTH ecosystem to eventually turn it into a thriving, economically profitable sector of the European technology landscape
  - Lean start-up & customer discovery business modeling methodologies

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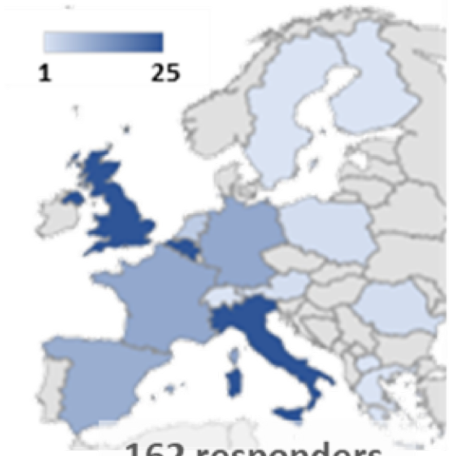
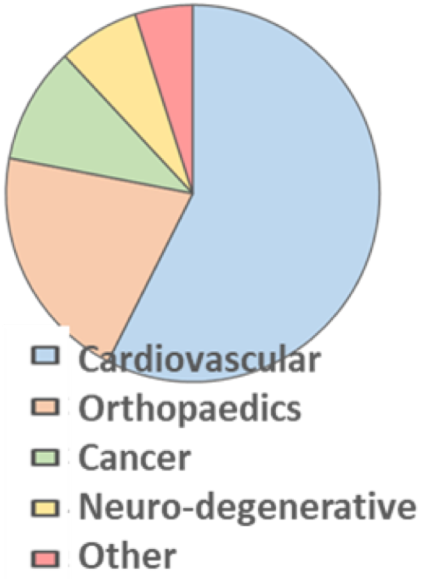
User community



162 responders
32-71 year old
All levels



Strengths	Weakensses
Awareness Confidence Accuracy Trust	Required technical expertise Access to computing resources CM&S is slow Still limited to a few fields
Opportunities	**Threats**
Trust Growth of cases; methods and data Applications in teaching Digital generation of healthcare providers	Regulatory approval Level of awareness in certain terms Mistrust/over expectations Data

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- **Sustainability**

Sustainability

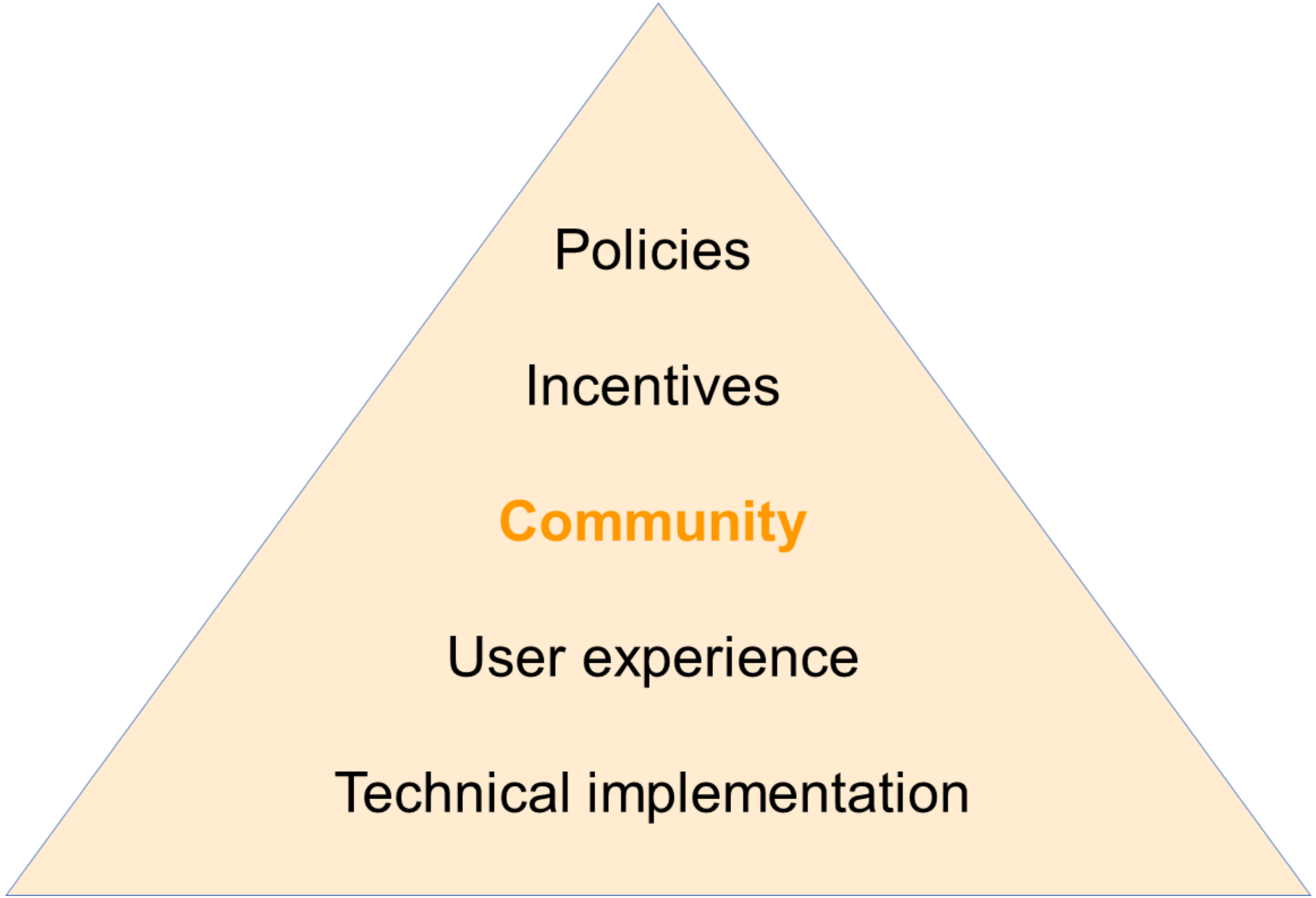
- Sustainability plan
  - Survey of providers & user communities
  - Internal assessment of costs
  - Conceptualisation of the marketplace mechanism
  - Proof-of-concept software architecture

