Review of evidence requirements for HealthTech

REPORT BY THE DECISION SUPPORT UNIT

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EXECUTIVE SUMMARY

The objective of this report was to develop an overview of reported evidence requirements or related considerations around clinical efficacy or effectiveness, and/or safety (and any specification of preferred study designs), for HealthTech from relevant organisations internationally.

The websites of a total of 61 agencies and organisations across 34 countries, as well as 4 regional or international entities (e.g. European Commission, WHO) were searched for relevant documentation. This search was supplemented by reference checking of included documents.

The final total was 26 documents from/describing 21 agencies from across 13 countries, plus 5 documents from 4 regional/global entities (Europe, WHO). The majority of relevant agencies and documents were identified from North America (2 countries, 7 agencies and 13 documents) and Europe (9 countries plus three EU-wide bodies, a total of 12 agencies and 11 documents), with fewer in Asia/Australasia (2 countries, 5 agencies and 5 documents) and none from Central & South America or Africa.

The overview found that it is generally the case that few of the identified documents from the HTA or regulatory agencies outlined evidence standards or preferences more specific or detailed than those outlined by NICE. Only agencies in a few countries had similar detailed study design requirements or preferences (Australia, France, Ireland, Singapore, USA, Wales), and, like NICE, some of these agencies tended to report some preferences for 'local' studies or data also (Australia, Singapore, Wales). As with NICE, some countries' evidence requirements sometimes also specified a role for real world data or evidence (RWD/RWE) and three also stated a preference for evidence on diagnostic HealthTech that extends beyond test accuracy to demonstrate health outcome benefits (Australia, Ireland, Singapore).

As a point of difference from NICE, two countries also stated a preference for RCT-based indirect comparisons over non-RCT evidence or 'single-arm trials', if appropriate, in the absence of relevant RCT evidence for devices (Australia, Ireland).

Three also included published systematic reviews or meta-analyses within their evidence hierarchies (Finland DiGi-HTA, Australia ASERNIP-S, Wales), and four specified ‘minimum’ evidence requirements or standards, e.g. as a minimum only quantitative controlled or comparative studies were acceptable (EU Member State Coordination Group on HTA, Germany’s DiGA, Australia’s MDHTAC and ICER/PHTI in the US).

Some agencies also clarify that their stated preferences can differ depending on the nature, characteristics, classification or ‘level of risk’ associated with the HealthTech. Based on the documents identified, the remaining countries and agencies had less detailed evidence requirements. These might simply involve a requirement for non-specific objective evidence of device or DHT ‘performance’ or ‘efficacy and safety’.

The majority of the documents concerned devices and HealthTech generally rather than DHTs specifically, but the evidence requirements for the latter, where reported, were rarely very different

This overview is limited to data from English language documents from the most easily identified HTA and regulatory agencies. On the whole, only some of the major agencies in France, Australia, Singapore, Wales and the USA specify detailed evidence requirements similar to the NICE ESF for DHTs in terms of study designs and basic evidence ‘hierarchies’ (e.g. a preference for RCTs). None of the agencies with English language documents had no stated clinical evidence requirements at all, but the requirements for the majority, where reported in relevant documents, appear to outline only very general evidence around HealthTech’s performance (efficacy, effectiveness and accuracy), safety and risks, without reference to study designs or evidence hierarchies. Only two agencies reported that no clinical evidence standards were currently in place for DHTs, but this was because the requirements were in the process of being developed (Austria, Belgium).

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ABBREVIATIONS AND DEFINITIONS

Abbreviation	Definition / Meaning
ACE	Agency for Care Effectiveness
AETS ISCIII	Agencia de Evaluación de Tecnologias Sanitarias
AETS Mendoza	Agencia de Evaluacion de Tecnologias Sanitarias de Mendoza
AETSA	Andalusian Health Technology Assessment Department
AETSU	Agency of Health Technology Assessment of Uruguay
Agenas	The Agency for Regional Healthcare
AHRQ	Agency for Healthcare Research and Quality
AI	Artificial Intelligence
AIHTA	Austrian Institute for Health Technology Assessment
ANS	Agência Nacional de Saúde Suplementar / National Regulatory Agency for Private Health Insurance and Plans
AOTMiT	Agency for Health Technology Assessment and Tariff System
AP-HP	Assistance publique - Hopitaux de Paris
AQuAS	Agència de Qualitat i Avaluació Sanitàries de Catalunya
ARGMD	Australian Regulatory Guidelines for Medical Devices
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures - Surgical
AVALIA-T	Galician Agency for Health Technology Assessment
BfArM	Federal Institute for Drugs and Medical Devices
C2H	Centre For Outcomes Research And Economic Evaluation For Health
CDA-AMC	Canada’s Drug Agency
CDE	Centre for Drug Evaluation
CE	Conformité Européenne
CED	Coverage with Evidence Development

Abbreviation	Definition / Meaning
CMS	Centres for Medicare & Medicaid Services
CNEDiMTS	Medical Device and Health Technology Evaluation Committee
COA	Clinical Outcome Assessment
CONITEC	National Committee for Technology Incorporation
DHQI	The Danish Healthcare Quality Institute
DHT / DHTs	Digital Health Tech / Digital Health Technology / Technologies
DiGA	Digital Health Applications / Digital Health Application
DIGEMID	General Directorate of Medicines, Supplies and Drugs
DMEPOS	Durable Medical Equipment, Prosthetics, Orthotics, and Supplies
DMT / DMTs	Digital Medical Technologies / Digital Medical Technology / Technologies
DSU	Decision Support Unit
DVSV	Federation of Social Insurances / Dachverband der Sozialversicherungsträger
EBM	Evidence-Based Medicine
EC	European Commission
EG	Example
EMA	European Medicines Agency
EP / EPs	Essential Principles / Essential Principle
ESF	Evidence Standards Framework
EU	European Union
FDA	Food & Drug Administration
FinCCHTA	Finnish Coordinating Centre for Health Technology Assessment
G-BA	The Federal Joint Committee / Gemeinsamer Bundesausschuss

Abbreviation	Definition / Meaning
GCP	Good Clinical Practice
GÖG	Gesundheit Österreich GmbH
HAS	Haute Autorité de Santé
HealthTech	Health Technology
HIQA	Health Information and Quality Authority
HTA	Health Technology Assessment
HTACG	HTA Coordination Group
HTAIn	Health Technology Assessment of India
HTD	Health Technology Developer
HTW	Health Technology Wales
IACS	Health Sciences Institute in Aragon
ICER	Institute for Clinical and Economic Review
IDE	Investigational Device Exemption
IECS	Institute for Clinical Effectiveness and Health Policy
IHE	Institute of Health Economics
IMDRF	International Medical Device Regulators Forum
INEAS	National Authority for Assessment and Accreditation in Healthcare
INESSS	Institut national d'excellence en santé et en services sociaux
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
KCE	Belgian Health Care Knowledge Centre
MAH	Marketing Authorisation Holder

Abbreviation	Definition / Meaning
MaHTAS	Health Technology Assessment Section, Ministry of Health Malaysia
MASC / MSAC	Medical Services Advisory Committee
MCIT	Medicare Coverage of Innovative Technology
MD	Medical Devices / Medical Device
MDHTAC	Medical Devices and Human Tissue Advisory Committee
MHRA	Medicines & Healthcare products Regulatory Agency
MOST	Multiphase Optimisation Strategy
NDX	National Digital Exchange
NECA	National Evidence-based Healthcare Collaborating Agency
NICE	National Institute for Health and Care Excellence / National Institute of Health and Care Excellence
NIHDI	National Institute for Health and Disability Insurance
NIHO	National Institute for Value and Technologies in Healthcare
NIPH	Norwegian Institute of Public Health
OH	Ontario Health
OSTEBA	Basque Office for Health Technology Assessment
PCCP / PCCPs	Predetermined Change Control Plans
PCT	Pragmatic Clinical Trials
PL	Prescribed List
PMA	Pre-Market Approval Application
pVE	Evidence of Positive Effect / Positive Healthcare Effect
R&N	Reasonable and Necessary
RCT / RCTs	Randomised Controlled Trial / Trials
RER	Region Emilia-Romagna

Abbreviation	Definition / Meaning
RWD	Real-World Data
RWE	Real-World Evidence
SBU	Swedish Agency for Health Technology Assessment and Assessment of Social Services
SCHARR	Sheffield Centre for Health and Related Research
SFOPH	Swiss Federal Office of Public Health
SHTG	Scottish Health Technology Group
SK-NRCHD	Salidat Kairbekova National Research Centre for Health Development
SMART	Sequential Multiple Assignment Randomised Trial
TGA	Therapeutic Goods Administration
UETMIS[SS]	Health and Social Services Technology Assessment Unit
UK	United Kingdom
UVT	HTA Unit in A. Gemelli Teaching Hospital
WHO	World Health Organisation
ZIN	Zorginstituut Nederland
ZonMw	The Netherlands Organisation for Health Research and Development

1. BACKGROUND

This report concerns HealthTech, i.e. medical devices, diagnostics and digital health interventions, including artificial intelligence (AI). This excludes pharmaceuticals.

NICE does not have stated evidence standards for HealthTech generally but does outline some general standards or preferences for Digital HealthTech (DHT). The NICE (2022) Evidence Standards Framework (ESF) is a series of 21 evidence standards for Digital HealthTech (DHT), covering Design factors (1-9), Describing Value (10-13), Demonstrating Performance (14-16), Delivering Value (17-18), and Deployment (19-21). Each standard is specified as applying to some or all DHTs depending on the level of risk associated with that technology (categorised from 'A' for low risk to 'C' for high risk), with more numerous and rigorous standards being applied to technology deemed to represent higher levels of risk due to its role in diagnosing or treating a condition.

For the purposes of this work, the most relevant standard is number 14. This concerns the requirement to 'provide evidence of the DHT's effectiveness to support its claimed benefits'. The evidence requirements can depend on whether the technology is therapeutic or diagnostic.

The standard specified preferences for therapeutic DHTs are for UK evidence (or from a setting relevant to the UK health and social care system) and evidence that is comparative and prospective, i.e. randomised controlled trials (RCTs) are preferred over other designs to support the clinical management (treatment) of a specific condition 'where this study design is appropriate'. 'High-quality comparative real-world study designs' are also considered acceptable in the absence of experimental studies. It is important that the comparator in all such studies 'reflects the current NHS care pathway'. Test accuracy studies of DHTs – using an appropriate reference standard – are mentioned as being relevant to support diagnosis of a specific condition. So-called 'end-to-end' studies reporting 'downstream clinical consequences of the diagnosis or test outcome' are also seen as important for demonstrating clinical utility.

To inform evidence considerations, it is important that NICE are aware of any evidence preferences or requirements for HealthTech to be approved, purchased or used internationally. The aim of the current project therefore was to find and summarize any evidence requirements for HealthTech reported by HTA or regulatory agencies in countries and regions other than England, including if there is a lack of stated evidence requirements.

The agencies or organisations of interest, similar to the Medicines and Healthcare products Regulatory Agency (MHRA) and NICE in the UK and England, are either: 1) Health Technology Assessment (HTA) agencies or similar that specify evidence requirements for developing recommendations around the use of HealthTech within a particular health system or systems; or 2) regulatory authorities that specify clinical evidence requirements when establishing conformity with agreed standards for granting approval for the licensing of a HealthTech.

