Draft plan for Health technology assessment of medical devices and in-vitro diagnostics

Contents

Acknowledgements

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1.1 Introduction

Health Technology Assessment (HTA) for medical devices is a systematic process used to evaluate their clinical effectiveness, safety, cost-effectiveness, and broader impact on healthcare systems. Unlike pharmaceuticals, HTA for devices often considers factors such as usability, learning curves, and real-world performance. It helps decision-makers allocate resources efficiently and ensure that innovative technologies deliver value for patients and health systems.

Guidance is available from the World Health Organization through its "Health Technology Assessment of Medical Devices, Second Edition" (WHO Medical Device Technical Series, 2025)[1]. The following summarizes the key elements of this guidance for countries initiating HTA for medical devices, while details are available in the full publication.

1.1.1. Role of HTA in Health Systems

HTA is a multidisciplinary process that evaluates the clinical, economic, social, and ethical implications of health technologies. For medical devices, HTA ensures that adoption decisions are evidence-based and aligned with universal health coverage (UHC) goals. It links regulatory approval, health system integration, and lifecycle management, helping countries prioritize technologies that deliver value and avoid unnecessary spending.

1.1.2. Governance and Policy

Strong governance is essential for HTA implementation. Countries should establish national HTA committees with clear mandates, legal frameworks, and transparent processes. Decision-making should be accountable, inclusive, and based on evidence rather than opinion. Building policy capacity and stakeholder engagement ensures that HTA recommendations are trusted and integrated into health system planning.

[1] Health technology assessment of medical devices, second edition. Geneva: World Health Organization; 2025 (WHO medical device technical series). License: CC BY-NC-SA 3.0 IGO. Health technology assessment of medical devices, 2nd ed

1.1.3. HTA Methods for Medical Devices

Medical devices differ significantly from pharmaceuticals, requiring tailored assessment approaches. Unlike drugs, devices often have shorter lifecycles, frequent incremental innovations, and depend on user skill and infrastructure, making randomized controlled trials and cost-effectiveness analyses challenging. WHO recommends a life-cycle approach to HTA, applying it at different stages: pre-market approval, early adoption (horizon scanning), full HTA, procurement, and reassessment for disinvestment.

Key methodologies include:

- **Full HTA:** Comprehensive evaluation of clinical effectiveness, safety, economic impact, and social/ethical considerations. For devices, this must account for surgical dependencies, learning curves, and usability.
- **Horizon Scanning:** Early identification of emerging technologies to prepare health systems for adoption and manage disruptive innovations.
- **Rapid HTA:** Streamlined assessments for urgent decisions or resource-limited settings, trading depth for speed. Useful during emergencies or for devices with short lifecycles.
- **Living HTA:** Dynamic, continuously updated assessments incorporating new evidence, ideal for technologies with frequent updates.
- **Multi-Criteria Decision Analysis (MCDA):** Incorporates broader criteria beyond cost-effectiveness, such as technical characteristics, ease of implementation, and patient experience, enabling context-sensitive decisions.
- **Adaptive HTA:** Adapts existing HTA reports from other countries to local contexts by integrating local data on costs, epidemiology, and health system capacity.
- **Real-World Evidence (RWE):** Uses data from routine clinical practice to address evidence gaps, particularly relevant for devices where traditional trials are impractical.

These methods allow flexibility for LMICs, enabling timely and context-sensitive evaluations while promoting transparency and stakeholder engagement.

1.1.4. Challenges in LMICs

Low- and middle-income countries face barriers such as limited technical capacity, scarce financial resources, and inadequate local data. Capacity-building at individual, organizational, and system levels is critical. Networking with international HTA bodies and leveraging global resources can help overcome these challenges. Local data generation and context-sensitive methodologies are key for effective HTA in resource-constrained settings.

1.1.5. Special Topics

Emerging technologies like digital health, artificial intelligence, and 3D printing require adapted HTA frameworks. These innovations often lack traditional evidence and evolve rapidly, making conventional HTA methods inadequate. Real-world data can fill evidence gaps, while ethical considerations and equity must guide assessments. Emergency preparedness is another priority, with HTA playing a role in rapid decision-making during health crises.

1.1.6. International Collaboration

Global and regional networks such as HTAi, INAHTA, RedETSA, and HTAsiaLink support knowledge exchange, capacity-building, and harmonization of HTA practices. Collaborative initiatives reduce duplication, share resources, and strengthen HTA systems in LMICs. The EU HTA Regulation (2021/2282) exemplifies structured cooperation, requiring joint assessments while allowing local implementation. WHO encourages countries to leverage these partnerships for sustainable HTA development.

