From Prototype to Practice

Evaluating and Scaling Healthcare Digital Twins

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Research programs: Sustainability in all aspects of life

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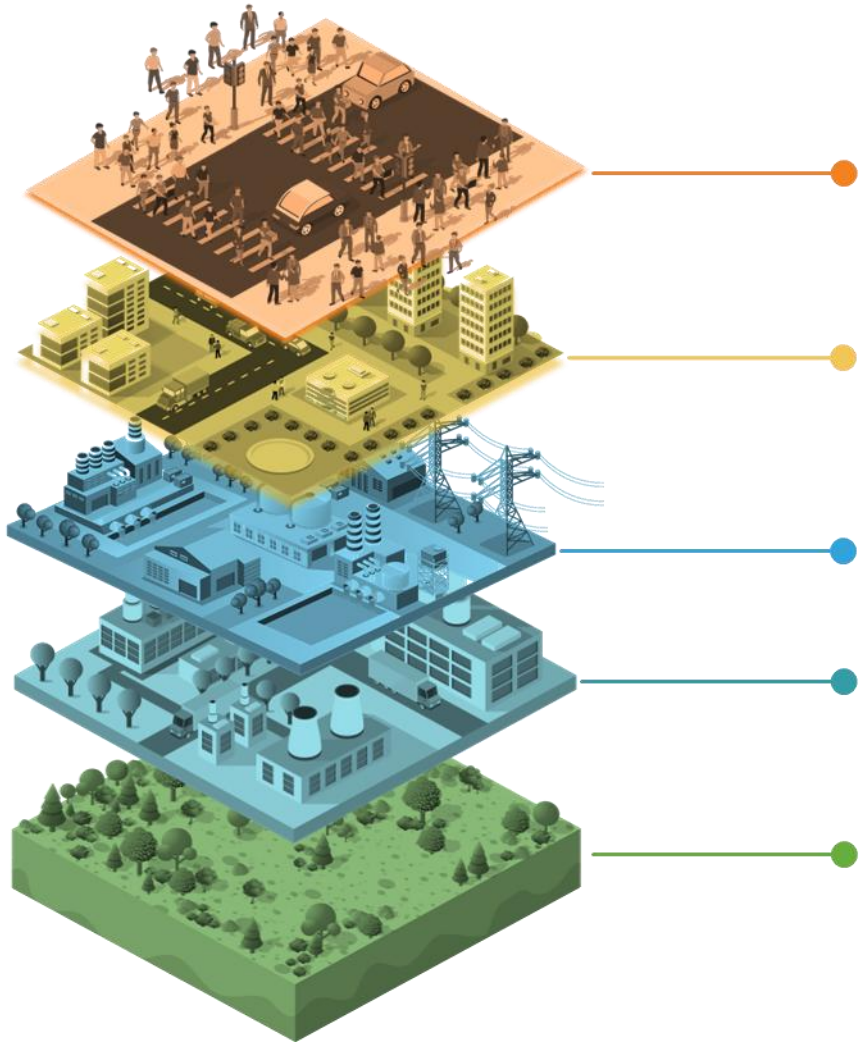
VISION ON TECHNOLOGY FOR A BETTER WORLD



SUSTAINABLE HEALTH

Various Human DTs ->VHT

SUSTAINABLE MATERIALS

Product Lifecycle DT

SUSTAINABLE ENERGY

Smart Grids DT

Renewable Energy Source DT

SUSTAINABLE CHEMISTRY

Biomass Conversion DT

Chemical Process Optimization DT

SUSTAINABLE LAND USE

Ecosystem and Biodiversity DT

Water Resource Management DT

Virtual Human Twin

JOURNEY TO PERSONALIZED HEALTHCARE

WHAT? A **virtual human twin (VHT)*** is a digital representation of a person's physiology, including its interaction with potential diseases.
WHY? A VHT is expected to contribute to **targeted prevention, early diagnostics, personalized prescription and treatment monitoring**.

Real world data

Encompasses all health data from a patient e.g., from:

HEALTH RECORD

IMAGING

SEQUENCING

LAB TESTS

Development of patient-specific predictive digital twin models for real time digital simulation of cells, tissues, organs or organ systems.

Access to dynamic high performance computing, data learning and model integration.

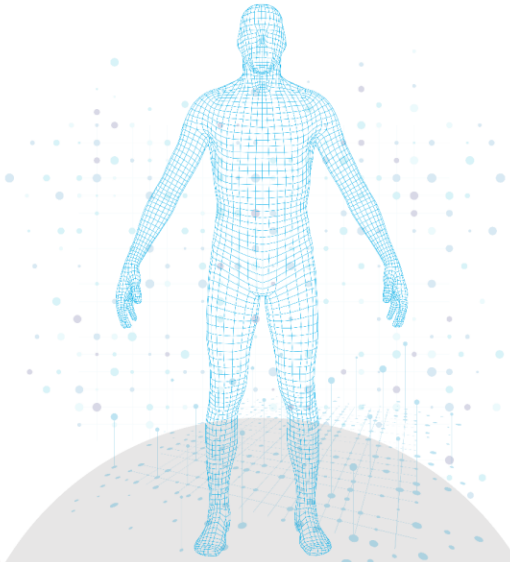
Regulation and validation

Computational models

Consent driven data access

Personal data storage and sharing infrastructure with consent driven access ensuring data privacy and protection.

System governemance, regulatory and certification processes are required in order to validate and standardize each model.



Virtual Human Twin

Integration of individual models into one virtual human twin, ready for implementation into medical services

Essential Development Areas

REGULATION AND VALIDATION

DEVELOPERS

Transparant traceble and secure testing environment

FRAMEWORK BASED ON REAL-WORLD DATA FOR CERTIFIED MEDICAL APPLICATIONS

CERTIFIED

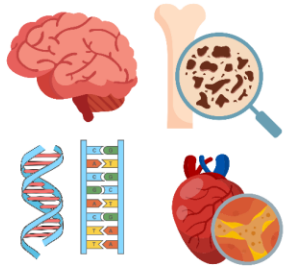
REGULATORY BODIES

Up-to-date legal guidelines and standardized evaluation

COMPUTATIONAL MODELS

DIGITAL TWIN MODELS

Patient-specific predictive computer models for cancer, cardiovascular diseases, epilepsy, osteoporosis, pharmacogenomics, intensive care applicatons,...