Good Simulation Practice

- Good Simulation Practice is defined as a set of rules and criteria for a quality system related to
  - the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of in silico studies …
  - aimed to complement / reduce, refine, or replace in vitro & in vivo testing

- In silico world grassroots initiative
- Supported by international stakeholders (FDA, EMA, DIN, …)

Join In Silico World Community of Practice on slack


Policies
Incentives
Community
User experience
Technical implementation

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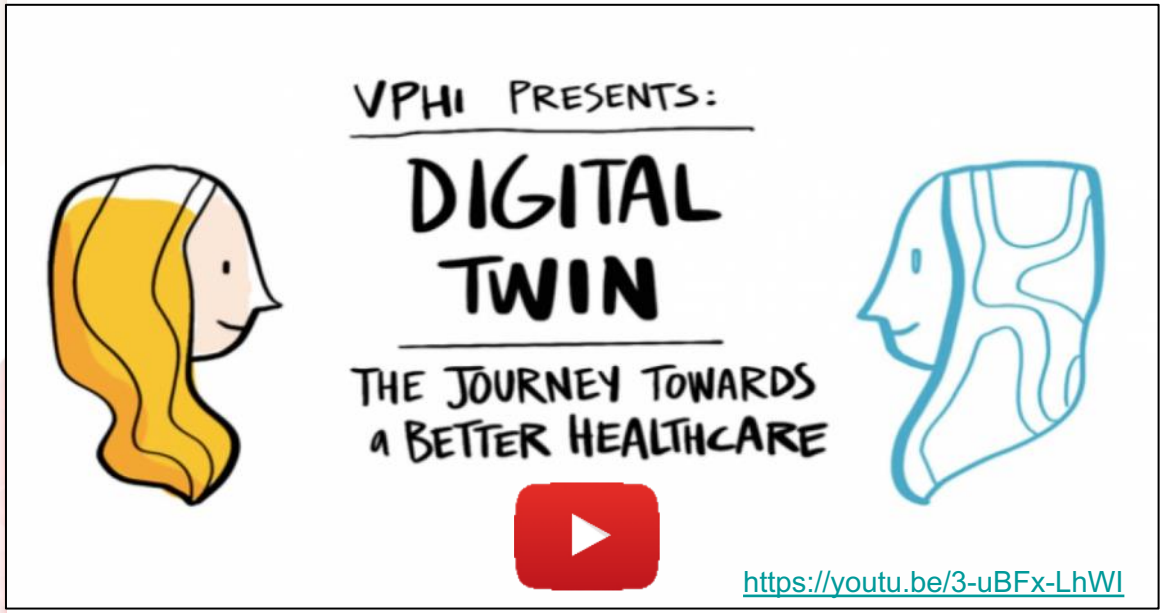

Thank you

http://www.vph-institute.org
http://insilico.world