1.2 EU HTA Regulation (2021/2282) for medical devices and in-vitro diagnostics

The Regulation (EU) 2021/2282[2] establishes a unified framework for joint HTAs across EU Member States, including Joint Clinical Assessments (JCAs) for new medicines and selected high-risk medical devices and in vitro diagnostics, alongside Joint Scientific Consultations (JSCs) to support health technology developers. The regulation mandates a single evidence submission by developers at the EU level and obliges Member States to give due consideration to JCAs in their national HTA processes. By harmonizing methodologies and reducing duplication, it aims to accelerate patient access to innovation while preserving national decision-making on economic and reimbursement aspects.

Two implementing acts govern and the legal requirements for HTA of high-risk medical devices and in vitro diagnostics for the JCA and JSC processes.

1.2.1 Implementing act on joint scientific consultations of medical devices and in-vitro diagnostic medical devices[3]

Commission Implementing Regulation (EU) 2025/117 of 24 January 2025 laying down rules for the application of Regulation (EU) 2021/2282 with regard to the procedures for joint scientific consultations on medical devices and in vitro diagnostic medical devices.

[2] European Commission. The Regulation (EU) 2021/2282 available at: https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-assessment_en

[3] European Commission. Implementing act on joint scientific consultations of medical devices and in-vitro diagnostic medical devices available at: Implementing regulation - EU - 2025/117 - EN - EUR-Lex

- **Purpose and Scope**

The implementing act establishes the framework for conducting Joint Scientific Consultations under the EU HTA Regulation, specifically for medical devices and IVDs. Its goal is to provide early, structured dialogue between developers and HTA bodies to align evidence generation plans with future assessment requirements. This helps ensure that clinical studies and data collection strategies meet both regulatory and HTA expectations, reducing duplication and accelerating access to innovative technologies.

- **Process and Timelines**

The act defines clear procedural steps for JSCs, including annual consultation windows, submission requirements, and timelines for responses. Developers must submit detailed documentation such as draft clinical protocols, study designs, and evidence plans. The HTA Coordination Group organizes consultations, supported by expert panels, and ensures that advice is delivered within specified deadlines to maintain predictability for manufacturers.

- **Stakeholder Engagement and Transparency**

JSCs involve a broad range of stakeholders, including clinical experts, patient representatives, and regulators, to ensure that advice reflects real-world needs and patient perspectives. The implementing act emphasizes transparency, requiring clear roles, responsibilities, and standardized templates for requests and feedback. This structured approach fosters trust and consistency across Member States.

- **Integration and Coordination**

The act allows for parallel consultations with regulatory bodies such as the EMA or notified bodies when device development overlaps with regulatory approval processes. This coordination minimizes duplication and aligns evidence requirements for both regulatory and HTA purposes, streamlining product development and supporting timely market entry.

1.2.2 Implementing act on joint clinical assessment of medical devices and in-vitro diagnostic medical devices[4]

Commission Implementing Regulation (EU) 2025/2086 of 17 October 2025 laying down, pursuant to Regulation (EU) 2021/2282 on health technology assessment, procedural rules for the interaction during, exchange of information on, and participation in, the preparation and update of joint clinical assessments of medical devices and in vitro diagnostic medical devices at Union level, as well as templates for those joint clinical assessments.

- **Purpose and Scope**
  The implementing act sets out detailed rules for conducting Joint Clinical Assessments under the EU HTA Regulation for high-risk medical devices and IVDs. Its

[4] European Commission. Implementing act on joint clinical assessment of medical devices and in-vitro diagnostic medical devices available at: Implementing regulation - 2025/2086 - EN - EUR-Lex

primary aim is to harmonize clinical evaluation across Member States by defining common methodologies, templates, and timelines for assessing comparative clinical effectiveness and safety. This ensures consistency and transparency while reducing duplication of national assessments.

- **Assessment Process**
  Manufacturers submit a single evidence dossier at the EU level, which is reviewed by the HTA Coordination Group and its designated subgroups. The JCA focuses exclusively on clinical domains—such as patient-relevant outcomes, safety, and effectiveness—without addressing economic or organizational aspects, which remain under national competence. The act specifies standardized reporting formats, procedural steps, and deadlines to ensure timely delivery of assessments.
- **Governance and Stakeholder Involvement**
  The implementing act emphasizes collaboration and transparency. It outlines roles and responsibilities for Member States, HTA bodies, and the Coordination Group, and includes mechanisms for stakeholder engagement, such as consultations with clinical experts and patient representatives. Clear timelines and templates are provided to guarantee predictability for developers and decision-makers.
- **Integration with Regulatory Processes**
  While JCAs are distinct from regulatory approval, the act encourages coordination with notified bodies and other regulatory authorities to align evidence requirements and avoid duplication. This integrated approach supports faster market access for innovative technologies while maintaining rigorous standards for clinical evaluation.