Research question: What are the stated requirements or related considerations for evidence of clinical efficacy or effectiveness and/or safety as reported by HTA and regulatory agencies internationally to get a funding or listing recommendation or other form of approval for HealthTech?

Objective: To develop an overview of reported evidence requirements or related considerations around clinical efficacy or effectiveness, and/or safety (and any specification of preferred study designs), for HealthTech from relevant organisations internationally.

2. METHODS

To be included in this report, documents had to satisfy the criteria outlined in Table 1:

Table 1: Eligibility criteria

	Inclusion	Exclusion
Technology	The guidance must be issued for specific types of HealthTech (e.g. digital HealthTech [DHT], interventional procedures etc.).	Pharmaceuticals
Evidence requirements	The document must include one or more statements concerning requirements, preferences or standards relating to evidence of clinical efficacy and/or safety of a HealthTech	No stated requirements
Countries / agencies	National HTA agencies, including those at international and regional level (e.g. EU, WHO), as well as national level.	England (and NICE)
	International regulatory agencies, e.g. from Europe [CE mark], Australia, Canada, and the United States	MHRA
Language	English	Documents not in English

CE: Conformité Européenne; EU: European Union; HTA: Health Technology Assessment; MHRA: Medicines & Healthcare products Regulatory Agency; NICE: National Institute of Health and Care Excellence; UK: United Kingdom; WHO: World Health Organization

In order to identify evidence requirements for recommendation or approval of HealthTech by relevant agencies, the websites of international HTA and regulatory organisations and agencies were searched for relevant documentation in English. This process mainly consisted of searching the website of each agency or organisation listed on the INAHTA Members List, although other relevant regulatory agencies, such as the Food & Drug Administration (FDA) in the USA, were also searched.

Website searches were conducted in April 2026 through a combination of browsing relevant sections of the website, such as those entitled ‘HTA’, ‘Publications’, ‘Reports’, ‘Guidelines’, ‘Methods/Methodology’ and similar, and/or using the website’s search function to search for relevant keywords such as ‘medical device’, ‘health technology’, ‘health technology assessments’, and then screening the results. For each website, relevant documents were either downloaded or webpages linked to for further, detailed

screening or an absence of relevant evidence was noted. This work was conducted by an information specialist (EP).

Reference checking of relevant included documents was also conducted by a reviewer (CC) to identify any relevant sources that had been missed by website searches.
The next stage consisted of detailed checking of the specified documents and webpages and extraction of any relevant (and related contextual) data or text on evidence requirements or preferences on demonstrating efficacy or safety to inform decision-making. These data were extracted into a form piloted on a set of known relevant documents and the final form agreed in consultation with NICE. The form included the following fields: country/region; agency and function; type of HealthTech; evidence requirements; document reference.

The information was then presented in a series of tables organised by geographical region and an overarching narrative summary for each was provided. This work was all conducted by a single reviewer (CC).

3. RESULTS

3.1. Searches and document selection

The websites of a total of 61 agencies and organisations across 34 countries, as well as 4 regional or international entities (e.g. European Commission, WHO) were searched for relevant documentation. The results of these searches are presented in Tables 2 and 3, organised by region and country.

A total of 16 different agencies' websites and related resources across 9 countries (Australia, Belgium, Canada, France, Ireland, Scotland, Wales, Singapore, USA) and 4 international entities (e.g. European Medicines Agency [EMA], European Commission [EC] [Joint Clinical Assessment] on HTA, EC Member State Coordination Group on HTA and World Health Organization [WHO]) were found to hold documents with relevant information in English on clinical evidence requirements (Table 2). No relevant information in English was found in documents sourced from the remaining 44 agencies' websites and related resources across 29 countries or international entities (Table 3).

In addition to the search results, evidence in English was identified from included documents for an additional five countries and agencies (the websites of some of these agencies had been searched but no English data found): Austria (AIHTA), Finland (DiGi-HTA), Germany (DIGA), Netherlands (NZa) and the Australian agency MDHTAC. Details of these additions are included in the Results tables.

The final total was 26 documents from/describing 21 agencies from across 13 countries, plus 5 documents from 4 regional/global entities (Europe, WHO). The majority of relevant agencies and documents were identified from North America (2 countries, 7 agencies and 13 documents) and Europe (9 countries plus three EU-wide bodies, a total of 12 agencies and 11 documents), with fewer in Asia/Australasia (2 countries, 5 agencies and 5 documents) and none from Central & South America or Africa. A country could have more than one relevant agency, and one agency might have more than one relevant document containing clinical evidence requirements for HealthTech (e.g. the US FDA had six identified separate documents with relevant content).

Table 2: Sources from search where documentary evidence retrieved

Country/ region	HTA agency / organisation	Main webpage	Guidance date	Guidance title/ topic	Document webpage url
EUROPE					
Belgium	KCE - Belgian Health Care Knowledge Centre	https://kce.fgov.be/en	2023	Evaluation of Digital Medical Technologies	https://kce.fgov.be/en/evaluation-of-digital-medical-technologies
France	Haute Autorité de Santé (HAS)	https://www.has-sante.fr/	2021	Pathway of medical devices in France	https://www.has-sante.fr/jcms/p_3213810/en/pathway-of-medical-devices-in-france
France	Haute Autorité de Santé (HAS)	https://www.has-sante.fr/	2021	Methodology for the clinical development of medical devices.	https://www.has-sante.fr/upload/docs/application/pdf/2021-09/guide_methodology_for_the_clinical_development_of_md.pdf
Ireland	Health Information and Quality Authority (HIQA)	https://www.hiqa.ie/	2019	Guidelines for Evaluating the Clinical Effectiveness of Health Technologies in Ireland	https://www.hiqa.ie/reports-and-publications/health-technology-assessment/guidelines-evaluating-clinical-effectiveness
Scotland	Scottish Health Technology Group (SHTG)	https://shtg.scot/	2023	Evidence Framework	https://shtg.scot/what-we-do/evidence-framework/
Wales	Health Technology Wales	https://healthtechnology.wales/	2024	Appraisal Process Guide	https://healthtechnology.wales/about/our-appraisal-process/
EU	European Commission (Joint Clinical Assessment)	https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-	2025	Guidance on filling in the Joint Clinical Assessment dossier template of a Medical Device	https://health.ec.europa.eu/publications/guidance-filling-joint-clinical-assessment-jca-dossier-template-medical-devices-and-vitro-diagnostic_en

Country/ region	HTA agency / organisation	Main webpage	Guidance date	Guidance title/ topic	Document webpage url
		assessment/joint-clinical-assessments_en			
EU	European Commission (Joint Clinical Assessment)	https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-assessment/joint-clinical-assessments_en	2024	Guidance on the validity of clinical studies for joint clinical assessments	https://health.ec.europa.eu/publications/guidance-validity-clinical-studies-joint-clinical-assessments_en
EU	European Commission	https://health.ec.europa.eu/	2025	Briefing Document template for HTA Coordination Group (HTACG) Joint Scientific Consultation (JSC) for Medical Devices (MD)	https://health.ec.europa.eu/health-technology-assessment/key-documents_en?f%5B0%5D=topic_topic%3A227&f%5B1%5D=topic_topic%3A236
EU	European Medicines Agency	https://www.ema.europa.eu/en/homepage	last updated 2025	Questions and answers on implementation of the medical devices and in vitro diagnostic medical devices Regulations ((EU) 2017/745 and (EU) 2017/746)	https://www.ema.europa.eu/en/human-regulatory-overview/medical-devices
NORTH AMERICA					
Canada	Health Canada	Home - Canada.ca	2026	Guidance on clinical evidence requirements for medical devices: Submitting clinical evidence - Canada.ca	Guidance on clinical evidence requirements for medical devices: Submitting clinical evidence - Canada.ca
Canada	Institut national d'excellence en santé	https://www.inesss.qc.ca/en/index.html	2024	A GUIDE TO SUPPORT VALUE ASSESSMENT	https://www.inesss.qc.ca/en/methodology/methodology-documents.html

Country/ region	HTA agency / organisation	Main webpage	Guidance date	Guidance title/ topic	Document webpage url
	et en services sociaux (INESSS)				
USA	Agency for Healthcare Research and Quality (AHRQ)	https://www.ahrq.gov/	2022	Analysis of Requirements for Coverage With Evidence Development (CED) – Topic Refinement	https://www.ahrq.gov/research/findings/ta/index.html
USA	Institute for Clinical and Economic Review (ICER)	https://icer.org/	2023	The 2023 Value Assessment Framework	https://icer.org/our-approach/methods-process/value-assessment-framework/
USA	Institute for Clinical and Economic Review (ICER) / PHTI	https://icer.org/	2023	ICER-PHTI Assessment Framework for Digital Health Technologies	https://icer.org/assessment/icer-phti-assessment-framework-fordigital-health-technologies/#timeline
USA	U.S. Food & Drug Administration (FDA)	https://www.fda.gov/	2016	Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/leveraging-existing-clinical-data-extrapolation-pediatric-uses-medical-devices
USA	U.S. Food & Drug Administration (FDA)	https://www.fda.gov/	2025	Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices
USA	U.S. Food & Drug Administration (FDA)	https://www.fda.gov/	2024	Predetermined Change Control Plans for Medical Devices	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/predetermined-change-control-plans-medical-devices

Country/ region	HTA agency / organisation	Main webpage	Guidance date	Guidance title/ topic	Document webpage url
USA	U.S. Food & Drug Administration (FDA)	https://www.fda.gov/	2023	Content of Premarket Submissions for Device Software Functions	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-device-software-functions
ASIA & AUSTRALASIA					
Australia	Medical Services Advisory Committee (MASC)	https://www.msac.gov.au/		Guidelines for preparing assessments for the Medical Services Advisory Committee	
Australia	Australian Safety and Efficacy Register of New Interventional Procedures -Surgical (ASERNIP-S)	https://www.surgeons.org/research-audit/research-evaluation-inc-asernips		General guidelines for assessing, approving and introducing new procedures into a hospital or health service	https://www.surgeons.org/research-audit/research-evaluation-inc-asernips/publications
Singapore	Agency for Care Effectiveness (ACE)	https://www.ace-hta.gov.sg/		Medical Technologies Evaluation Methods and Process Guide	
Global	WHO	https://www.who.int/	2025	Health technology assessment of medical devices, 2nd ed	https://www.who.int/publications/i/item/9789240110878

Table 3: Sources / agencies searched but no documents identified containing relevant data in English