PERSONALIZED RISK PREDICTION AND TREATMENT

Real-world data learning, dynamic feedback and model integration

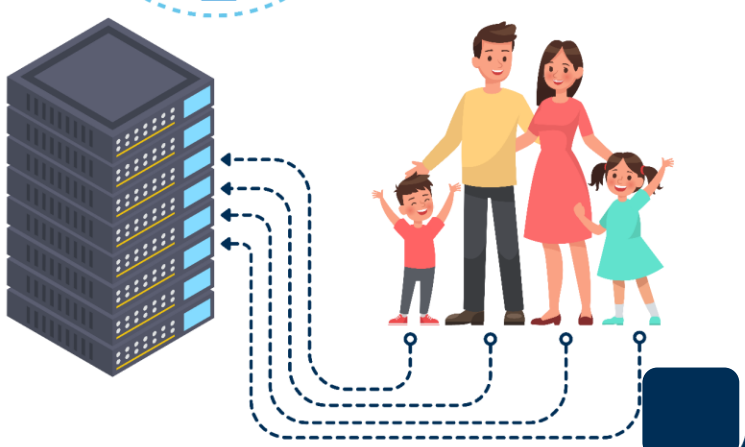
HIGH PERFORMANCE COMPUTING

CONSENT DRIVEN DATA ACCESS

Patients can allow selective access to data for personalized healthcare and/or research purposes

CONSENT DRIVEN ACCESS

PERSONAL DATA STORAGE AND PROTECTION

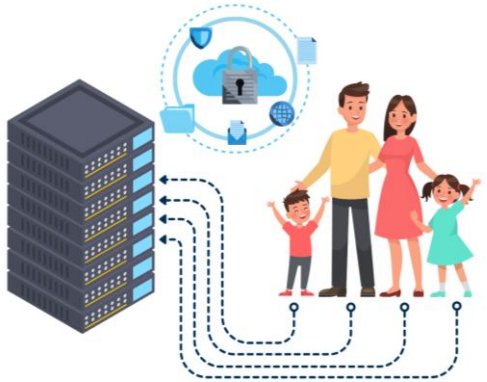


Phases of PMs towards DT enabled healthcare

COMPLEXITY

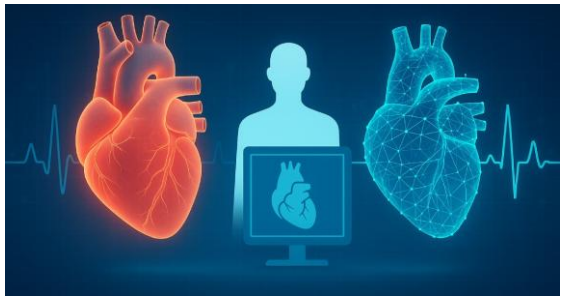
I. Enable storage & sharing

Personal data and DT models storage, ethical and legal compliant, and quarriable for different applications



II. Precision Medicine: Independent Digital Twins enter healthcare

Clinicians routinely consult patient-specific digital twins—living computational models continuously updated with genomics, imaging, and sensor streams—to forecast trajectories and rehearse treatments. Conventional clinical wisdom is fused with simulation-driven evidence under robust guardrails, bringing faster, safer, and more equitable care.



III. Multimodal decision making (DT enabled healthcare)

Clinicians supported by expert AI agents: traceable and referenced to guidelines e.g. radiology, cancer genomics