At the end of 2025, the HTA Coordination Group adopted some specific guidance for the JSCs and JCAs of medical devices and in vitro diagnostics with the join process for these types of products to be initiated in 2026. The summaries are available below and the full guidance is available from the references.

1.2.3 Guidance regarding the HTA CG recommendation for the selection of Medical Devices (MD) and In Vitro Diagnostic Medical Devices (IVD)for Joint Clinical Assessments (JCA)[5]

- The guidance defines eligibility for JCA under the HTAR for high-risk technologies: medical devices (Class IIb/III with expert panel scientific opinions) and IVDs (Class D with expert panel views). Eligibility criteria do not imply automatic selection. The selection criteria are applied at different stages of the technology life cycle and for different purposes.
- Formalised 3-step selection procedure:

[5] Member State Coordination Group on HTA. Guidance on the HTACG recommendation for the selection of medical devices and in vitro diagnostic medical devices for JCA. Available at: Guidance on the HTACG recommendation for the selection of medical devices and in vitro diagnostic medical devices for JCA - Public Health

1. Identification: The EMA submits a quarterly report to the HTA secretariat, no later than 15 days after each quarter, listing all eligible devices, manufacturers, and notified bodies, and the expert panel's opinion or views.

2. Recommendation: The HTA CG, supported by the JCA SG, assesses the devices and recommends those that should undergo a JCA.

3. Adoption: The European Commission adopts an Implementing Decision selecting the devices, following the HTA CG's recommendation.

- For a device to be selected, it must fulfil at least one of the following criteria (Article 7(4) HTAR). The interpretation of criteria may differ depending on the technology and clinical context.
  1. Unmet Medical Needs: no satisfactory diagnosis/treatment method in the EU, or major therapeutic advantage.
  2. First in Class: No certified EU alternative with the same mechanism of action or technological approach, including first use in a new indication or device if the first one is not yet certified.
  3. Potential Impact: expected benefit on patient survival, quality of life, or safety, or a high economic/organisational impact on healthcare systems (impact on patient, public health, and healthcare system level)
  4. Advanced Technology: Incorporation of AI, machine learning, or complex algorithms.
  5. Cross-border Dimension: The assessment applies significantly to several EU/EEA countries.
  6. Union-wide Added Value: The JCA provides better outcomes than assessments only at the MS level.
- The selection follows a quarterly cycle coordinated by the JCA Subgroup (SG). MS submit positions and justifications using a standardised Selection Table template. A small group of JCA SG members and chairs drafts a recommendation proposal based on MS responses. The JCA SG approves the draft where consensus is reached, or revises and approves it in writing, after which it is formally adopted by the HTA CG during a meeting or in writing.
- HTA Secretariat informs HTDs of the recommendation and, if selected, the reasons. HTDs submit the certificate of conformity and instructions for use within 7 days of certification or request (whichever is later), or via EUDAMED, where information is fully available.

1.2.4 Procedural Guidance for JCA medical devices and in vitro diagnostic medical devices (IVDs)[6]

The guidance describes the process from the start of the JCA on high-risk medical devices/ IVDs through assessment, endorsement, publication, and updates. The selection process is out of scope for this procedural guidance. It aims to harmonize clinical evaluation across Member States, reduce duplication, and ensure timely, transparent assessments.

- Applies to high-risk medical devices (Class III) and in vitro diagnostic devices (Class D).
- Focuses exclusively on clinical domains: comparative effectiveness, safety, and patient-relevant outcomes.
- Economic, organizational, and reimbursement aspects remain under national competence.

Key Procedural Elements

- **Initiation:** The HTA Secretariat requests the certificate of conformity and instructions for use from the Health Technology Developer (HTD) within 7 days (counting from whichever event occurs later) and informs the relevant notified body and expert panel (via EMA).

- **Scoping:** The JCA Subgroup appoints an Assessor and Co-Assessor (ASR, CO-ASR), who develop a proposed assessment scope based on the PICO framework, drawing on available scientific opinions and expert input. The JCA Subgroup reviews and finalises the scope within 60 days (or 10 days after the Commission decision, if later). The final scope is sent to the HTD, which initiates the dossier submission period. A scope clarification meeting may be requested from the HTD.

- **Dossier submission**: The HTD submits a JCA dossier containing clinical evidence, supporting analyses, and justification aligned with the agreed PICO within 100 days, with a possible 30-day extension in justified cases.

    - The European Commission, in consultation with the ASR and CO-ASR, verifies whether the dossier meets legal requirements within 15 working days. If deficiencies remain after a second request for missing information, the JCA is discontinued.