Country/region	HTA agency/organization	Main webpage	Notes
EUROPE			
Austria	Austrian Institute for Health Technology Assessment (AIHTA)	https://aihta.at/page/homepage/en	Documents not in English (but English summary found in another document)
Austria	Federation of Social Insurances (Dachverband der Sozialversicherungsträger), (DVSV)	https://www.sozialversicherung.at/cdscontent/?contentid=10007.821628&portal=svportal	No eligible documents
Austria	Gesundheit Österreich GmbH, (GÖG)	https://goeg.at/en	Documents not in English
Denmark	The Danish Healthcare Quality Institute, (DHQI)	https://www.sundk.dk/about/	Documents not in English
Finland	Finnish Coordinating Center for Health Technology Assessment, (FinCCHTA)	https://fincchta.fi/	No available documents
France	Assistance publique- Hopitaux de Paris (AP-HP)	https://www.aphp.fr/	No eligible documents
Germany	The Federal Joint Committee (Gemeinsamer Bundesausschuss), G-BA	http://www.g-ba.de	Documents not in English
Germany	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG)	https://www.iqwig.de/en/	Documents not in English
Italy	The Agency for Regional Healthcare (Agenas)	https://www.agenas.gov.it/	No eligible documents
Italy	RER – Regione Emilia-Romagna	https://salute.regione.emilia-romagna.it/	No eligible documents
Italy	UVT – HTA Unit in A. Gemelli Teaching Hospital		Website not found

Netherlands	Zorginstituut Nederland (ZIN)	https://www.zorginstituutnederland.nl/	No eligible documents
Netherlands	The Netherlands Organisation for Health Research and Development (ZonMw)	https://www.zonmw.nl/en	No eligible documents and some documents not in English
Norway	Norwegian Institute of Public Health (NIPH)	https://www.fhi.no/en/	No eligible documents
Poland	Agency for Health Technology Assessment and Tariff System (AOTMiT)	https://www.aotm.gov.pl/	Documents not in English
Spain	Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS)	https://aquas.gencat.cat/ca/inici	No eligible documents
Spain	Galician Agency for Health Technology Assessment (AVALIA-T)	https://acis.sergas.gal/	Documents not in English
Spain	Agencia de Evaluación de Tecnologias Sanitarias (AETS ISCIII)	https://www.isciii.es/en/agencia-evaluacion-tecnologias-sanitarias-sobre-nosotros	Documents not in English
Spain	Andalusian Health Technology Assessment Department (AETSA)	https://www.aetsa.org/	Documents not in English
Spain	Health Sciences Institute in Aragon, (IACS)	https://www.iacs.es/	Documents not in English
Spain	Basque Office for Health Technology Assessment (OSTEBA)	https://www.euskadi.eus/web01-a2ikeost/en/	Documents not in English
Slovakia	National institute for Value and Technologies in Healthcare (NIHO)	https://niho.sk/	Links to EUnetHTA methods (searched separately)
Sweden	Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU)	https://www.sbu.se/en/	No eligible documents
Switzerland	Swiss Federal Office of Public Health (SFOPH)	https://www.bag.admin.ch/en	Documents not in English

EU	EUnetHTA	https://tools.eunethta.be/	Archived site/documents; linked to EU Commission site (searched separately)
NORTH AMERICA			
Canada	Canada's Drug Agency (CDA-AMC)	https://www.cda-amc.ca/	No eligible documents (too general, not healthtech specific)
Canada	Institute of Health Economics, (IHE)	https://ihe.ca/	No eligible documents
Canada	Ontario Health (OH)	https://www.ontariohealth.ca/	No eligible documents
SOUTH & CENTRAL AMERICA			
Argentina	Agencia de Evaluacion de Tecnologias Sanitarias de Mendoza (AETS Mendoza)	https://aets.com.ar/	Documents not in English
Argentina	Institute for Clinical Effectiveness and Health Policy (IECS)	https://iecs.org.ar/en/	No eligible documents
Brazil	Agência Nacional de Saúde Suplementar/ National Regulatory Agency for Private Health Insurance and Plans (ANS)	https://www.gov.br/ans/pt-br	No eligible documents
Brazil	National Committee for Technology Incorporation, (CONITEC)	https://www.gov.br/conitec/pt-br	Documents not in English
Colombia	Instituto de Evaluación Tecnológica en Salud (IETS)	https://iets.org.co/	No eligible documents
Peru	General Directorate of Medicines, Supplies and Drugs, (DIGEMID)	https://medenvoyglobal.com/in-country-representation/peru-digemid/	No eligible documents
Uruguay	Agency of Health Technology Assessment of Uruguay (AETSU)	https://aetsu.org.uy/	Documents not in English; links to WHO guidance

ASIA & AUSTRALASIA			
China	Center for Drug Evaluation (CDE)	https://www.cde.org.tw/cdeen/	No available documents
India	Health Technology Assessment of India, Ministry of Health & Family Welfare (HTAIn)	https://htain.dhr.gov.in/	Unable to access website
Japan	Center For Outcomes Research And Economic Evaluation For Health (C2H)	https://c2h.niph.go.jp/en/	No eligible documents
Kazakhstan	Salidat Kairbekova National Research Center for Health Development (SK-NRCHD)	http://www.rcrz.kz	Unable to access website
Malaysia	Health Technology Assessment Section, Ministry of Health Malaysia, (MaHTAS)	https://hq.moh.gov.my/medicaldev/cawangan-penilaian-teknologi-kesihatan/	No available documents
New Zealand	PHARMAC – NEW ZEALAND	https://www.pharmac.govt.nz/	No eligible documents
South Korea	NECA – National Evidence-based healthcare Collaborating Agency, KOREA	https://www.neca.re.kr/	No eligible documents
AFRICA			
Tunisia	National Authority for Assessment and Accreditation in Healthcare (INEAS)	https://www.ineas.tn/fr	Documents not in English
GLOBAL			
International	International Medical Device Regulators Forum (IMDRF)	IMDRF “Software as a Medical Device": Possible Framework for Risk Categorization and Corresponding Considerations (2014)	Nothing on evidence standards, just categories of devices

3.2. Evidence requirements by region and country

The key edited data on evidence requirements are presented in the Appendix in Tables 5a, 5b (Europe), 6a, 6b, 6c (North America), 7 (Asia and Australasia) and 8 (Global).

3.2.1. Europe

For Europe, relevant data were identified from nine countries (nine agencies) (Austria (AIHTA), Belgium (KCE), Finland (FinCCHTA/DiGi-HTA), France (HAS/CNEDiMTS), Germany (BrArM/DiGA), Ireland (HiQA), the Netherlands (NZa), Scotland (SHTG) and Wales (HTW), as well as for the region more broadly (European Commission/European Union) (Table 4). Each country had a single relevant document, except for France, which had two relevant 'Guides'. And information from a third document.

It should be noted that the information presented on the clinical evidence requirements for DHTs in Austria, Finland and France are extracted from a report produced by the Belgian Health Care Knowledge Centre (KCE) (Evaluation of Digital Medical Technologies, 2023)*. The KCE compiled these data as part of the process in developing its own evidence standards and requirements (unspecified in the document and ongoing). The source documents were not available in English (see Table 3) and so were not extracted directly for this report. It should also be noted that, in terms of HealthTech, all of these clinical evidence requirements concerned DHTs only, except for France, for which requirements for devices are also presented.

3.2.1.1. Austria*

*Austrian Institute of Health Technology Assessment (AIHTA)**

The development of evidence requirements for DHTs was reported to be 'ongoing' in the Belgium KCE guide for the Evaluation of Digital Medical Technologies (DMTs) (2023) .

The evidence requirements did include specifying study designs (e.g. RCT is the preferred evidence) but there was no comment on prioritising local data. It is noted that the requirements were similar to NICE.

3.2.1.2. Belgium

*Health Care Knowledge Centre (KCE)**

The guide for the Evaluation of Digital Medical Technologies (DMTs) (2023) specifies only the most basic evidence requirements for reimbursement. The development of these requirements was reported to be 'ongoing' in this document.

The evidence requirements do not include specifying study designs (e.g. RCT is the preferred evidence) or prioritising local data.

The 'requirements' for reimbursement of DHTs – beyond regulatory approval – were stated as 'a demonstration of socio-economic value' (undefined).

3.2.1.3. Finland

*DiGi-HTA**

The Belgium KCE guide for the Evaluation of Digital Medical Technologies (DMTs) (2023) specifies clinical evidence requirements for DHTs both for medical benefit and organisational improvement.

The evidence requirements did include specifying study designs (e.g. RCTs, observational studies etc.) but noted that this could also include evidence from Cochrane reviews. There was no comment on prioritising local data.

The requirements could be different depending on class of DHT. RCTs of 'similar HealthTech products' would also be considered.

3.2.1.4. France

Medical Device and Health Technology Evaluation Committee (CNEDiMTS) part of Haute Autorité de santé (HAS)

Following regulatory approval (CE mark), the clinical evidence requirements for medical devices submitted to CNEDiMTS for reimbursement listing are outlined in two documents: Methodology for the clinical development of medical devices.

Methodology Guide. Assess Health Technologies (2021) and Pathway of medical devices in France. Guide. Assess Health Technologies (2021).

The evidence requirements include specifying study designs (e.g. RCT is the preferred evidence) but not prioritising local data.

The requirement is for 'conclusive clinical studies'. Multi-centre, double-blind RCTs are considered the preferred evidence, but the choice of other experimental designs is permissible as long as justification can be provided that this alternative design is more suitable for the device. It is also acknowledged that the choice of study design is dependent on the device itself (use and purpose), the existence of alternatives and size of relevant patient population etc..

*According to the Belgium KCE summary document, the requirements outlined by CNEDiMTS for DHTs are similar to those given above for devices, i.e. no specific rules on type of studies (or size) to prove clinical benefits, but RCTs are considered gold standard and the decision to use other types of studies must be justified.

3.2.1.5. Germany

Federal Institute for Drugs and Medical Devices (BfArM)

The Fast-Track Process for Digital Health Applications (DiGA) appears in the Guide for Manufacturers, Service Providers and Users (2020) and specifies clinical evidence requirements. These underpin the required Evidence of Positive Effect (pVE) of a DHT. This effect 'may derive either from the area of medical benefit or from the area of patient-relevant improvement of structure and processes'. A manufacturer must prove such an effect in a defined patient group.

The evidence requirements did include specifying study designs (e.g. RCTs, cohort studies) but not prioritising local data (only that the comparator is 'oriented on the reality of healthcare').

Numerous different designs are listed as acceptable, but no preferred hierarchy of study designs is presented. The most important characteristic is that they are

'quantitative comparative' studies, with the minimum being a 'retrospective comparative' design. The presence of a control is crucial to demonstrate that the application of the DHT has value relative either to alternatives or not applying it.

3.2.1.6. Ireland

Health Information and Quality Authority (HIQA)

The Guidelines for Evaluating the Clinical Effectiveness of Health Technologies in Ireland (2018) specifies clinical evidence requirements for all technologies, including pharmaceuticals and Health Tech.

The evidence requirements include specifying study designs (e.g. RCT is the preferred evidence) but not prioritising local data.

RCTs are considered the preferred evidence unless unavailable. The preferences do not quite follow the standard hierarchy of study designs but, in the absence of RCTs, extends to a preference for indirect comparison over to single arm data.

3.2.1.7. Netherlands

Dutch Health Authority (Nederlandse Zorgautoriteit, NZa)

The Belgium KCE guide for the Evaluation of Digital Medical Technologies (DMTs) (2023) specifies clinical evidence requirements for DHTs both for medical benefit and organisational improvement.

The evidence requirements did not include specifying study designs, and there was no comment on prioritising local data.

The statement only specified evidence on relative effectiveness of the new technology versus current standards.

