# Challenges and opportunities for digital therapeutics: key requirements to demonstrate value across the EU, England and the US

**Kipentzoglou N[1], Zegaoui Y[1], Satherley A[1], Whitehouse J[1], Thompson A[2].**

[1]Lightning Health, London, [2]University of Manchester

## Introduction

Digital therapeutics (DTx) deliver medical interventions using evidence-based, clinically evaluated software to treat, manage, and prevent a broad spectrum of diseases and disorders.[1]

The potential value of DTx is increasingly recognised by regulators and payers, with a record $14.7 billion invested into US digital health companies in H1 2021.[2]

To ensure healthcare systems recognise the value of DTx, assessment pathways must reflect their dynamic nature and the process of iterative improvements, whilst ensuring the cost-effective use of healthcare resources.

## Methods

A comprehensive review was conducted covering the EU, England, and US to identify processes for the evaluation of DTx, clinical/HEOR evidence requirements, and the implications for patient access. Insights were also obtained from manufacturers and budget holders.

## Research findings

### United States

#### The Digital Health Software Precertification (Pre-Cert) Program

The Digital Health Software Precertification (Pre-Cert) Program from the FDA is a pilot scheme that takes the new approach of regulating the company rather than the product.

The goal is to provide more efficient regulatory oversight of Software as a Medical Device (SaMD) products[3], to ensure patients' safety while leaving DTx innovators free to improve their products.

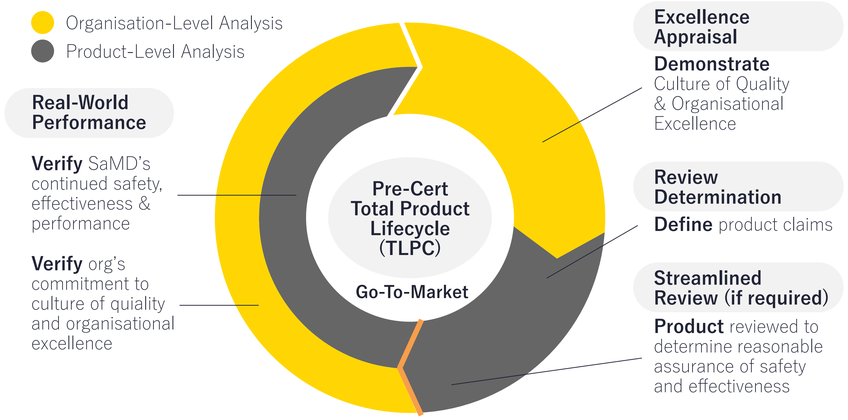


**Figure 1.** Proposed key components of a future Pre-Cert Program

The TPLC approach enables the evaluation and monitoring of a SaMD from premarket development to postmarket performance.[4] This involves 'excellence appraisal' to pre-certify a company, 'review determination' to determine the premarket review pathway, 'streamlined review' using information gained from the pre-certification process, and 'real world performance' based on how a product performs with patients.

#### Reimbursement for DTx in the US

A key challenge for uptake of DTx in the US is the business case for formulary inclusion by health plans. This is evolving, with Express Scripts and CVS Health from 2019 covering DTx in health plans.[5,6] Blue Cross Blue Shield[7], Medicaid[8], and Highmark Health[9] have also added digital solutions to their benefits lists.

US formulary committees typically consider the clinical outcomes, therapeutic value, effective usability, security/privacy standards, and cost-effectiveness for a new DTx. Payer insight suggests the key value driver is offset spending for costly chronic conditions, in particular prevention/management for diabetes and cardiovascular disease.

### Germany

Germany passed the Digital Care Act ('Digitale Versorgung Gesetz') in 2019[10], creating the fast-track process for digital health applications (DiGA) and enabling doctors to prescribe reimbursed DTx to publicly insured patients.

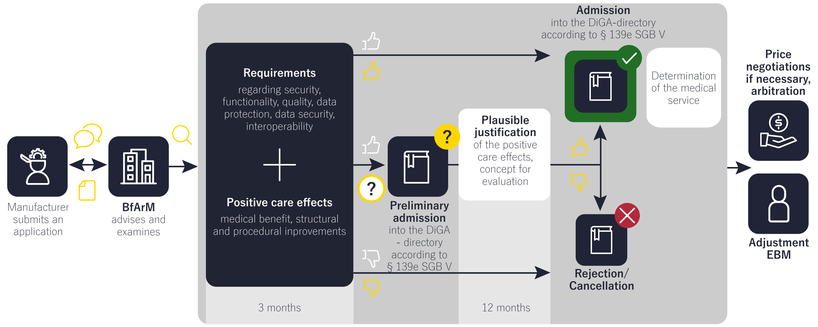


**Figure 2.** The fast-track process for digital health applications in Germany

#### DTx assessment process in Germany:

- Manufacturers register their CE-marked device (class I or IIa) at BfArM with information on product security, functionality, quality, data protection and data security, interoperability, and positive effects on healthcare through comparative studies[11]
- If product requirements are met and the evidence of positive effects on health care is provided, this results in inclusion in the DiGA register
- If sufficient evidence does not yet exist, there can be preliminary admission in the DiGA register with a 12–24-month test phase. If required evidence can be shown, this results in a final admission into the DiGA register[12]

#### Pricing for DTx in Germany:

- For 12 months after admission to the DiGA register, the price is set by the manufacturer
- After inclusion in the DiGA register, there is a price negotiation between the manufacturer and the GKV-SV, after which the negotiated price applies
- If there is no agreement, the arbitration board sets the reimbursement price within 3 months[13]

### Belgium

In 2021, INAMI-RIZIV announced a reimbursement scheme for DTx that are CE marked medical devices, with close alignment to the fast-track process for DTx in Germany.