- **Assessment phase**: Following confirmation of dossier completeness, the Assessor and Co-Assessor jointly draft the JCA and summary reports. The JCA Subgroup reviews

[6] Member State Coordination Group on HTA. Procedural Guidance for JCA medical devices and in vitro diagnostic medical devices. Available at: https://health.ec.europa.eu/publications/procedural-guidance-jca-medical-devices-and-vitro-diagnostic-medical-devices_en

drafts for quality and coherence. Revised drafts must be finalised within 165 days from Commission confirmation.

    - The Health Technology Developer has 7 days to identify factual inaccuracies or request confidentiality for commercially sensitive information; only fact-based comments are considered.

- **Endorsement & publication**: The HTA Coordination Group endorses the JCA and summary reports within 30 days. Where consensus cannot be reached, divergent scientific opinions are included. The Commission verifies procedural compliance and publishes the reports.
- **Updates**: Where new evidence becomes available, the HTA Coordination Group decides whether an update is required. Updates follow the same procedural logic and timelines but apply only to the relevant sections of the assessment.

1.2.5 Questions and Answers on general methodological and procedural issues for joint clinical assessments[7]

This Q&A clarifies practical and methodological requirements for Joint Clinical Assessments (JCAs) under the EU HTA Regulation, focusing on evidence standards, dossier completeness, and handling of PICOs (Population, Intervention, Comparator, Outcomes).

Key Requirements for HTDs

- **Address All PICOs**: Health Technology Developers (HTDs) must respond to every PICO in the dossier, even if they disagree with its relevance. All decisions and deviations must be justified.
- **Evidence Gaps**: If data is unavailable, HTDs must provide the closest relevant analyses, explain deviations, and justify why remaining data is informative. Cross-referencing is allowed for duplicate results across different PICOs. If there is an evidence gap, the dossier is considered incomplete, depending on the appropriateness of the HTD's justification for the lack of comparative data. Unjustified gaps may render the dossier incomplete.
- **Subgroup Analyses**: If a subgroup overlaps with another PICO population, both reporting requirements apply (e.g., interaction tests for subgroups, outcome results for full population). For broader trial populations, HTDs should explore valid subpopulation analyses. If a trial population is wider than the PICO requirement, the

[7] Member State Coordination Group on HTA. Questions and Answers on general methodological and procedural issues for joint clinical assessments. Available at: Questions and Answers on general methodological and procedural issues for joint clinical assessments - Public Health

HTD should explore whether a scientifically valid subpopulation analysis can be conducted to meet the PICO definition.

- **Outcome Reporting**: All outcomes in the assessment scope must be included in subgroup analyses, except safety outcomes by System Organ Class (SOC) and Preferred Term (PT).

Additional Methodological Rules

- **Therapeutic Indication**: HTDs cannot propose a different indication than that submitted to EMA; the JCA scope is based on the EMA indication. The JCA Subgroup bases the assessment scope on the therapeutic indication proposed to the EMA.
- **Complete Dossier**: All available evidence must be included in the initial submission (version V0.1), with full data, analyses, and documentation for verification. The dossier must contain complete and up-to-date information, data, analyses, and underlying documentation to allow the assessor/co-assessor to verify accuracy.
- **Indirect Comparisons**: If no direct comparison exists, HTDs should use indirect methods, anchored approaches are preferred over unanchored.
- **Individualized Treatment**: When a single treatment is not suitable for all patients, actual treatment choices depend on individual characteristics. When treatment varies by patient characteristics, the comparator may be a bundle of options. The "individualized treatment" comprises a bundle of treatment options that represents the comparator. The JCA defines one PICO against the individualized treatment comparator, and the analysis yields one effect estimate comparing the intervention against the overall group of patients receiving any option from the individualized treatment arm. Definitions are found in the glossary of the Coordination Group's Guidance on the Scoping Process.

1.2.6 Guidance on filling in the Joint Clinical Assessment dossier template of a Medical Device[8]

This guidance provides a comprehensive framework for HTDs to develop a structured, transparent, and methodologically sound JCA dossier for medical devices under EU law.

- **Purpose and Scope**

This guidance is designed to support Health Technology Developers (HTDs) in completing the Joint Clinical Assessment (JCA) dossier template, as outlined in Annex I of Implementing Regulation 2025/2086. It serves as a practical tool to ensure that submissions are structured and aligned with regulatory requirements. In addition, the guidance complements other methodological documents developed under

[8] Member State Coordination Group on HTA. Guidance on filling in the Joint Clinical Assessment dossier template of a Medical Device. Available at: Guidance on filling in the Joint Clinical Assessment dossier template of a Medical Device

Regulation (EU) 2021/2282, providing consistency across health technology assessments. All evidence presented in the dossier must adhere to internationally recognized standards of evidence-based medicine, ensuring transparency, reliability, and scientific rigor throughout the assessment process. The overall process, structure, and methodological principles are the same for both MDs and IVDs, with specific additional requirements for IVDs due to their diagnostic nature.