3.2.1.8. Scotland

Scottish Health Technology Group (SHTG)

The Evidence Framework (2023) mirrors the general domains of the NICE ESF for DHTs but is to apply to all HealthTech, specifying some clinical evidence preferences for demonstrating or supporting the claimed benefits of a technology.

The evidence requirements include only a broad specification of study design (e.g. experimental and quasi-experimental interventional studies) and prioritising local data (care options that reflect current NHS Scotland care pathways).

There is only a stated preference for 'interventional studies', and when it is not 'possible, ethical or relevant' to conduct such a study, then the framework asks if there are any observational studies. Standards are also applied to real-world evidence, i.e. to assess whether the technology performed to its expected level.

3.2.1.9. Wales

Health Technology Wales (HTW)

The Health Technology Wales Appraisal Process Guide (2024) specifies clinical evidence preferences for HealthTech.

The evidence requirements include specifying study designs (e.g. RCT is preferred) and prioritising local data (comparisons with current treatment and care options).

RCTs are considered the preferred evidence unless unavailable. The preferences follow a standard hierarchy of study designs e.g., where RCTs are unavailable or not feasible then non-RCTs and observational studies are acceptable; and data from single arm studies are only to be included if there are no comparative data. Data can also be used from 'well-conducted' secondary analyses.

3.2.1.10. Europe region

The European Union also has two bodies related to HTA that provide some information on clinical evidence requirements: the European Commission (Joint Clinical Assessment) and the Member State Coordination Group on HTA. Inevitably perhaps, these bodies have very general requirements around the provision of evidence

following international standards of evidence-based medicine (EBM), including that all relevant efficacy, effectiveness and safety data for a device or other HealthTech is made available, including 'high-quality real-world data' such as 'those provided by internationally recognised disease registries', although it is also noted that evidence below a minimum level for internal and external validity and statistical precision might be excluded if sufficient higher level evidence is available.

The European Medicines Agency (EMA) evidence requirements for regulatory approval are summarised in Table 5b. This largely consists of the provision of evidence on a device's 'performance and safety' and its compliance / conformity with the agency's requirements on Medical Devices Regulation (EU) 2017/745 (MDR). These General Requirements can be summarised as: 'devices shall achieve the performance intended by their manufacturer and … are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users…'. This includes requirements that a manufacturer specifies and justifies the level of clinical evidence necessary to demonstrate conformity with the safety and performance requirements of the regulation, including post-marketing surveillance. In the event that these evidence requirements are met, a device can acquire a Declaration of Conformity, the CE mark (Conformité Européenne).

All of the European HTA agencies require regulatory approval from the EMA before a device or DHT can 'move' to evaluations for reimbursement or similar listings. The regulatory requirements detailed above are also explained in many of the HTA agency guidance documents cited in Table 5a, as well as additional documents such as the French Haute Authorité Santé (HAS) Pathway of medical devices in France Methodology guide (2022). This latter document is not specifically included in any tables because its key content is covered in Table 5b.

3.2.2. North America region

For North America relevant data were identified for the USA from one public organisation that makes determinations concerning listing of technologies on their plans (CMS), three HTA agencies (AHRQ, ICER, PHTI) (Table 6a) and one regulatory agency, the FDA (Table 6b). For Canada, two agencies were identified, one HTA (INESSS) and one regulatory (Canada Health) (Table 6c). It should be noted that, in terms of HealthTech, the clinical evidence requirements presented concern – where specified - DHTs, devices and, in some cases, other 'items and services'.

3.2.2.1. USA

The data for non-regulatory agencies in the US are presented in Table 6a.

CMS and AHRQ

The evidence requirements for the listing of 'items and services' on plans from the Centers for Medicaid and Medicare Services (CMS) are limited and covered both by the CMS documents and the HTA Agency for Healthcare Research and Quality (AHRQ), which outlines additional evidence requirements for listing/reimbursement on the CMS programs.

The evidence requirements did not include specifying study designs or prioritising local data.

Items and services need only be demonstrably 'reasonable and necessary for the diagnosis of treatment of illness or injury', i.e. that they are 'safe and effective' and not 'experimental or investigational'.

When CMS decides that there is insufficient evidence to conclude definitively that an item or service is "reasonable and necessary," including FDA-approved products, it may issue a Coverage with Evidence Development (CED) decision, which allows patients to access these select medical items and services, with coverage, on the condition that there is prospective collection of agreed upon clinical data (AHRQ, 2022). The evidence requirements for this are outlined by the AHRQ and include 'evidence of net benefit', clinically meaningful differences demonstrable for the

technologies according to case-by-case agreed ‘evidentiary thresholds’ (set by the sponsors/investigators of the technology), for the primary outcomes, and to reflect the diversity of the local patient populations.

ICER

The Value Assessment Framework (2023) specifies clinical evidence requirements for devices.

The evidence requirements include specifying study designs (e.g. RCT is the preferred evidence) but do not specifically prioritise local data.

RCTs and systematic reviews/meta-analyses are considered the preferred evidence but no limits are placed on study designs (e.g. observational designs, including cohort and case-control studies, are valued for providing longer term evidence of benefits and harms) or approach (e.g. indirect comparisons are accepted in the absence of head-to-head RCTs). Weight is also placed on the value of Real World Evidence (RWE) to complement existing experimental data.

ICER & PHTI

The Assessment Framework for Digital Health Technologies (2023) specifies clinical evidence requirements for different ‘tiers’ of DHTs, like NICE, determined by their function and the level of risk to patients.

The evidence requirements include specifying study designs (e.g. RCTs, quasi-experimental and observational studies) and prioritising local data in the highest risk tiers.

The evidence requirements follow a general hierarchy, with the highest risk DHTs requiring higher levels of evidence (including some local data) relative to simple evidence of health outcomes or test accuracy in cases where the DHTs are considered to be low risk.

For the lowest risk devices, the minimal requirements concern ‘accuracy’ and the ‘maximum’, empirical data on health improvement. For the moderate risk devices, the

minimal requirements concern ‘an evaluation of accuracy and precision’ against an established gold-standard and the ‘maximum’ (for the ‘highest risk’ devices of this type) might require RCTs. For the highest risk devices, the minimal requirements are evidence from ‘high-quality quasi-experimental or observational studies’, and the ‘maximum’, depending on the level of ‘high risk’ associated with the DHT, ranged from RCTs demonstrating efficacy to RCTs that include relevant ‘local data’ (i.e. conducted in populations and health systems of interest).

The data for regulatory agencies in the US are presented in Table 6b.

FDA

The FDA has produced a series of six relevant documents, five of which are listed here (dating from 2013 to 2025), specifying clinical evidence requirements devices, and one of which concerns DHTs (2023).

The evidence requirements include specifying study designs (e.g. ‘valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts’ [FDA, 2018)). No mention is made about prioritising local data.

The many guidance documents are consistent in their summary of evidence requirements. The overall principle is the requirement for ‘valid scientific evidence’ to ‘substantiate the safety and effectiveness of a device’ (2025, 2013); there must be a ‘reasonable assurance of safety and effectiveness’ (2025, 2024, 2018, 2013). Contained within this is the acceptance that the evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions (2016, 2013). The approach is generally inclusive and does not specifically follow an evidence hierarchy, with the exception of the principle ‘that evidence of effectiveness of a medical device must generally be obtained from well-controlled studies’ (2013). The DHT guidance, by contrast, requires only ‘objective evidence that the selected DHT appropriately assesses the clinical event or characteristic in the proposed participant population (e.g., step count or heart rate). DIFF from NICE REQS

3.2.2.2. Canada

The data for Canada are presented in Table 6c. From Canada, one document, from the Quebec HTA Agency (INESSS), outlined the clinical evidence requirements for HealthTech, but the document available in English was very basic.

The evidence requirements did not include specifying study designs and prioritising local data.

The document only states that criteria by which HealthTech should be assessed include clinical efficacy and safety.

A little more detail is provided on evidence requirements for regulatory approval for medical devices from Health Canada.

The evidence requirements did not include specifying study designs or prioritising local data, although a requirement is that the clinical evidence should demonstrate how the device affects ‘diverse subpopulations’.

Specific study designs are not mentioned, but a device ‘must have objective evidence to support its safety and effectiveness’ within the parameters set for its use. It is also explicit about the necessity to provide evidence on the risks and benefits – and uncertainties regarding this.

3.2.3. Asia & Australasia

For Asia and Australasia (Table 7), only agencies from Singapore (ACE) and Australia (MSAC, TGA, MDHTAC, ASERNIP-S) were found to report explicit evidence requirements for HealthTech. It should be noted that, in terms of HealthTech, the Singapore requirements relate to DHTs, where-as the Australian requirements mostly concern devices.

3.2.3.1. Singapore

From Singapore, one document, from the HTA Agency for Care Effectiveness (ACE), outlined the clinical evidence requirements for Medtech, investigative technologies and DHTs. The stated focus was on demonstrating the clinical benefits of the HealthTech.

The evidence requirements include specifying study designs (e.g. RCT is the preferred evidence for therapeutic HealthTech evaluations) and prioritising local data.
NICE ESF 14 is cited in the document to support the approach that the highest 'levels' of evidence are preferred, but alternative, lower levels of evidence can be accepted in their absence, e.g. non-RCTs if there are no RCTs; retrospective studies if there are no prospective studies).

For Medtech generally and therapeutic DHTs, the preference is for clinical evidence from RCTs directly comparing the HealthTech with the health system's current comparator, or comparative RWE studies for DHTs to demonstrate their impact on patient or clinically relevant outcomes and health system outcomes. In the absence of such evidence, 'lower levels of evidence without design or quality threshold restrictions are often considered, if they are relevant to the intended use and claimed benefits of the technology'. Beyond the preference for test accuracy studies, both 'investigative technologies' and diagnostic DHTs preferred 'end-to-end' evidence, i.e. evaluations not only of the accuracy of a diagnostic test, but also of the patient or clinical outcomes further down the line.

3.2.3.2. Australia

From Australia, documents were identified that outlined clinical evidence requirements for devices from a regulator (Therapeutic Goods Administration) and two HTA agencies (Medical Services Advisory Committee and Medical Devices and Human Tissue Advisory Committee), and for surgical procedures (which often make use of medical devices) from the Royal Australasian College of Surgeons.

Therapeutic Goods Administration (TGA)

The Australian Regulatory Guidelines for Medical Devices (ARGMD) (2024) and the Clinical evidence guidelines for medical devices (2023) from the TGA outline the clinical evidence requirements for devices.

These evidence requirements do not include specifying study designs and do not specifically prioritise local data.

The document states that the clinical evidence for such devices 'appropriate to the use and classification of the device' and needs to comply with Essential Principle 14, i.e. that the clinical evidence is 'sufficient to demonstrate an appropriate level of safety and performance when used for their intended purpose(s)'. Evidence from 'comparable devices' that are not deemed equivalent does not satisfy the requirements.

Medical Services Advisory Committee (MSAC)

The Guidelines for preparing assessments for the MSAC (2021) specifies clinical evidence requirements for both therapeutic and investigative technologies.

The evidence requirements include specifying study designs (e.g. RCT is the preferred evidence) and prioritising local data.