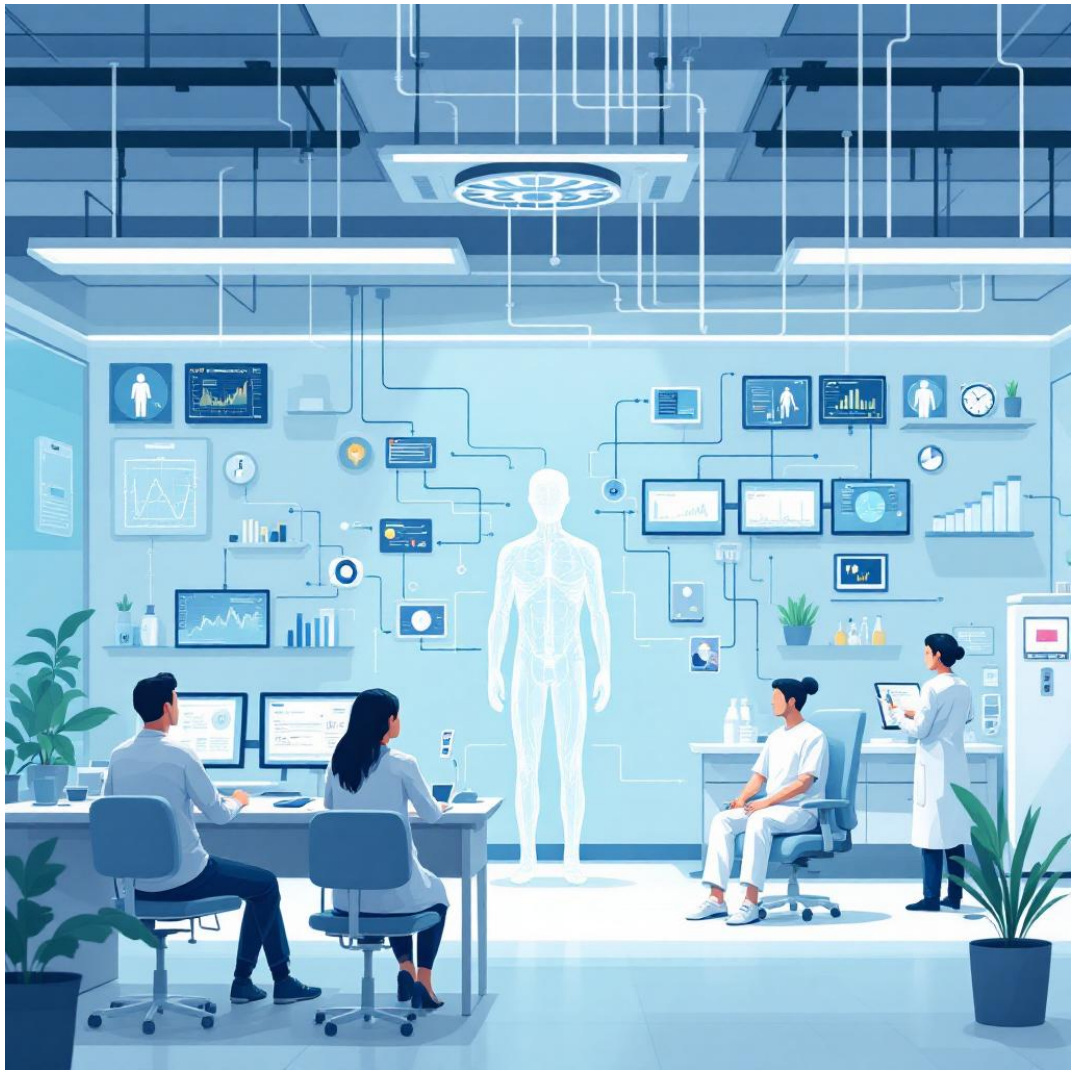
IMPACT

TIME to Practice

Prototype

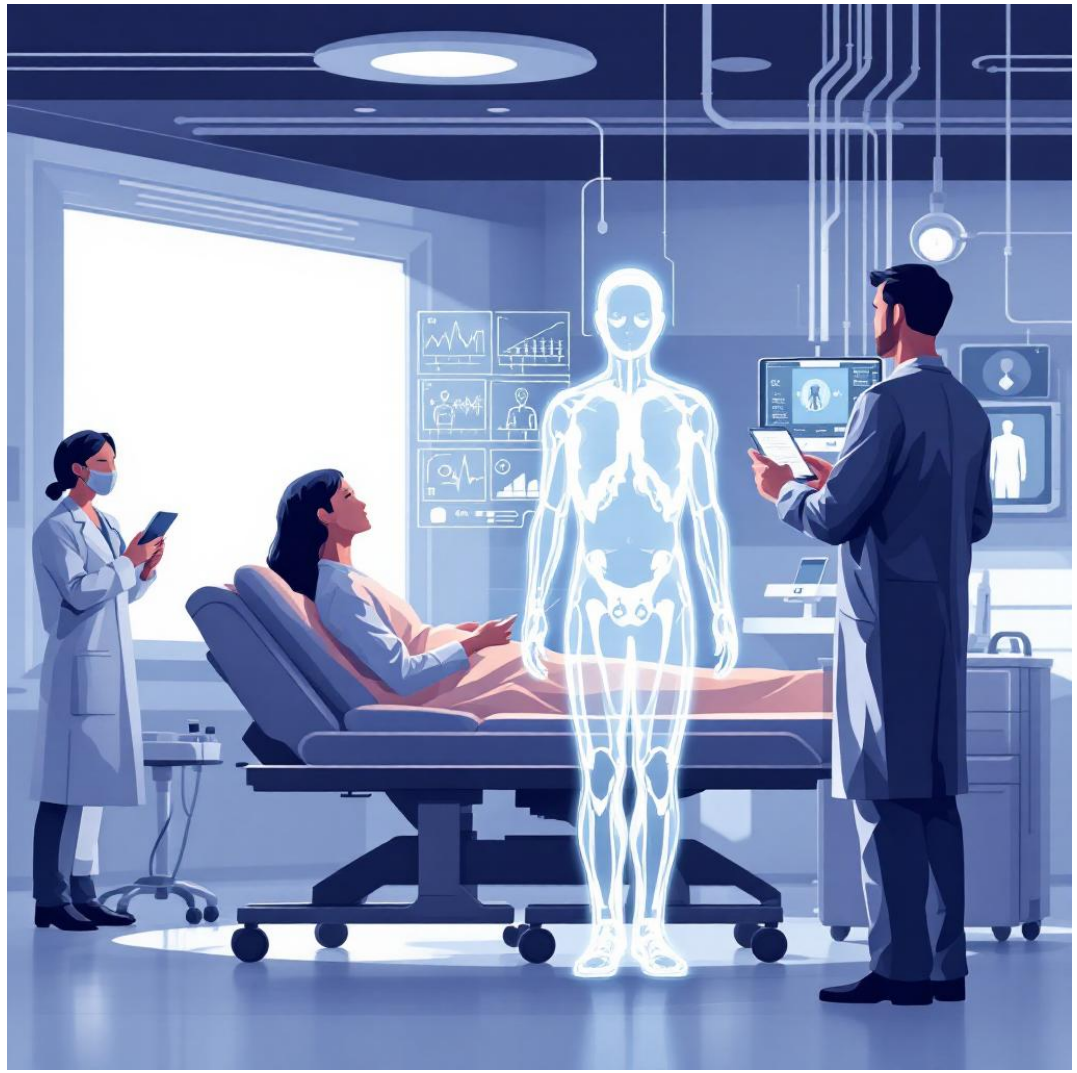
- **Clear Purpose**: Clinical use + explicit “not for” list (scope freeze).
- **No wobbling**: stable demo on retrospective data; sensible latency; basic fail-safes.
- **Credibility metrics**: shows confidence/uncertainty
- **Built in privacy** : minimal data, basic DPIA done; activity logs.
- **Ready for supervision**: lightweight docs (model card, data sheet) and simple exit criteria for Go/NoGO.