- **Dossier Structure and Format**

The Joint Clinical Assessment dossier must follow the structure provided in the official template. Each section of the template is presented in grey boxes, while this guidance offers explanatory text to assist in completing those sections. Information should be presented clearly and concisely, with a preference for tabular formats wherever possible to enhance readability and transparency. This structured approach ensures consistency across submissions and facilitates efficient review by assessment bodies.

Revision History & Confidentiality

The JCA dossier follows a structured versioning system, starting a version history section, with versions like V0.1 (initial), V0.2–V0.5 (updates), up to V2.0 for final publication.

There should be a dedicated confidentiality version (V0.5) where the HTD identifies and justifies confidential information, a public version (V1.0) for publication, and V2.0 following a completed update of a JCA. HTD may indicate and justify confidential information, which may be removed for public versions.

Content requirements

HTDs must provide a complete overview of the technology, including device identification, technical characteristics, clinical context, regulatory status in selected non-EEA jurisdictions, and requirements for use. For IVDs, additional technical detail is required, including an explicit description of the analyte or marker, the assay method principle, and whether the test is automated or quantitative.

The dossier must follow the Commission-defined PICO framework, define inclusion and exclusion criteria, exclude abstract-only studies, and be supported by systematic literature searches across MEDLINE, Cochrane, and study registries, with a search cut-off no more than three months before submission.
HTDs must justify analytical methods in line with Coordination Group guidance and specify comparator scenarios, including a single comparator, multiple comparators, or an individualized treatment comparator comprising a bundle of options.

Where studies are comparable, pairwise meta-analyses are required. For indirect comparisons, anchored methods are preferred. HTDs do not perform the risk-of-bias assessment but must provide sufficient information to enable assessment by the JCA team and must specify and justify methods for handling missing data.

Results must be presented separately for each PICO. Analyses should preferably use the intention-to-treat population, with deviations justified. Statistical results must clearly state whether analyses were pre-specified, adjusted for multiplicity, and assessed against a defined alpha level. Safety outcomes should be reported descriptively in the main results section, with analytical safety estimates reported in the appendix.

For MDs, this includes clinical investigation reports, the Clinical Evaluation Report (CER), post-market clinical follow-up documentation, expert panel opinions, and relevant prior HTA reports.

For IVDs, mandatory documentation centres on the Performance Evaluation Report (PER), clinical performance study plans and reports (CPSP), expert panel views issued during performance evaluation consultation, and full reference lists submitted in RIS format (Appendix D and C for MD and IVD, respectively).

Appendices (A–D)

- **A**: Tabular descriptions and methods of each included study.
- **B**: Risk-of-bias details and certainty assessments.
- **C**: Main clinical study results not covered in PICO sections.
- **D**: Documentation (search strategies, full texts, registry data from clinical trial or device registries), programming codes used for analyses, Clinical Evaluation Report (CER)/ Clinical Investigation Report (CIR), Post-Market Clinical Follow-up (PMCF) plans, expert opinions, Periodic Safety Update Reports (PSURs).

1.2.7 Template for dossier submission[9]

Pending

The Member State Coordination Group on HTA are currently finalizing the word template for the dossier submission for JCAs for medical devices and invitro diagnostics. They are working to see what minor tweaks would be needed in the current template used for medicinal products.

1.2.8 Updates in the EU regulation for medical devices[10]

The European Union has fundamentally reformed its regulatory framework for medical devices and in vitro diagnostic medical devices over the past decade to strengthen patient safety, transparency and regulatory oversight across the single market. The cornerstone of this reform is Regulation (EU) 2017/745 on medical devices (MDR) and Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR), which replaced the former EU directives and introduced a more robust, lifecycle-based regulatory approach. These

[9] Member State Coordination Group on HTA. pending
[10] European Commission: Medical devices – new regulations. Available at: https://health.ec.europa.eu/medical-devices-sector/new-regulations_en

regulations established stricter requirements for clinical evidence, post-market surveillance, traceability, and notified body oversight, reflecting the significant technological developments and increased complexity of medical devices over the last 20 years. The MDR became applicable in May 2021 and the IVDR in May 2022, marking a shift toward a harmonized and directly applicable EU regulatory system aimed at ensuring a high level of health protection while supporting innovation and market confidence across Member States.