RCTs are considered the preferred evidence unless their data are not applicable to Australia or none is available – highlighting, again, the importance of local data. The preferences follow the standard hierarchy of study designs, with comparative evidence preferred. This extends to preferences for indirect comparisons relative to single arm

data. Other than indirect comparison, these preferences also extend to investigative technologies, and a preference for ‘direct from test to health outcomes evidence’.

Medical Devices and Human Tissue Advisory Committee (MDHTAC)

The Member Guidelines (2021) specifies clinical evidence requirements.

The evidence requirements do not include specifying study designs but do prioritise local data. Comparative data are a requirement. A technology cannot be ‘less clinically effective’ than a relevant comparator.

The document only specifies ‘the best available evidence’ compared with other products on the local prescribed list (PL) or an alternative.

Royal Australasian College of Surgeons (ASERNIP-S)

The Guidelines for Assessing, Approving and Introducing New Surgical Procedures (undated) specifies a broad hierarchy of clinical evidence requirements.

The evidence preferences include specifying, first, publication types, i.e. systematic reviews or HTAs on the new procedure, and then, in their absence, study designs, with RCTs being the first cited. However, other study designs, including case series and case reports and other evidence are also deemed acceptable, although all evaluations should consider the ‘likely robustness’ of such evidence along with other factors.

Procedures that are likely to have wider coverage than others are also deemed to require more intensive evaluation of evidence.

3.2.4. Global

The only global agency with any reference to evidence requirements for devices and DHTs was the World Health Organization (WHO), which had a single document on HTA. See Table in the Appendix.

The evidence requirements did not include specifying study designs but do prioritise local data.

The document only specified ‘the best available evidence’ and ‘local data’. It accepted that such evidence might not be ‘robust’ for some novel HealthTech (with relatively ‘weak’ supporting studies), but that a wide range of evidence should be considered, as appropriate.

While these requirements are non-specific, they claim a basic consistency with the standards of NICE, Singapore ACE and the Australian Medical Services Advisory Committee (MSAC), all of which are cited by this guidance (p.33).

4. DISCUSSION

It is generally the case that few of the identified documents from the HTA or regulatory agencies detailed evidence standards or preferences more specific than those outlined by NICE for DHTs, e.g. with a preference for RCTs over non-RCT evidence, where appropriate.

Some agencies that detailed different study designs also specified that their evidence requirements could differ depending on: whether or not it was difficult to generate comparative evidence on account of the 'nature' or 'characteristics' of a technology (France [HAS], US [FDA]), such as its intended use or setting (e.g. if the technology was intended for rare disease populations, those with high unmet need or where there was no obvious comparator) (Australia [MSAC], WHO); or depending on whether there were different classifications of, or levels of 'risk' associated with a device or DHT (US [ICER/PHTI], Finland [Digi-HTA], and Australia [TGA]].

Only agencies in a few countries had similar detailed study design preferences or requirements to NICE (Australia, France, Ireland, Scotland, Singapore, USA, Wales), and some of these agencies also tended to report a preference for 'local' studies or data also (Australia, Scotland, Singapore, Wales). As with NICE, some countries' evidence standards also specified a role for real world data or evidence (RWD/RWE) and three also stated a preference for evidence on diagnostic HealthTech that extended beyond test accuracy to demonstrate health outcome benefits (Australia, Ireland, Singapore).

As a point of difference from NICE, two countries also stated a clear preference for RCT-based indirect comparisons over non-RCT evidence or 'single-arm trials', if appropriate, in the absence of relevant RCT evidence for devices (Australia, Ireland). Three also included published systematic reviews or meta-analyses within their overview of preferred study designs (Finland DiGi-HTA, Australia ASERNIP-S, Wales), and four specified 'minimum' evidence requirements or standards, e.g. as a minimum only quantitative controlled or comparative studies were acceptable (EC Member Group CHTA, Germany's DiGA, Australia's MDHTAC and ICER/PHTI in the US).

Based on the documents identified, the remaining countries and agencies had less detailed evidence requirements, which might simply involve a requirement for non-specific objective evidence of device or DHT ‘performance’ or ‘efficacy and safety’.

The majority of the documents concerned devices or HealthTech generally rather than DHTs specifically, but the evidence requirements for the latter, where reported, where rarely very different.

These overall findings are presented in Tables 4a and 4b.

Table 4a: Summary of evidence requirements by HealthTech

Evidence 'hierarchies'	Specified study designs without a hierarchy	Local data	Indirect comparisons	Real World Evidence	Evidence of intended performance, efficacy and/or safety
Devices or HealthTech generally					
- Australia (MSAC, ASERNIP-S*) - France (CNEDiMTS) - Ireland (HiQA) - USA (FDA, ICER*) - Wales (HTW)	- Australia (MDHTAC) ‡ - Scotland (SHTG)	- Australia (MSAC, MDHTAC) - Wales (HTW)* - WHO	- Australia (MSAC) - Ireland (HiQA)	- USA (FDA) - USA (ICER) - Wales (HTW)	- Australia (TGA) - Europe: EMA, EC JCA, EU CGHTA - Canada (Health Canada, INESSS) - USA (CMS, AHRQ) - WHO
Digital Health Technologies (DHTs)					
- Austria (AIHTA)† - Finland(DiGi-HTA)* - France (CNEDiMTS) - Singapore (ACE) - USA (ICER/PHTI)	- Germany (DiGA/BfArM)	- Singapore (ACE) - USA (ICER/PHTI) - WHO		- Europe (EMA) - Finland (DiGi-HTA) - Germany (DiGA/BfArM) - Singapore (ACE)	- Belgium (KCE)† - Netherlands (NZa) - Canada (Health Canada, INESSS) - Europe: EMA - USA (FDA)

*Includes Systematic review/meta-analysis as a type of evidence
†Not detailed/ongoing
‡'comparative data' rather than a specific design.

Table 4b: Summary of evidence requirements by country

Region / country	Agency	Device/DHT	Evidence 'hierarchies'	Specified study designs without a hierarchy	Local data	Indirect comparison	Real World Evidence	Evidence of intended performance, efficacy and/or safety
EUROPE								
Austria	AIHTA	DHT	●					
Belgium	KCE	DHT						●
Finland	DiGi-HTA	DHT		●			●	
France	CNEDiMTS	Devices/DHT	●					
Germany	DiGA/BfArM	DHT					●	
Ireland	HiQA	Devices	●			●		
Netherlands								●
Scotland	SHTG	HealthTech		●	●			
Wales	HTW	HealthTech	●		●			
Europe	EMA	Devices/DHT					●	●
	EU CGHTA	Devices						●
	EC JCA	Devices						●
NORTH AMERICA								
USA	FDA	Devices	●				●	●
	CMS	Devices						●
	AHRQ	Devices						●
	ICER	Devices	●			●	●	
	ICER/PHTI	DHT						
Canada	Health Canada	Devices/DHT						●
	INESSS	Devices/DHT						●

ASIA & AUSTRALASIA								
Australia	MSAC	Devices	●		●	●		
	MDHTAC	Devices		●	●			
	ASERNIP-S	Devices	●					
	TGA	Devices						●
Singapore	ACE	DHT	●		●		●	
Global								
WHO		Devices/DHT			●			●

DHT: Digital Health Technology

4.1. Limitations

It should be noted that this report does not include any documents in languages other than English or that might have been made available via agencies or resources that were not checked or interrogated by the searches. As a result, it might have missed detailed evidence requirements for HealthTech as specified by a number of countries and agencies internationally, as well as other documents in English that the search and reference checking might have missed. The summary is therefore unlikely to be comprehensive. The identification of sources was largely conducted by a single information specialist (EP), and the identification, extraction and analysis of all relevant data, within documents identified as potentially relevant, was only conducted by a single reviewer (CC).

5. CONCLUSION

This report provides an overview of the reported evidence requirements and related considerations around clinical efficacy and/or safety for HealthTech from relevant organisations internationally. The overview presented is limited to data from English language documents from the most easily identified HTA and regulatory agencies. On the whole, only some of the major agencies in France, Australia, Singapore, Wales and the USA specify detailed evidence standards or requirements similar to the NICE ESF for DHTs in terms of study designs and evidence 'hierarchies' (e.g. a preference for RCTs). Some agencies also clarify that their stated preferences can differ depending on the characteristics, intended use, classification and 'level of risk' associated with the HealthTech. The clinical evidence preferences or requirements for the majority, where reported in relevant documents, appear to outline more general evidence around HealthTech's performance (efficacy, effectiveness and accuracy), safety and risks, without reference to study designs or evidence 'hierarchies'.

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APPENDIX

Table 5a: European national agencies: evidence requirements

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
Austria	Austrian Institute of HTA (AIHTA) / HTA	DHTs	Clinical evidence requirements (ongoing): Mirror those of Tier C of NICE's ESF: Minimum high-quality observational or quasi-experimental comparative studies and at best (best practice standard) RCTs, demonstrating benefits in relevant outcomes Stakeholders are involved in discussions	KCE, Evaluation of Digital Medical Technologies (2023) Table 15, pp.112-13.
Belgium	KCE - Belgian Health Care Knowledge Centre / HTA	DHTs	Only apps that have completed levels M1 (CE marking and GDPR) and M2 (interoperability and connectivity) of the [validation] pyramid can start the integration process in the M3 level (reimbursement).	KCE, Evaluation of Digital Medical Technologies (2023)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
	Recommendation		The Digital Medical Technology (DMT) has to demonstrate a social-economic added value. Only apps that have completed levels M1 and M2 of the pyramid can start the integration process in the M3 level. The intention of the National Institute for Health and Disability Insurance (NIHDI) is not to reimburse mobile apps per se, but their use within the context of a specific care process (see below section 2.5). An app can be either temporarily reimbursed (M3-), if its socio-economic value is still uncertain, or structurally reimbursed (M3+) if its socio-economic value is adequately proven.	
Finland	DiGi-HTA Network / HTA	DHTs	Clinical and/or organisational evidence requirements: Both medical benefits and / or improvements in organisation (e.g. care processes) considered. Study types: RCTs, Cochrane reviews, observational studies, and case studies. Specific requirements for a DMT decided on a case-by-case basis (may differ for class I vs class III DMTs). No general rules specified. Ongoing studies and RWD might be considered. If similar products are on the market for which RCTs exist, the evidence will be considered (Digi-similar RCTs).	KCE, Evaluation of Digital Medical Technologies (2023) Table 15, p.110.
France	Medical Device and Health Technology Evaluation Committee (CNEDiMTS) part of	Devices	**3.3. Studies to demonstrate the clinical benefit** The design of the studies essential to demonstrating the clinical benefit of the new MD must be based on the different feasibility and development studies**.** Depending on the stakes, the studies selected can be superiority, equivalence or non-inferiority studies.	Pathway of medical devices in France. Guide. Assess Health Technologies (2021)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
	Haute Authorité de Santé (HAS)/ HTA Recommendation		The type of trial with the best level of evidence to demonstrate the clinical superiority of a new MD [medical device] over the reference strategy is a randomised, controlled trial… The randomised, controlled trial, in addition to having to fulfil standard methodological criteria, must also be clinically relevant… It is possible that this trial, depending on the specific characteristics of the MD, cannot be controlled and randomised. In this case, the people conducting the project can use other experimental plans suitable to the context. In all cases, this strategy must make it possible to clearly explain and justify alignment between the methodological choices made and the expected level of demonstration to show a benefit of the device assessed… Trials are preferably multicentre….The theoretical estimate of the number of patients to be included is essential… Once CE marking has been obtained, surveillance and medical device vigilance must be put in place in order to continuously assess the risks associated with the use of the MD.	