Maturation & Evaluation



- **Clinically credible**: shadow-mode (and limited live) results hit predefined accuracy/timeliness targets across sites; no harmful patterns.
- **Safe to try in the wild** : clear human override, visible audit trail, tested fail-safe behavior in the actual workflow.
- **Utility & Usability tested** : clinicians complete tasks faster/safer; short training works; explanations are understood.
- **Governed & lawful**: certification applications are in place; secure environment validated; data sharing/permits compliant.
- **Change-ready**: update/rollback process tested; monitoring dashboards live; versioning and release notes in order.
- **Evidence packaged**: concise impact/RWE summary mapped to MDR/IVDR and payer/HTA questions.

Deployment in Practice

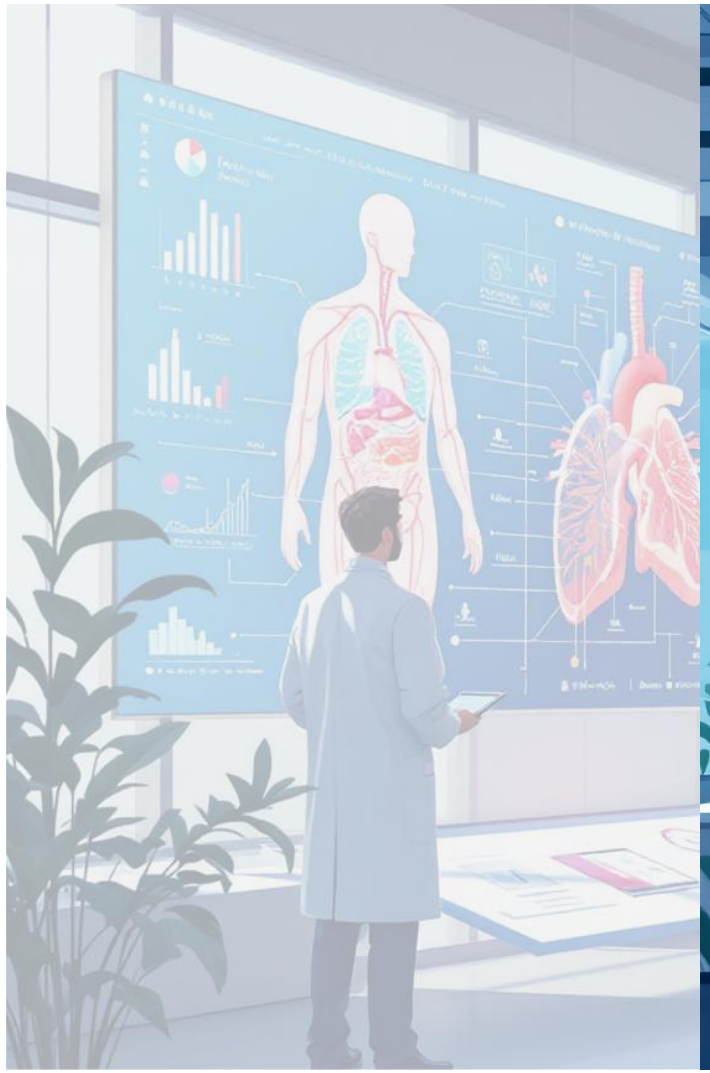


- **Accredited & scoped**: conformity assessment/CE mark labeling matches the tested use—no mission creep.
- **Operationally steady**: Service Level Agreements met; seamless EHR/device integration; role-based access; full traceability.
- **Continous Monitoring**: live performance, bias/drift alerts, incident response & Corrective and Preventive Action loop tested.
- **Secure & resilient**: vulnerability management, backups, recovery drills; periodic re-validation after updates.
- **People & trust**: trained clinicians; patient-facing explanations; responsibilities and escalation paths clear.

Prototype

Maturation & Evaluation

Deployment in Practice



- Multi-stakeholder, multi-experience
- Certification/approvals
- Data realism & drift
- Safety & accountability
- Security & interoperability
- Evidence & economics