At the same time, the Commission acknowledges that implementation of the new framework has proved challenging, particularly due to notified body capacity constraints and the risk of medical device shortages. In response, the EU has adopted targeted amendments to extend transitional periods, remove sell-off deadlines, and allow for a gradual roll-out of EUDAMED, the central EU database for medical devices.

In December 2025, the European Commission proposed a targeted revision of the MDR and IVDR to simplify requirements, reduce administrative burden, improve digitalization, and introduce more proportionate rules, especially for lower-risk devices, well-established technologies and small and medium-sized enterprises, while maintaining high safety standards. This proposal aims to make the regulatory system more predictable, efficient and sustainable, ensure continued availability of medical devices, and future-proof the framework to respond to innovation and evolving patient needs, subject to adoption by the European Parliament and EU Council.

This is a major proposal (2025) 1023 to simplify and rebalance MDR and IVDR, responding to sustained implementation concerns. The EU has moved decisively from a “hard reset” MDR/IVDR implementation to a phased, pragmatic stabilization strategy, while preparing a second-generation reform (MDR 2.0 / IVDR 2.0) that emphasizes proportionality, sustainability and supply security without abandoning patient-safety goals. The key features of the proposal are summarized below.

Simplification & Proportionality

- Removal of the 5-year maximum certificate validity
- Replaced by risk-based periodic reviews by notified bodies
- Reduced administrative burden for SMEs
- Lighter requirements for well-established technologies (WETs)

Clinical Evidence Flexibility

- Broader definition of admissible clinical data:
    - Published literature
    - Real-world evidence
    - Bench and in-silico data
- Easier demonstration of equivalence, including removal of the requirement for contracts with equivalent product manufacturers

Reclassification of Certain Devices

- Potential down-classification of:
    - Reusable surgical instruments

    - Accessories to implantables
    - Large categories of medical software (modification of MDR Rule 11)
- This could significantly reduce notified body involvement for some products.

Reduced Post-Market Burden

- Less frequent PSUR updates
- Extended serious-incident reporting timelines (from 15 to 30 days for non-critical incidents)
- Simplified change management after certification

1.3 Special topics – digital health technologies

As highlighted in section 1.1 in the special topics, HTA for digital health technologies is a growing area where methods are still evolving. The following international EU and OECD projects are now working on the methods for these kinds of health technologies. A recent editorial[11] explores how HTA can enable the responsible, evidence-based integration of artificial intelligence (AI) into healthcare systems at a time when AI technologies are expanding rapidly across clinical specialties. The authors emphasize that health systems are under pressure to determine which AI tools to invest in, as the pace of commercialization accelerates and AI begins to influence diagnostics, care pathways, and organizational processes. Traditional HTA has only recently started adapting to AI, and existing evaluation efforts remain fragmented, focused on selective domains such as ethics or developer guidance rather than producing a comprehensive, comparable evidence base.

Drawing on three major initiatives and projects (MAS-AI, AI-MIND, and EDiHTA), the review illustrates emerging models for assessing AI across its lifecycle, from early development to full implementation. These projects introduce structured assessment pathways, early-phase and full-phase HTA models, and multi-stakeholder approaches that bring together clinicians, patients, AI developers, ethicists, and legal experts. By highlighting these examples, the authors argue that HTA must evolve into a harmonized, multidimensional, and collaborative process capable of capturing AI's risks, benefits, and context-specific performance. This evolution, they conclude, is essential to compare AI systems fairly, support safe adoption, and ensure AI delivers real-world value for patients and health systems.

1.3.1 EDiHTA[12]

The EDiHTA project is a major EU-funded Horizon Europe initiative (2024–2028) aimed at developing the first flexible, inclusive, validated, and ready-for-use European Health

[11] Di Bidino R, Fasterholdt I, Daugbjerg S, Cicchetti A. Unlocking AI's value: the HTA approach to responsible healthcare integration. BMJ Digital Health & AI. 2026;2:e000250. https://doi.org/10.1136/bmjdhai-2025-000250

[12] The EDiHTA project: Available at: https://edihta-project.eu/

Technology Assessment (HTA) framework specifically for Digital Health Technologies (DHTs) such as telemedicine, mobile health apps, and AI tools. Existing HTA methods struggle to capture the unique value, risks, and context-specific benefits of digital technologies; EDiHTA fills this gap by co-creating a comprehensive evaluation framework with HTA agencies, clinicians, policymakers, regulators, patients, industry, and research institutions. The resulting framework will be tested across real-world pilot sites in leading European hospitals, supported by an interactive digital platform, and informed by legal, ethical, privacy, and European Health Data Space (EHDS) requirements. Its overarching goal is to create a harmonized, stakeholder-driven approach for assessing DHTs across Europe to improve decision-making and support sustainable digital health adoption.