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
			1: Assessment of the benefit of MDs [medical devices] must be based on conclusive clinical studies... While randomised, controlled clinical trials are generally considered to be the gold standard methodology to demonstrate the efficacy of a health product, in line with the principles of Evidence Based Medicine, these are sometimes difficult to implement for medical devices … **3.1. Double-blind, randomised controlled trials** Although the conditions of the study design may differ from routine clinical practice, double-blind, randomised controlled trials remain the essential reference for the assessment of any health product… The choice of a methodology other than a randomised controlled trial must always be explained and justified by the manufacturer… [Differences with drugs for HealthTech] Therefore, the learning curve for operators must be taken into account when assessing surgical or interventional techniques. **7. In practice** The choice of clinical evaluation plan depends entirely on the context: the action sought by the use of the medical device, the existence of alternatives, the size of the target population, etc. These different parameters must be taken into account when choosing the type of study to be implemented.	Methodology for the clinical development of medical devices. Methodology Guide. Assess Health Technologies (2021)
France*	Medical Device and Health Technology	DHTs	Clinical and/or organisational evidence requirements: Criteria to be met:	KCE, Evaluation of Digital Medical

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
	Evaluation Committee (CNEDiMTS) part of Haute Authorité de Santé (HAS)/ HTA Recommendation		DHT must be considered innovative (by CNEDiMTS), in terms of clinical patient benefit or improvement in the organisation of care, based on first data available vs relevant comparators. No specific rules on type of studies (or size) to prove clinical benefits, but RCTs considered gold standard and decision to use other types of studies should be justified.	Technologies (2023) Table 15, pp.109-110.
Germany	Federal Institute for Drugs and Medical Devices (BfArM) / HTA Recommendation	DHT (DiGA, Digital Health Application).	4.2: Evidence that a DiGA has a pVE can only be provided for a defined patient group or several defined patient groups. Only for these patient groups can the DiGA be prescribed and reimbursed in case it is listed in the DiGA directory. 4.2.2.: The manufacturer must prove at least one positive healthcare effect… **4.3 General Requirements for Studies to Prove a Positive Care Effect** In order to prove a positive healthcare effect, a manufacturer must present the results of a comparative study which shows that the application of DiGA is better than not applying it. … The choice of the comparison group must be oriented on the reality of healthcare. **4.3.1 Choice of Methods** …The prerequisite is that they are quantitative comparative studies and that the chosen methodology is adequate for the chosen object of investigation. **4.5.1 Justification of the Improvement of Healthcare**	The Fast-Track Process for Digital Health Applications (DiGA) according to Section 139e SGB V A Guide for Manufacturers, Service Providers and Users (2020)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
			DiGA manufacturers who apply for provisional listing must plausibly demonstrate that their DiGA can achieve one or more pVE for a specific patient group… **4.6 Specific Requirements for Study Types and Study Designs** An application for listing in the directory requires at least the submission of a retrospective comparative study: case-control studies, retrospective cohort studies or intra-individual comparisons are possible…If DiGA contain diagnostic instruments, i.e. a measurement and interpretation of vital data, a survey of users on physical or mental conditions, a survey of pain sensation, etc., additional studies on test quality must be submitted. **4.6.1 Study to Verify Positive Care Effects** … In order to ensure this, quantitative studies must be submitted, regardless of the selected pVE to be verified. Purely qualitative research results are not sufficient… Observational analytical studies, such as case / control studies or cohort studies are acceptable study designs since they provide for a control group and can be conducted retrospectively or prospectively, depending on the research question. Before and after comparisons are also permitted. Furthermore, experimental intervention studies such as non-randomised or randomised controlled trial (RCT) are also suitable for demonstrating positive healthcare effects… other alternative study designs and methods such as	

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
			Pragmatic Clinical Trials (PCT), Sequential Multiple Assignment Randomised Trial (SMART) or Multiphase Optimisation Strategy (MOST) may also be useful, depending on the care context of the DiGA and the evidence sought…	
Ireland	Health Information and Quality Authority (HIQA) / HTA Recommendation	Health Tech	**3.1.3 Types of study** Evidence to support the effectiveness of a technology should be derived by clearly defined methods. Where available, evidence from high quality RCTs should be used to quantify efficacy… In the event that RCT evidence is not available and it is not possible to estimate treatment effect through indirect methods, then data from single arm studies may be available.	Guidelines for Evaluating the Clinical Effectiveness of Health Technologies in Ireland (2018)
Nether-lands	Dutch Healthcare Authority (NZa) / Approval / Licensing	DHTs	Clinical and/or organisational evidence requirements: The criterion 'state-of-the-art of science and clinical practice' considers the relative effectiveness of the new diagnosis or treatment vs current standard. Aspects considered include: the comparator used for the evaluation, target group, outcomes, and if relative effect is large enough to be clinically relevant. Standard principles of evidence-based medicine are applied in this process.	KCE, Evaluation of Digital Medical Technologies (2023) Table 15, pp.111-112.
Scotland	SHTG / HTA	HealthTech	Evidence of clinical benefits: Demonstrating benefits. Are there high quality, relevant studies available?	Evidence Framework (2023)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
	Recommendation		Were these studies done in a setting relevant to the Scottish health and social care system? Did the studies show improvements in relevant outcomes? For technologies that treat a specific condition. Are there interventional studies (experimental or quasi-experimental design) that support the claimed benefits of the technology? Did they show improvements in relevant outcomes? Is the comparator a care option that reflects the current NHS Scotland care pathway? In a novel, innovative or transformative technology, the setting may not reflect the Scottish pathway, but it should still be able to demonstrate excellent performance and high value. For technologies that diagnose a specific condition. Do they support the claimed benefits of the test? This may include test accuracy studies, using an appropriate reference standard, or a concordance study to show agreement with current practice. When it is not possible, ethical or relevant to conduct an interventional study. Are there observational studies? Real World Evidence: Did the technology perform its intended purpose to the expected level?	
Wales	Health Technology Wales / HTA	HealthTech	7.3.1.1 Types of evidence included We consider all types of evidence as potentially relevant to our rapid evidence reviews. However, we give priority to evidence that compares the effectiveness	Health Technology Wales

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits (Selected relevant text from documentation)	Document (reference)
	Recommendation		of a technology or model of care and support with current treatment or care options, and that measures effectiveness in as unbiased a manner as possible. For example, if we identify relevant and well-conducted randomised controlled trials, we may choose to report only results from these and not from non-randomised or observational studies. Similarly, where randomised controlled trials are unavailable or not feasible, we look for other sources of evidence from non-randomised or observational studies that compare the technology or model of care and support of interest with current practice or standard care. We will usually only include data from single-arm studies (where there is no control group) if no comparative evidence is available… We will also prioritise evidence from well-conducted secondary studies, such as systematic reviews or health technology assessments undertaken by other agencies, where these are available. Depending on their exact relevance to our work, they can be used as a source of … outcome data to be used directly in our own evidence synthesis.	Appraisal Process Guide (2024)

Table 5b: European regional agencies: evidence requirements

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
EU	European Medicines Agency (EMA) / Regulator Approval	Medicinal products co-packaged with Devices	**p.1:** For medical devices that form an integral product with a medicinal product (Regulation (EU) 2017/745, second subparagraph of Article 1(8) and 1(9)), new requirements to provide an EU declaration of conformity issued by the medical device manufacturer, or a certificate of conformity (so-called hereafter EU certificate) or an opinion from a notified body designated under Regulation (EU) 2017/7452 for the type of device in question are applicable in certain circumstances (Art. 117). **2.2** The submission of evidence of compliance with the general safety and performance requirements of the with the Medical Devices Regulation (EU) 2017/745 (MDR) in the marketing authorisation dossiers of integral DDCs did not apply to MAAs submitted before 26 May 2021, i.e. the date of application of the MDR. **3.3** It is the responsibility of the applicant/MAH to ensure that the medical devices co-packaged with the medicinal product meet the applicable general safety and performance requirements set out in MDR Annex I … [ANNEX I: GENERAL SAFETY AND PERFORMANCE REQUIREMENTS CHAPTER I: GENERAL REQUIREMENTS 1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are	Questions and answers: for applicants, marketing authorisation holders of medicinal products and notified bodies regarding medicines used in combination with medical devices (2020)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.]	
EU	European Commission (Joint Clinical Assessment [JCA]) / HTA Methods Guidance	Devices	p.2: The provision of information, data, analysis and other evidence in the dossier shall follow international standards of evidence-based medicine. 4.3 … It is a methodological requirement that all data on the relative effectiveness and relative safety of the medical device are provided for all original clinical studies and for evidence syntheses, respectively.	Guidance on filling in the Joint Clinical Assessment dossier template of a Medical Device (2025)
EU	Member state coordination group on HTA / HTA	General (includes drugs)	HTA requires the relative effectiveness of an intervention to be determined as correctly and precisely as possible… it is therefore essential that a JCA contains a description of both “the relative effects of the health technology” and “the degree of certainty of the relative effects, taking into account the strengths and limitations of the available evidence”.	Guidance on Validity of Clinical Studies (2024)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
	Methods Guidance		… Although HTA usually requires a high target certainty of results (e.g. RCT evidence for new medicinal products), it is necessary to assess all available data, as submitted by the Health Technology Developer (HTD). Nevertheless, there might be justification to not assess the evidence that ranges below a minimum level of internal validity, external validity, or statistical precision in detail, if the PICO question can be sufficiently answered on the basis of higher certainty results.	
EU	EMA / HTA Methods Guidance	DHT	- Consideration should also be given to meeting the requirements of any additional current legal and regulatory frameworks …the sponsor remains ultimately responsible for ensuring that the conduct of the clinical studies and the final data generated by those studies comply with the regulatory requirements. For a **clinical outcome assessment (COA)**: -Content validity … -Construct validity… -Reliability… Evaluating reliability, convergent validity and ability to detect change are also important psychometric properties to establish… - Where relevant, diagnostic and prognostic performance (sensitivity and specificity) as well as sensitivity to change in clinical status should be demonstrated... At present, studies using high-quality real-world data (such as those provided by internationally recognised disease registries) would be considered another potential means to achieve validation of endpoints, if such	Questions and answers: Qualification of digital technology-based methodologies to support approval of medicinal products (2020)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			real-world evidence is of acceptable quality, robust enough, and ideally *a priori* agreed upon with the regulators.	