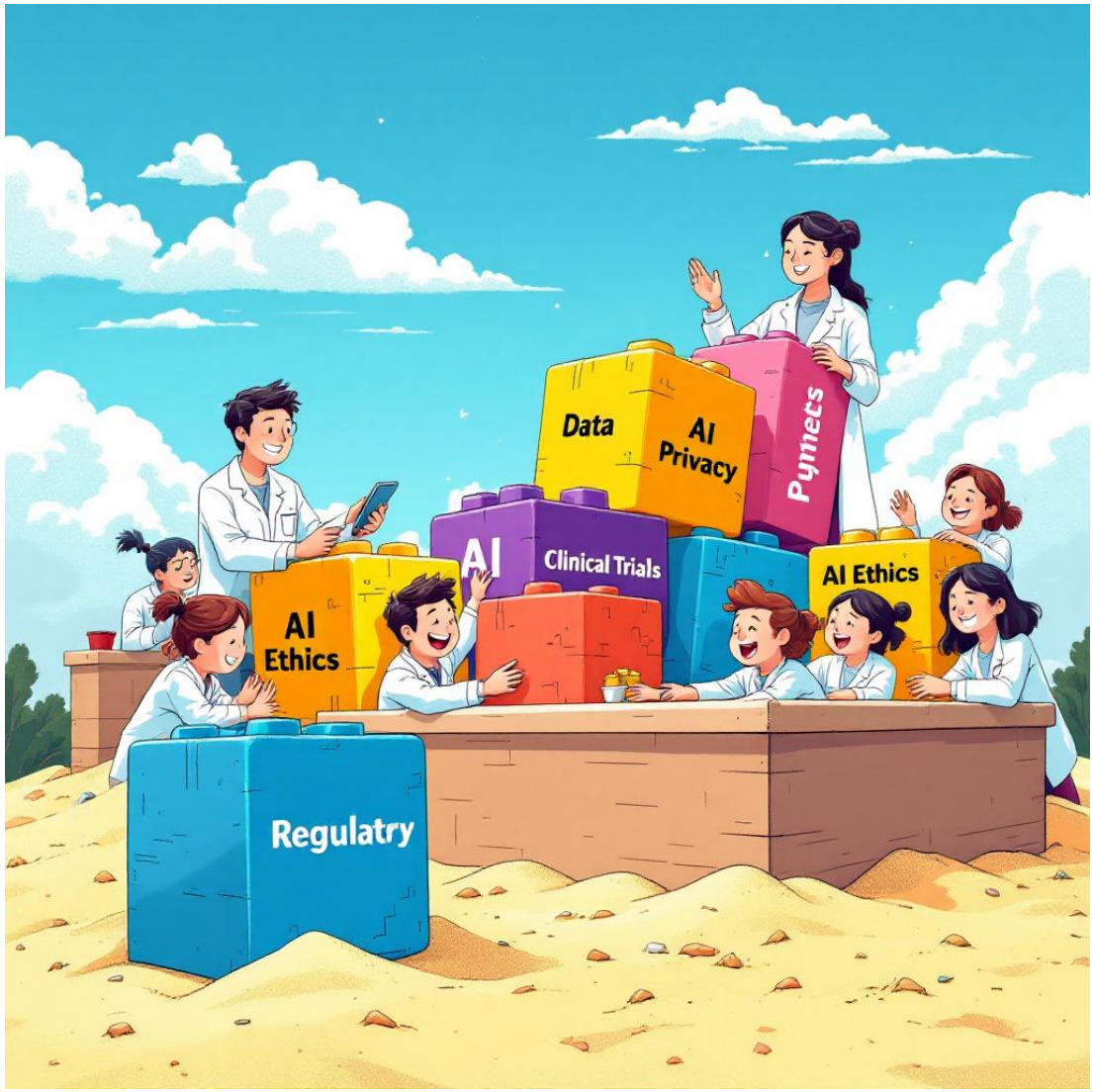
The wave of Digital Twin Models & Applications

- The current pace of discovery in healthcare innovation is far outpacing the ability of our existing regulatory and evaluation framework to keep-up.
- **Collective tidal wave of digital healthcare innovations and Digital Twin models** from Cardiovascular digital twins; physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) “dosing twins”; musculoskeletal/orthopedic twins in prosthesis design &/ gait optimization; Pulmonary ventilation–perfusion twins for optimizing ventilator settings; Oncology therapy-selection twins; metabolic twins” for type 1 diabetes; Neuro-twins for seizure forecasting and closed-loop stimulation; cell-therapy twins to predict CAR-T expansion/toxicity*;* AI Powered Mental Health Twins…
- **We need a new paradigm complementary to existing healthcare regulatory system in EU.**

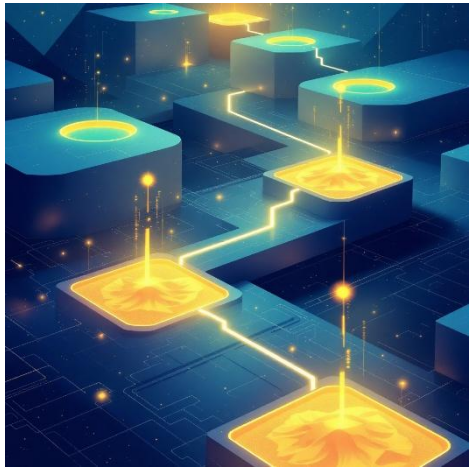
What is a Regulatory Sandbox ?

- A regulatory sandbox is a controlled environment, established to understand the opportunities and risks associated with specific innovations and to develop an appropriate regulatory environment to accommodate them effectively. (*OECD definition*[1]) *Regulators' Perspective*

- Regulatory sandboxes "for developing evidence about how a new product, technology, or business model (innovation) works and the outcomes it produces"—seek to promote innovation in highly regulated sectors, giving innovators access to regulatory experts. Regulatory sandboxes are … in which innovators can test new products and services; find out if business models are viable and how new technologies work in the market; introduce an innovation to market potentially more quickly and at lower cost; and *find out what consumer protection safeguards may be needed* in the context of their innovations. (*Regulatory Sandboxes for Digital Health by World Bank Group*[2]) *Innovators' Perspective*



The relevance of regulatory sandboxes and current challenges



- **Controlled testing environment** — Sandboxes let regulators and innovators trial novel regulatory approaches safely before real-world deployment.
- **Bridging regulatory gaps** — They help address challenges posed by cutting-edge health technologies (e.g., AI decision support, digital biomarkers, ATMPs) that outpace traditional frameworks.
- **Agile and flexible** — Time-limited and adaptable frameworks enable temporary deviations from standard rules to explore tailored solutions.
- **Faster evidence generation** — Facilitate real-world data collection and iterative refinement of complex technologies to meet safety and efficacy standards.

- **Early stakeholder collaboration** — Encourage dialogue between innovators, regulators, and other actors to clarify compliance under new EU regulations (AI Act, DMA, DSA, EHDS).
- **Global early pilots** — Only a few health-focused sandboxes exist (e.g., Canada, UK MHRA AI Airlock, Singapore telemedicine…), showing promising but limited progress.
- **Need for scale and standardisation** — Current initiatives are small, fragmented, and not yet equipped to fully address fast-evolving innovation complexity.

European Legislations towards Regulatory Sandboxes

- **AI Act — Regulation (EU) 2024/1689 (core enabler)**
- Creates **AI regulatory sandboxes** (Member States must have at least one operational by **2 Aug 2026**) and allows **real-world testing (RWT)** of high-risk AI outside sandboxes under authority supervision (Articles 57–61). Critical for structured, supervised evaluation of digital-twin CDSS and device-embedded AI before/alongside market access. Also provides limited allowance to **further process personal data within sandboxes** for projects in the public interest (Art. 59)

- **MDR & IVDR — Regulations (EU) 2017/745 and 2017/746 (device rulebook)**
- The primary conformity-assessment framework for digital-twin solutions that qualify as **software as a medical device (SaMD)** or as AI embedded in medical/IVD devices (risk classification, clinical evaluation, PMCF/PMPF). Essential for aligning sandbox/RWT evidence with market-access documentation and notified-body expectations.