Purpose: Create the first Europe-wide HTA framework tailored to digital health technologies (DHTs) to assess their real-world added value.

Scope: Assessment of multiple DHT types: including telemedicine, mApps, artificial intelligence tools, across different technology readiness levels and territorial levels (national, regional, local).

Co-creation: Developed jointly with HTA agencies, clinicians, hospitals, patient groups, regulatory bodies, and policymakers, ensuring inclusiveness across the value chain.

Duration & Funding: 48-month Horizon Europe project (Jan 2024–Jan 2028) with €8 million in EU funding.
Consortium: 16 partners from 10 European countries, including HTA agencies, universities, hospitals, patient organizations, and expert bodies.
Piloting: Framework will be **tested in five major European hospitals** and through an open piloting programme involving DHT developers.
Expected Outputs:

- Map of HTA stakeholders in Europe
- Analysis of legal/privacy/regulatory requirements (incl. European Health Data Space)
- Interactive digital platform guiding users through HTA processes
- A fit-for-purpose digital HTA framework for Europe

Intended Impact: A harmonized, practical, user-friendly HTA approach enabling better digital health decision-making and supporting health system sustainability.

1.3.2 ASESS-DHT[13]

ASSESS-DHT is a Horizon Europe project (2024–2026) focused on developing a harmonized, fit-for-purpose European framework for assessing Digital Health Technologies (DHTs). Building on existing HTA tools and international models such as Germany's DiGA and France's

[13] The ASSESS-DHT project. Available at: https://assess-dht.eu/

PECAN, the project aims to streamline and consolidate assessment methods while incorporating essential criteria—including privacy, cybersecurity, interoperability, usability, data handling, and evaluation of AI-based and dynamic, continuously learning technologies. The project adopts a four-pillar structure covering consolidation of current evidence, toolkit and framework development (including phased and fast-track pathways), real-world testing through case studies, and long-term sustainability. Ultimately, ASSESS-DHT seeks to support a coherent digital single market by enabling consistent, trustworthy, and efficient HTA of digital technologies across Europe, aligned with the EHDS.

Purpose: Develop a generic European digital HTA framework to evaluate innovative DHTs, addressing methodological gaps and supporting digital transformation of health systems.

Scope: Covers telemedicine, wearables, mHealth apps, AI-driven tools, digital therapeutics (digiceuticals), remote monitoring systems, digital twins, clinical decision support systems, and more.

Alignment with EU policy: Framework aligned with the EHDS Regulation proposal and relevant data protection, cybersecurity, and interoperability standards.

Methodological focus:

Incorporates assessment of:

- Privacy and cybersecurity
- Data storage, handling, quality, and governance
- Interoperability and usability
- AI transparency and lifecycle considerations
- Dynamic/iterative DHTs that improve over time

Uses lessons from DiGA (Germany) and PECAN (France) to develop phased, adoption-friendly, and fast-track pathways for DHT approval.

Four-pillar structure:

1. **Consolidation & preparation** — mapping and synthesizing existing assessment frameworks.
2. **Toolkit development** — creating the new assessment framework, pathways, checklists, and manuals.
3. **Testing & validation** — via real-world case studies.
4. **Uptake & sustainability** — stakeholder engagement, usability testing, and dissemination.

Duration & Funding: 36-month Horizon Europe project (Jan 2024–Dec 2026) with over €6 million in EU funding.

Expected Outputs:

- Overarching DHT assessment manual
- Special pathways for AI, DTx, and rapidly evolving technologies
- A European evidence repository for DHT evaluations
- Tools enabling payers and decision-makers to use the framework

Intended Impact: Increase the EU-wide adoption of trustworthy, effective DHTs and support a coherent digital single health market for patients, clinicians, health systems, and developers.

1.3.3 OECD

The Organisation for Economic Co-operation and Development (OECD) also reviewed how HTA for digital medical devices has been occurring in many OECD countries and published their findings in 2025. The OECD Health Working Paper No. 177 (2025)[14] examines how several OECD countries are adapting health technology assessment (HTA) to evaluate digital medical devices, a category that includes fast-evolving tools such as digital therapeutics, remote monitoring systems, mobile applications, and AI-enabled diagnostics. The paper highlights that while digital health innovations present major opportunities for improving care, they also introduce challenges for payers and governments, particularly in determining coverage, pricing, and value under increasing budget pressures.

A key barrier identified is the absence of a common taxonomy for digital medical devices and the difficulty of applying traditional HTA methods, built for pharmaceuticals and hardware devices, to technologies that evolve rapidly, rely on real-time data, and interact dynamically with users. Several countries: including France, Germany, Israel, Korea, Spain, and the United Kingdom, are developing or refining dedicated assessment pathways for specific types of digital devices. Through desk research and interviews, the report maps these national approaches, focusing on remits, evaluation methods, evidence requirements, and coverage pathways.