Table 6a: North America 'Coverage' programs and HTA agencies: evidence requirements

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
USA	Centers for Medicare & Medicaid Services (CMS) Coverage on Insurance plans (National coverage determinations, NCDs)	Items and services	In general, for an item or service to be considered for Medicare coverage it must: **1.** Fall within at least one benefit category established in Section 1861 of the Social Security Act (the Act): Durable Medical Equipment, Prosthetics, Orthotics, and Supplies (DMEPOS); 2. Not be specifically excluded by the Act; and 3. Be "reasonable and necessary" (R&N) for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member (§1862(a)(1)(A) of the Act). Medicare Program; Medicare Coverage of Innovative Technology (MCIT) and Definition of ''Reasonable and Necessary''(CMS–3372–F): An item or service must be (1) safe and effective, (2) not experimental or investigational, and (3) appropriate for the Medicare patients.	CMS.gov Medicare Coverage of Items and Services | CMS Centers for Medicare & Medicaid, editor: Federal Register; 2021. p. 2987-3010
USA	Agency for Healthcare Research and Quality (AHRQ) / HTA	Items and services	Table 5. Final Proposed Requirements … C. The rationale for the study is supported by scientific evidence and study results are expected to fill the specified knowledge gap and provide evidence of net benefit.	Analysis of Requirements for Coverage With Evidence Development (CED)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
	Coverage on Insurance plans		D. Sponsors/investigators establish an evidentiary threshold for the primary outcome(s) so as to demonstrate clinically meaningful differences with sufficient precision. E. The CED study is registered with ClinicalTrials.gov and a complete protocol is delivered to CMS. … I. The primary outcome(s) for the study are clinically meaningful and important to patients. A surrogate outcome that reliably predicts these outcomes may be appropriate for some questions. J. The study population reflects the demographic and clinical diversity among the Medicare beneficiaries who are the intended users of the intervention. This includes attention to the intended users' racial and ethnic backgrounds, gender, and socio economic status, at a minimum.	– Topic Refinement (2022)
USA	ICER / HTA Recommendation	Devices	p.4: ***Acceptance of Multiple Forms of Evidence*** Patients, clinicians, and policymakers are most interested in evidence on the comparative clinical effectiveness of care options, but this does not mean that ICER's value framework limits the type of evidence to be considered to the results of randomized controlled trials (RCTs). p.5: When available, high-quality RCTs and systematic reviews of RCTs provide evidence that is least susceptible to many scientific biases. However,	Value Assessment Framework (2023)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			head-to-head RCTs of active comparators are uncommon, especially for interventions near the time of regulatory approval. Without direct head-to-head evidence, insights into comparative clinical effectiveness may require indirect comparisons through formal network meta-analysis. Complementing these sources of information is evidence derived from many different analytic approaches and that are available from a wide range of sources. Although more vulnerable to some important confounding biases, observational methodologies such as cohort studies, case-control studies, and long-term disease and drug registries often provide helpful evidence, particularly on longer-term outcomes. As will be described in greater detail later in this document, we also have a commitment to explore how “real-world” observational evidence can contribute to a more comprehensive and accurate view of the risks, benefits, and costs associated with any intervention. This commitment extends not only from using available published sources, but includes the possibility of working with life science companies, patient groups, or data aggregator companies to develop and analyze new sources of real-world evidence in a way that will meet the evidentiary standards relevant to the questions being addressed p.13: 2.3 ICER’s evaluation of comparative clinical effectiveness is grounded in a systematic review of all available evidence….	

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			ICER's judgements around comparative clinical effectiveness are informed by evidence arising from multiple sources. When available, high-quality RCTs or their meta-analyses provide evidence that is least susceptible to certain scientific biases. When benefits and harms occur over the course of many years, or when harms are rare but clinically important or even catastrophic, evidence from high quality published peer-reviewed studies using observational data and methodologies such as cohort studies, case-control studies, and long-term disease and drug registries may be used… ***Real-World Evidence*** RWE may help complement other types of evidence … RWE often has greater vulnerability to known and unknown biases that create limitations in our ability to rely on it when making judgments about relative effectiveness of different care options. Nonetheless, we understand that RCTs have their own limitations and are often inadequate to address all questions relevant to assessments of comparative clinical effectiveness… Patient-reported outcome studies and studies that capture broader patient and family effects of treatment are especially desired as they can provide evidence usually not included in clinical trials… p.14: In summary, we have a flexible and inclusive approach to sources of evidence, which stresses the importance of the rigor of clinical trial while	

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			augmenting such evidence with data from other real-world or grey-literature sources	
USA	ICER & PHTI / HTA Recommendation	Digital HealthTech	Pp.13-15, and Table 3: Safety and effectiveness Tier 1 DHTs are universally low risk since they are user-initiated and not integrated into clinical care, … The minimum evidence standard requires only that the DHT provides accurate information (e.g., heart rate measured from the mobile app gives accurate and reliable information compared to a gold standard). The best evidence standard for these DHTs would also include empirical data on the perceived behavior change or health improvement by end-users… Quantitative valid measures are preferred for self-reported outcomes. Tier 2 is focused on diagnostic and prognostic DHTs, …For diagnostic DHTs at the lower bounds of moderate risk, minimum evidence only requires the evaluation of accuracy and precision against a well-established gold standard. .., DHTs posing higher risk require greater certainty that the information provided produces improved health outcomes within reasonable risk related to false positive and false negative findings. For example, with high-risk diagnostics (e.g., cancer diagnosis), an RCT demonstrating that use of the diagnostic DHT improves patient outcomes may be required …	ICER-PHTI Assessment Framework for Digital Health Technologies (2023)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			Tier 3 encompasses professionally-directed preventative and therapeutic health management interventions. These DHTs have direct clinician involvement and measurable clinical outcomes… Tier 3a interventions are for preventative health or health behavior management under clinician supervision…Tier 3a DHTs that are low risk should, as a minimum, have evidence from high quality observational or quasi-experimental studies with an appropriate comparator and assessment of clinically relevant patient outcomes. Tier 3a DHTs that are moderate risk should have evidence from an RCT demonstrating clinical efficacy… Tier 3b interventions are therapeutic interventions for clinically diagnosed conditions and they are considered moderate to high risk… Tier 3b interventions are therapeutic (e.g., app that delivers CBT for opioid use disorder) or directly guide a medical or surgical intervention (e.g., software that creates 3D reconstruction images and determines location for optimal needle placement for a lung biopsy). The minimum evidence requirement for moderate risk Tier 3b interventions is a well-conducted RCT demonstrating clinical efficacy. As for high-risk Tier 3a interventions, the study may be conducted in a selected population using surrogate outcomes, and short-term follow-up may be acceptable. High-risk Tier 3b interventions require at least one additional RCT that evaluates the clinical effectiveness of the intervention in patient	

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			populations and health systems of interest. RCTs for all Tier 3b DHTs should capture patient-important outcomes, compare the new DHT to a reasonable active comparator (e.g., well-managed standard of care), and demonstrate durability of treatment effect to a pre-established timepoint guided by expert opinion.	

Table 6b: North America Food & Drug Administration (FDA): evidence requirements

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
USA	FDA / Regulator Approval	Devices	p.1, 1.0: The final rule, effective one year after publication, is codified at 21 CFR parts 807, 812, and 814.3 … p.3: [FDA] requires sponsors and applicants to provide statements regarding the conduct of clinical investigations. … These regulations address data quality and integrity and human subject protection and are considered part of FDA's GCP regulations... pp.4-5: Good clinical practice (GCP) is defined in 21 CFR 812.28(a)(1) as "a standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical investigations in a way that provides assurance that the data and results are credible and accurate and that the rights, safety, and well-being of subjects are protected." p.11: (6) As defined in 21 CFR 860.7, valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. The evidence required may vary according	Acceptance of Clinical Data to Support Medical Device Applications and Submissions Frequently Asked Questions - Guidance for Industry and Food and Drug Administration Staff (2018)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use. Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.	
USA	FDA / Regulator Approval	Devices	p.6: Reasonable assurance of safety and effectiveness and substantial equivalence of devices with PCCPs [he documentation describing what modifications will be made to an EXISTING device] – A PCCP is part of the device marketing authorization.	Pre-determined Change Control Plans (2024) Draft
USA	FDA / Regulator Approval	Devices	Guidance (non-binding) p.6: In order to make decisions about the effectiveness and safety of a medical device in pediatric patients, FDA considers the totality of the evidence available. As with any PMA, HDE or *de novo* request, FDA will still consider clinical data (whether extrapolated or not) alongside other forms of scientific evidence from assessments of device performance (e.g., preclinical testing, engineering models, biocompatibility, virtual patient simulations, statistical models) to determine whether the sponsor has demonstrated a reasonable assurance of safety and effectiveness (or probable benefit, for HDEs)… p.8:The agency recognizes that the amount and type of evidence required will depend on a number of factors, including the nature of the device, what is	Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices - Guidance for Industry and Food and Drug Administration Staff (2016)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			already known about the product in the adult population (if relevant), what is known or can be extrapolated about the device to the pediatric population, and the underlying disease or condition being treated. In some cases, well-designed bench and animal testing will be sufficient to evaluate the device. In others, clinical data may be needed to evaluate the safety and effectiveness of the device." p.10: The specific threshold for approval addressed under PMDSIA for the use of extrapolated data is "reasonable assurance of effectiveness." … both PMA approval and granting a *de novo* request require a reasonable assurance of safety and effectiveness,	
USA	FDA / Regulator Approval	Devices	Guidance (non-binding) p.18, footnote 50: Software performance and functional requirements generally include, but are not limited to, requirements related to algorithms or control characteristics for therapy, diagnosis, monitoring, alarms, analysis, and interpretation with full text references or supporting clinical data, if necessary .	Content of Premarket Submissions for Device Software Functions -Guidance for Industry and Food and Drug Administration Staff (2023)
USA	FDA / Regulator	Devices	Guidance (non-binding)	Use of Real-World Evidence to

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
	Approval		p.2: Many of the considerations and best practices for generating RWE are derived from the same principles that govern generation of clinical evidence from traditional clinical studies, which are generally referred to as good clinical practice (GCP). As with all clinical evidence, FDA's assessment of RWE provided in support of a particular regulatory decision will be evaluated as part of the totality of information available to FDA. Per 21 CFR 860.7(c)(1), "[a]lthough [a] manufacturer may submit any form of evidence to the Food and Drug Administration in an attempt to substantiate the safety and effectiveness of a device, the agency relies upon only valid scientific evidence to determine whether there is reasonable assurance that the device is safe and effective." … The standard of valid scientific evidence will apply, as appropriate, regardless of the source of clinical evidence provided. pp.5-6…. While [the guidance] does describe the factors that FDA considers when evaluating relevance and reliability of RWD, it does not provide a specific set of criteria or other scoring tools for determining the suitability of any specific RWD source for generating RWE for a particular regulatory decision…. this guidance describes the circumstances under which clinical evidence generated from RWD may be used to support a variety of FDA decisions based on the existing evidentiary standards.	Support Regulatory Decision-Making for Medical Devices - Guidance for Industry and Food and Drug Administration Staff (2025)