- **European Health Data Space (EHDS) — Regulation (EU) 2025/327 (data access at scale)**
- Establishes **HealthData@EU** for cross-border **secondary use** of health data, **data-permit** mechanisms, and **secure processing environments**—the practical pipes to train/validate digital twins on multi-country datasets under harmonised governance. Enters into force **26 Mar 2025**; staged implementation via implementing acts.

European Legislations towards Regulatory Sandboxes

- **GDPR — Regulation (EU) 2016/679 (privacy baseline)**
- Governs processing of special-category health data and research exemptions; remains the backbone for lawful data use in development, validation, and RWT. Interlocks with AI Act's sandbox-specific data-processing carve-out.

- **HTA Regulation — Regulation (EU) 2021/2282 (evidence for adoption)**
- Applicable from 12 Jan 2025; introduces Joint Clinical Assessments (JCAs) and Joint Scientific Consultations. Frames the evidence standards payers/HTA bodies will expect for digital-twin-enabled interventions (e.g., comparative effectiveness, real-world evidence generated via sandboxes/RWT feeding into reimbursement decisions)

- **NIS2 — Directive (EU) 2022/2555 (operational cybersecurity)**
- Imposes risk-management and incident-reporting duties on **essential/important entities** including the **health sector**; creates a baseline cyber posture for hospitals and vendors deploying twin-enabled services in RWT pilots. Member States had to transpose by **Oct 2024**; enforcement now rolling nationally.

Regulatory Sandbox ???

Prototype

~~Maturation & Evaluation~~

Deployment in Practice

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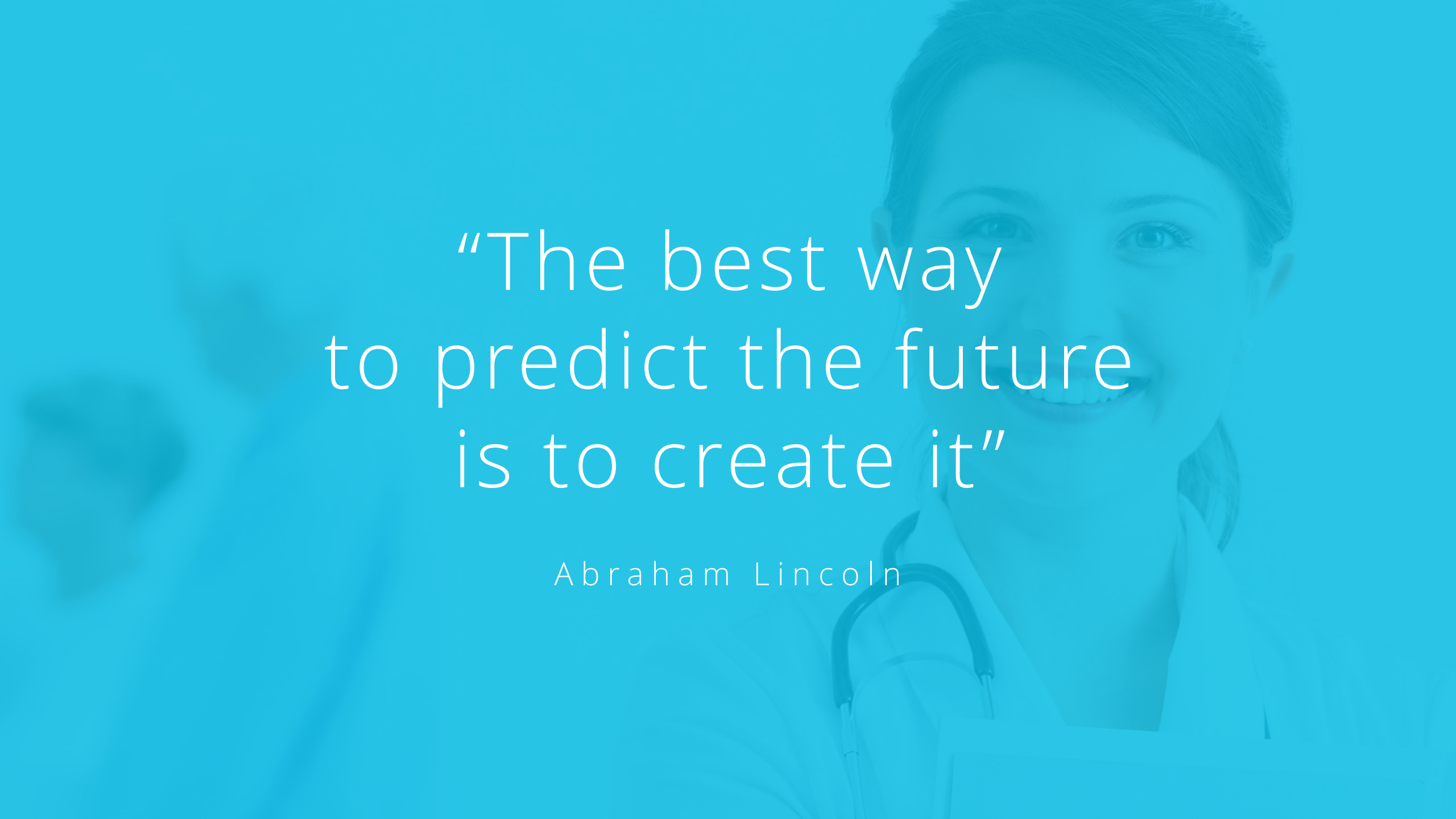
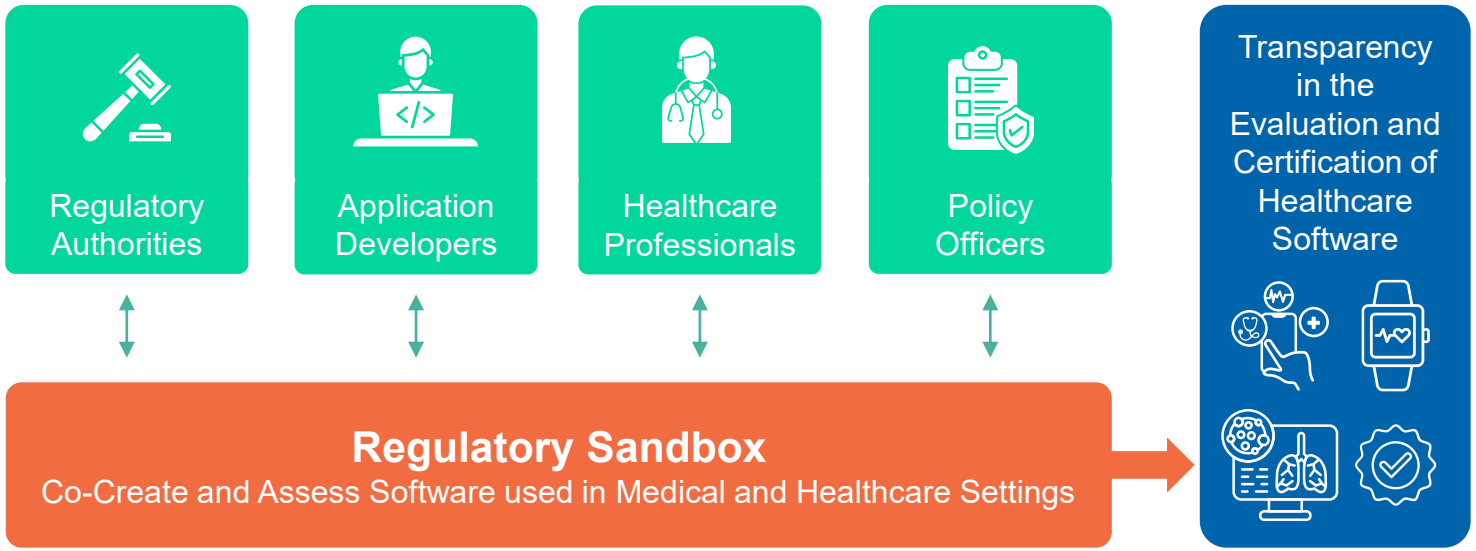