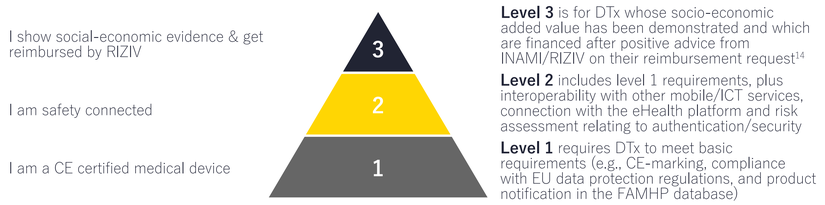


**Figure 3.** The Belgian mHealth Validation Pyramid

#### For products that meet level 1 and 2, the manufacturer can apply for reimbursement

- The manufacturer submits information to INAMI-RIZIV on how the DTx works, the existing healthcare process and future implications of using the DTx, and budget impact
- A working group evaluate the submission and submit advice (positive/negative) to the insurance committee, based on clinical evidence, integration into the healthcare system, improvement/potential to complement current practice, and budget impact
- Based on the advice of the working roup, the insurance committee decide on reimbursement.[15,16]

### England

#### DTx reimbursement in England is a decentralised process, with decision making by CCGs

To support NHS Commissioners, NICE has developed a risk-based approach to DTx reimbursement within its evidence standards framework.[17]

#### The NICE evidence standards framework for digital health technologies

| Clinical effectiveness | Economic impact |
|---|---|
| High-quality observational or quasi-experimental studies with relevant outcomes (including comparative data), a commitment to ongoing data on the usage and value of the DTx in the NHS, and quality and safeguarding requirements. | Information must be collected on the DTx user population size, care pathways, health/other outcomes from use, cost/resource use, and utilities (if cost-utility analysis is appropriate). The type of economic analysis will depend on the financial consequences of adopting the DTx. |

- **Low financial commitment:** Cost-consequence or budget impact analysis
- **High financial commitment:** Cost-utility analysis or cost-consequence analysis (if cost-utility analysis is not possible) and budget impact analysis

#### CCG level decision making

Despite NICE evidence standards, there is no centralised reimbursement model for DTx in England. Each CCG may have different submission requirements and containing budget impact is likely to be the key consideration within annual budget cycles.

### Key implications for manufacturers of DTx

| Core requirements | Details |
|---|---|
| **Quality management** | • Each DTx should have a Quality Management Scheme (QMS) certified according to ISO 13485 |
| **Information security management (ISM)** | • For any DTx capturing personal information, an ISO-compliant ISM system should be in place (e.g., ISO 27001) |
| **Interoperability in healthcare systems** | • Healthcare systems increasingly require interoperability with other mobile/ICT systems (e.g., electronic patient record systems) |
| **Clinical effectiveness** | • Positive impact vs SoC (medical outcomes or process of patient care)<br>• High quality intervention studies or RCTs should have an active comparator (or use historical controls if not possible) |
| **Real world evidence collection** | • Mechanisms should be in place for ongoing collection of usage data and patient outcomes to inform payer requests for post-launch data |
| **Economic value demonstration** | • Budget impact and cost-consequence modelling are likely to be most appropriate for DTx value demonstration |

### Recommendations for DTx manufacturers

**Develop an evidence-based value proposition to show relevant value for patients and healthcare systems**:

Early involvement of patient and public representatives is essential.

**Plan for reimbursement requirements from the start of DTx development:**

Requirements for QMS, information security, interoperability and evidence of clinical/economic value should inform the development strategy.

**Follow standardised frameworks for DTx to ensure alignment across markets:**

ISO standards for DTx are recognised across countries to inform quality/reliability
In the US, the AMCP has recognised NICE evidence standards for DTx.[18]

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Abbreviations. AMCP: Academy of Managed Care Pharmacy; DTx: Digital Therapeutics; BfArM: (German) Federal Institute for Drugs and Medical Devices; CCG: Clinical Commissioning Group; FAMHP: (Belgian) Federal Agency of Medicines and Health Products; FDA: (US) Food and Drug Administration; GKV-SV: (German) National Association of Statutory Health Insurance Funds; ICT: Information and Communication Technology; IMDRF: International Medical Device Regulators Forum; MDR: (European) Medical Devices Regulation; NICE: National Institute for Health and Care Excellence; INAMI-RIZIV: (Belgian) National Institute for Health and Disability Insurance; QMS: Quality Management Scheme; SaMD: Software as a Medical Device; TPLC: Total Product Life Cycle

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