Country / Region	**Agency / HTA or regulator** **Recommendation / Decision**	**HealthTech (e.g. digital, device, interventional procedure)**	**Evidence requirements/standards to demonstrate benefits**	**Document (reference)**
USA	FDA / Regulator Approval	Devices (Therapeutic, Diagnostic, Multi-use)	Guidance (non-binding) p.8: ***3.1 The Statutory Standard for Approval of a PMA: Reasonable Assurance of Safety and Effectiveness*** (pre-market approval application (PMA)) As indicated by Sections 513(a)(1)(C) of the FD&C Act, a PMA must provide reasonable assurance of safety and effectiveness of the device. … In addition, FDA has, through regulation, interpreted the statutory standard for approval of a PMA as follows: *21 CFR 860.7(d)(1). There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use.* *21 CFR 860.7(e)(1). There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence,* p.9: ***3.2 Valid Scientific Evidence***	Design Considerations for Pivotal Clinical Investigations for Medical Devices - Guidance for Industry, Clinical Investigators, Institutional Review Boards and Food and Drug Administration Staff (2013)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			The regulations state that the safety and effectiveness of a device will be determined on the basis of valid scientific evidence. 21 CFR 860.7(c)(1). Valid scientific evidence is defined through regulation as follows: *21 CFR 860.7(c)(2) Valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. The evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use. Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.* *21 CFR 860.7(e)(2) The valid scientific evidence used to determine the effectiveness of a device shall consist principally of well-controlled investigations, as defined in [21 CFR 860.7](f), unless [FDA] authorizes reliance upon other valid scientific evidence which [FDA] has determined is sufficient evidence from which to determine the effectiveness of a device, even in the absence of well-controlled investigations. [FDA] may make such a*	

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			determination where the requirement of well-controlled investigations in [21 CFR 860.7](f) is not reasonably applicable to the device. Thus, one key principle evident in 21 CFR 860.7 is that evidence of effectiveness of a medical device must generally be obtained from well-controlled studies (as described in 21 CFR 860.7(f)). However, the regulations provide FDA with some flexibility regarding its determination of the type of evidence that may be considered valid scientific evidence to demonstrate the safety of a medical device. p.10: FDA believes that in most cases, clinical data will be necessary to demonstrate effectiveness for a device … The results of the study must provide sufficient evidence for FDA to make a determination of reasonable assurance of safety and effectiveness, as defined in the regulations above.. **3.3**…. FDA relies on valid scientific evidence to determine whether there is reasonable assurance that the device is safe and effective. p.11**, 3.4**…In any case, the scientific rigor necessary for a clinical study and the robustness of evidence that need to be collected are not dependent on whether an [Investigational Device Exemption] IDE is required in order to initiate the study.	
USA	FDA / Regulator	DHTs	p.11, C: **Verification, Validation, and Usability Evaluations of Digital Health Technologies**	Digital Health Technologies for

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
	Approval		For the purposes of this guidance, verification is confirmation by examination and provision of objective evidence that the parameter that the DHT measures (e.g., acceleration, temperature, pressure) is measured accurately and precisely. Validation is confirmation by examination and provision of objective evidence that the selected DHT appropriately assesses the clinical event or characteristic in the proposed participant population (e.g., step count or heart rate). p.12: Depending on the DHT and its context of use, verification and validation may begin with benchtop studies, progress to testing in healthy volunteers, and continue in individuals representing the population to be studied in the clinical investigation.43 These studies should include demonstration that the clinical event or characteristic to be assessed (e.g., step count or heart rate) is consistently and appropriately measured in the population of interest	Remote Data Acquisition in Clinical Investigations Guidance for Industry, Investigators, and Other Stakeholders (2023)

Table 6c: Canadian agencies: evidence requirements

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
Canada	Institut national d'excellence en santé et en services sociaux (INESSS), Quebec / HTA Recommendation	Tests and procedures; Medical devices and equipment; Digital technologies	p.3: Assessors include: Health and Social Services Technology Assessment Unit (UETMIS[SS]) p.5: The approach presented in this guide is based on two frameworks: The framework for assessing the value of interventions in health and social services (INESSS, 2021). The framework for responsible innovation in healthcare (Silva et al., 2018) p.5, Table 1: Main Value Criteria>Clinical Dimension>Clinical efficacy •Adverse effects •Effects on quality of life and health •Care and services experience	A GUIDE TO SUPPORT VALUE ASSESSMENT (2024)
Canada	Health Canada / Regulator Licensing	Devices	All medical devices must be safe and effective for their intended use(s) (and 'must have objective evidence to support the claims of safety and effectiveness'). Clinical evidence should demonstrate: • the device is safe and effective when used as per the statement on indications for use and • how the device affects diverse subpopulations, such as women and gender-diverse people, racialized minorities, pediatric and older populations (when applicable) Manufacturers must also provide information on both:	Medical Devices Regulations (sections 10-20) (Accessed May 2026) Guidance on clinical evidence requirements for medical devices: Submitting clinical

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			• the risks and the benefits associated with using the device and • the uncertainty associated with how accurately they can define the risks and the benefits of the device Health Canada will issue a medical device licence if the application (and clinical evidence) demonstrates that: • the device meets the requirements and • the benefits of the device outweigh the identified risks and • the uncertainties relating to the benefits or adverse effects associated with the device are not significant	evidence - Canada.ca

Table 7: Asian and Australasian agencies: evidence requirements

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
Australia	Therapeutic Goods Administration (TGA) / Regulator	Devices	**Essential principles (EP) 14**: Every medical device requires clinical evidence, appropriate for the use and classification of the device, demonstrating that the device complies with the applicable provisions of the Essential Principles.	Australian Regulatory Guidelines for Medical Devices (ARGMD) (2024)
	Approval	Devices	Clinical Evaluation Procedures: p.17: Clinical evidence requirements. Clinical evidence comprises clinical data and its evaluation pertaining to a medical device. … From this information, an acceptable benefit-risk profile may be demonstrated for a medical device, by showing that it performs as intended and that all identified undesirable effects and hazards …are outweighed by the benefits. p.19: Why clinical evidence is required. All medical devices supplied in Australia must have clinical evidence sufficient to demonstrate an appropriate level of safety and performance when used for their intended purpose(s). pp.19-20: Requirements for different device classifications. Medical devices are classified according to their level of risk … Further, the classification, design and use of the device are relevant factors when considering the nature,	TGA Clinical evidence guidelines: for medical devices (2023)

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			type, and range of evidence appropriate to being able to demonstrate compliance with applicable provisions of the EPs. EP 14 itself notes that every medical device requires clinical evidence, appropriate for the use and classification of the device, demonstrating that the device complies with the applicable provisions of the EPs. …. Evidence from comparable devices that are not substantially equivalent may support or supplement direct or indirect clinical evidence. This does not generally represent sufficient clinical evidence for the purpose of demonstrating compliance with the EPs - except for certain categories of lower risk devices, whose clinical effects are well understood and characterised…	
Australia	Medical Services Advisory Committee (MSAC) / HTA (Health services and technologies)	Technologies	pp.61-62 : Randomised controlled trials are considered the best study design to minimise systematic error, if these are not available or not sufficient (e.g. because they are too small for replicability of results to be certain or they are not directly applicable to the target setting in Australia), other study designs should be presented…	Guidelines (2021) Guidelines for preparing assessments for the Medical Services Advisory Committee

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
	Funding recommendation (including circumstances of funding)		MSAC's preference for study designs is as per the hierarchy in the NHMRC levels of evidence for interventions…. MSAC has a preference for comparative study designs (such as cohort studies with a concurrent or historical control) over noncomparative studies (such as case series). However, there will be situations where no comparative studies have been performed (such as for rare diseases, where trial evidence is difficult to generate). Indirect comparisons are preferred over presenting only single arm data, which do not allow MSAC to consider comparative safety and effectiveness. p.64: Evidence without treatment switching is preferred. p.97. Presentation of direct from test to health outcomes evidence The principles for presenting direct clinical trial evidence of the effect of an investigative health technology on patient health outcomes are similar to those for presenting clinical trial evidence for a therapeutic technology. That is, MSAC's preference for study designs is as per the hierarchy in the NHMRC levels of evidence for interventions… Direct from test to health outcomes evidence is preferred to linked evidence …Single-randomised direct from test to health outcomes trial evidence comparing health outcomes from new test strategy and existing test strategy, where test information is used to derive treatment condition (preferred option for assessment of any claim regarding the clinical utility of a test)… If a clinical reference standard is available, the	

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			accuracy of the proposed test against this clinical reference standard would be preferred over the nonclinical reference standard in most cases. p.113: Tests have become more sensitive over time, and definitions of disease or disease stage have changed over time. Therefore, more recent studies are generally preferred. p.128: Preference will be given to evidence of health outcomes where the treatments provided are available to patients in Australia. The health benefit of a test that is only demonstrated through the subsequent use of a treatment only available in a trial setting should not be considered.	
	Medical Devices and Human Tissue Advisory Committee / HTA Listing recommendations	Devices	The MDHTAC's recommendations and advice are based on an assessment of comparative clinical effectiveness and cost-effectiveness of products using the best available evidence compared with other similar products already listed on the Prescribed List (PL) or alternative treatments. It is one of the eligibility requirements that there is evidence available that the product is no less clinically effective than the comparator [either listed on the PL or, if there are no appropriate comparators listed on the PL, the alternative treatments]. (Member Guidelines 2023)	Member Guidelines – Medical Devices and Human Tissue Advisory Committee (2023) Terms of Reference – Medical Devices and Human Tissue Advisory Committee

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
Australia	ROYAL AUSTRALASIAN COLLEGE OF SURGEONS / ASERNIP-S	Surgical procedures	2. ASSESSMENT 2.1 Prior evaluation It is important to establish the safety and effectiveness of the new procedure. …. Issues that should be considered include: • Has the technique been evaluated before? … If no systematic reviews or health technology assessments on the new procedure are available, then it may be useful to examine randomised controlled trials of the procedure. These could be identified using bibliographic databases such as PubMed (www.ncbi.nlm.nih.gov/pubmed/). However, for both logistical and ethical reasons there may be very few or no published randomised controlled trials on the procedure. Therefore, it may be necessary to assess the procedure based on available case series or case reports, as well as industry reports, laboratory studies, or reports of experiences of the technique in Australian and New Zealand facilities. • How reliable is the evaluation? Interpretation of assessments should take into consideration the likely robustness of the evidence, as indicated by the type of study design; whether studies were large enough to show reliable results for morbidity and mortality; and any possible confounding factors, such as the age of patients.	General Guidelines for Assessing, Approving & Introducing New Surgical Procedures into a Hospital or Health Service

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
			• How wide-ranging or complex is the procedure? A procedure with a wide application or one that is highly technological is likely to require more intensive consideration and evaluation, e.g. laparoscopic techniques.	

Table 8: Global agencies: evidence requirements

Country / Region	Agency / HTA or regulator Recommendation / Decision	HealthTech (e.g. digital, device, interventional procedure)	Evidence requirements/standards to demonstrate benefits	Document (reference)
Global	WHO / HTA Guidance	Devices, including DHT	**5.2:** HTA must be based on the best available evidence based on the best available, preferably local, data. Context-appropriate data are required to enable all stakeholders (policy-makers, clinicians and patients) to make informed healthcare decisions **Table 3** Principle 6 HTAs should consider a wide range of evidence and outcomes **7.1:** Full HTA medical devices…the quality and level of evidence generated in clinical studies for new devices may be less robust due to factors such as a lack of appropriate comparators, randomization and blinding (108, 110), which may not be feasible due to the nature of the technology; … There is currently no agreement on a standard definition of what constitutes a DHT or on a framework for their assessment. …	Health technology assessment of medical devices. Second edition. WHO medical device technical series (2025)