“The best way
to predict the future
is to create it”
Abraham Lincoln

Real-world-data enable assessment for health regulatory decision making : Advancing Innovative Medical Software in Europe

REALM consortium is creating a **collaborative framework** tailored to the European healthcare landscape by establishing a **regulatory sandbox** in cooperation with regulatory authorities, to work together on improving and evaluating innovative medical device software.

This approach fosters cross-border cooperation, aligns with European standards, and **accelerates the safe integration of cutting-edge technologies**, ultimately benefiting patients and healthcare practitioners.



The REALM platform components

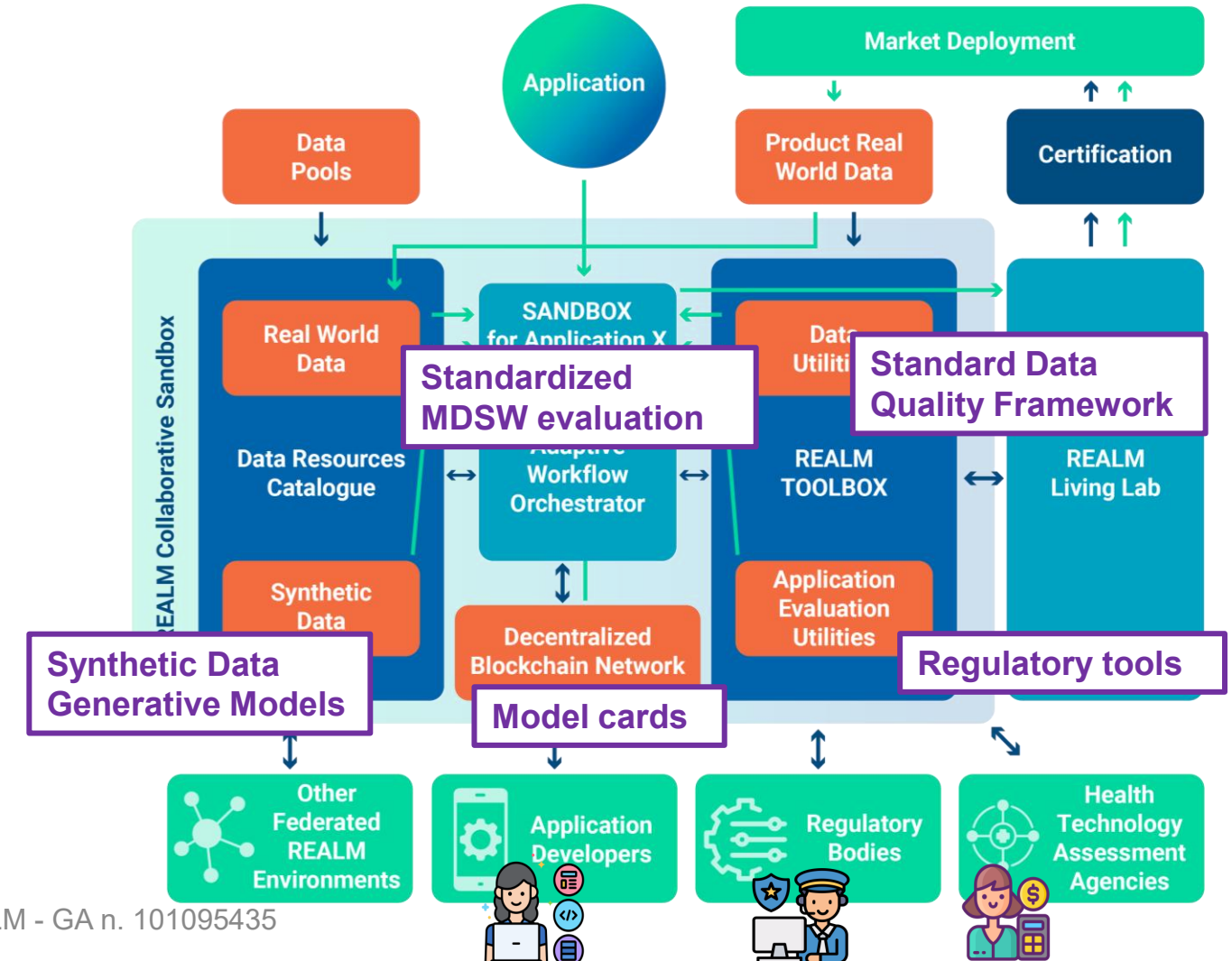
Stakeholders:

- **Application/Product Developer**
  - Industry
  - Academia
- **Regulatory agencies**
  - Notified bodies
  - National competent authorities
  - European Medicines Agency (EMA)
- **Data providers**
  - Data Analysis and Real-World Interrogation Network (DARWIN EU)
  - Healthcare providers, Biobanks, etc.
- **Health Technology Assessment Bodies**

Developer

Regulator

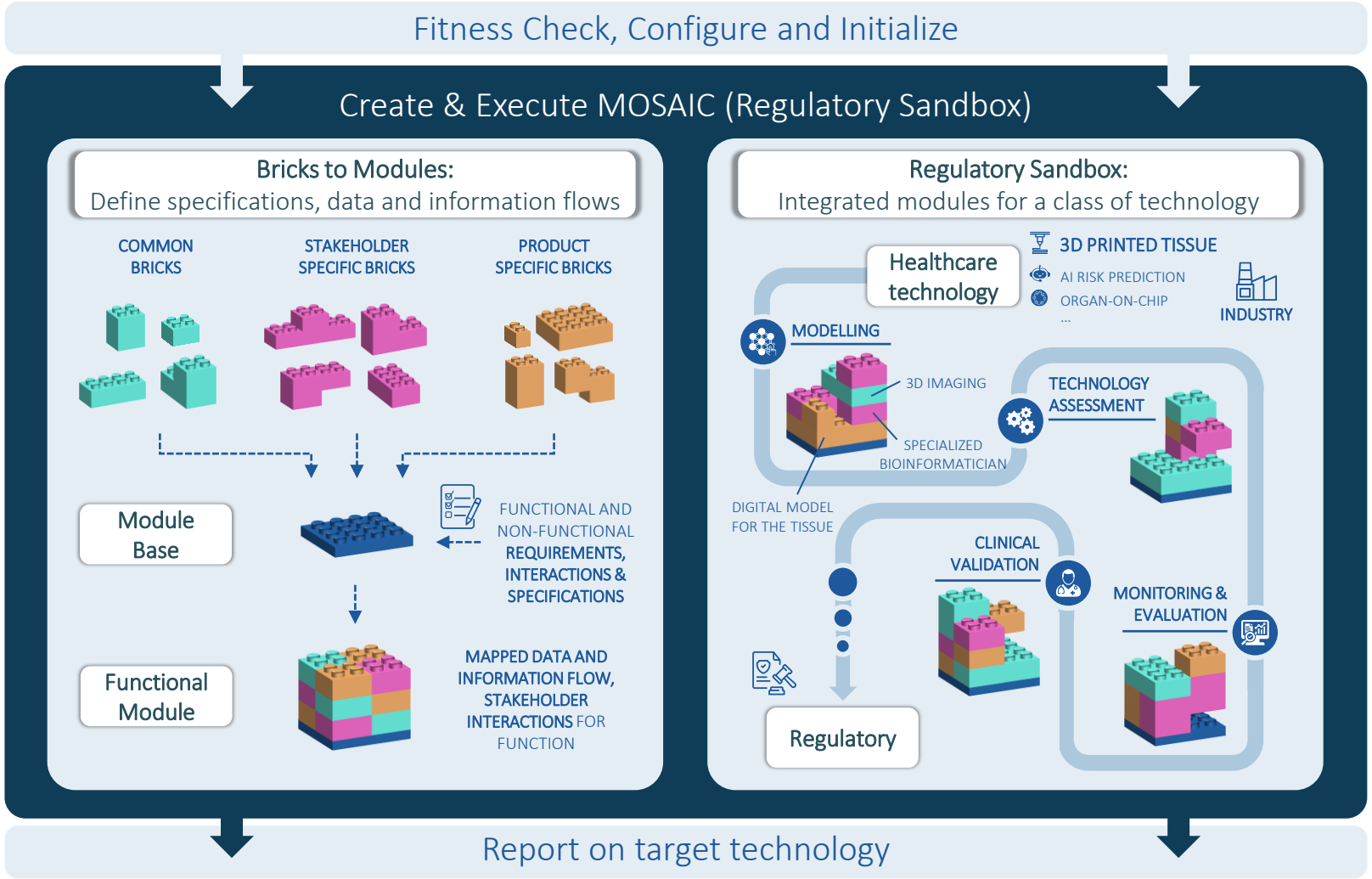
HTA assessor



https://realm-ai.eu/

Can we create a more generalized Regulatory Sandbox Implementation for all healthcare innovation crossborder in EU ?

Possibly –> Teaser … Upcoming



Actors & stakeholders for Implementation

- Digital Twin Application developers
- Notified Bodies
- National Competent Authorities
- HTA agencies
- TEF HEALTH
- EHDS
- AI Factories
- VHT Platform
- REALM
- …

Questions?

Interested? Please contact:

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