The paper identifies common challenges such as ensuring appropriate clinical evidence, dealing with fast innovation cycles, assessing privacy and cybersecurity risks, and evaluating adaptive or AI-based systems. It also highlights emerging good practices, including developing clearer definitions, adjusting evidence standards, incorporating real-world performance data, promoting methodological convergence, and exploring more harmonized international HTA approaches. Overall, the report contributes to global discussions on how health systems can better integrate digital medical devices while ensuring safety, clinical benefit, and efficient use of public resources.

[14] OECD Health Working Paper No. 177, Towards identifying good practices in the assessment of digital medical devices: Insights from several OECD countries. Available at: https://www.oecd.org/en/publications/towards-identifying-good-practices-in-the-assessment-of-digital-medical-devices_b485ee1f-en.html

1.4 Peer learning

1.4.1 INFARMED

In 2015, Portugal implemented a major reform of its national HTA system with the creation of the Sistema Nacional de Avaliação de Tecnologias de Saúde (SiNATS) through Decree-Law No. 97/2015, published on 1 June 2015. This legislation formally expanded HTA beyond pharmaceuticals to include medical devices and all other health technologies, representing a shift toward a unified, transparent, and comprehensive evaluation model governed by INFARMED – National Authority of Medicines and Health Products.

Objectives and Scope of SiNATS

SiNATS was designed to support evidence-based decisions on the adoption, pricing, reimbursement, and monitoring of health technologies within the National Health Service (SNS). Its scope explicitly includes medical devices, pharmaceuticals, diagnostics, and other health interventions across both public and private sectors. SiNATS evaluates technologies across multiple dimensions:

- Relative clinical effectiveness / therapeutic value
- Economic value (cost-effectiveness, cost-utility, or cost-minimization)
- Budget impact and affordability
- Organizational impact and sustainability
- Other value considerations, such as unmet need or equity implications

This multidimensional assessment allows INFARMED to issue decisions on price setting, financing / reimbursement, risk-sharing agreements, and post-market reassessment, the latter representing a new ex-post evaluation paradigm introduced by SiNATS.

Legislative and Governance Framework

The Decree-Law No. 97/2015 reorganized HTA governance and mandated the development of complementary Ordinances (e.g., Ordinance No. 195-C/2015) to operationalize assessment procedures and decision criteria. SiNATS created a system of structured stakeholder engagement, including six discussion forums to ensure transparency in processes and consultation with patients, clinicians, experts, and industry.

To operationalize technical work, INFARMED established a multidisciplinary Commission for the Evaluation of Health Technologies, comprising clinicians, pharmacists, economists, and methodologists, responsible for issuing HTA recommendations. This governance model was further strengthened during revisions to SiNATS in 2017, which introduced stricter timelines: 30-day deadlines for generics/biosimilars and under 180 days for new molecules, supporting faster decision-making and reducing historic approval delays.

For medical devices there are two pathways:

1. full comparative HTA and evidence assessment and evaluation report and
2. a rapid assessment for similar medical devices ("me-too") where there is only the validation of specific technical requirements and validation of the price proposal.

For example, in 2024 for new medical devices 4 went through the full pathway and 110 the rapid assessment. This has the co-payment provided by SHS for outpatient setting and 100% reimbursement by NHS for inpatient settings.

Feature	Full Comparative HTA	Rapid Assessment (Similar Devices)
Purpose	Evaluate new/innovative devices; determine added value	Validate equivalence and price for similar devices
Evidence Required	Full clinical + economic + organizational	Technical documentation + compliance + price
Depth of Review	High (therapeutic, economic, system impact)	Low (technical + price validation)
Typical Duration	Several months (no legal deadline)	Weeks (faster, simplified; no legal deadline)
Decision Outputs	Price, reimbursement, usage conditions, ex-post monitoring	Price validation, inclusion in procurement pathways
Legal Basis	SiNATS (Decree-Law 97/2015)	Same legislation, simplified application

HTA Process for Medical Devices

Although early Portuguese HTA focused primarily on medicines, the 2015 reform expanded systematic assessment to medical devices. Under SiNATS, medical devices undergo:

1. **Clinical evaluation** (effectiveness, comparative value, safety)
2. **Economic evaluation** (type depends on availability of added therapeutic value; for example, cost-minimisation for equivalent technologies)
3. **Decision on pricing and reimbursement**, including potential conditional approval or risk-sharing mechanisms
4. **Monitoring and post-market reassessment** for technologies already in use

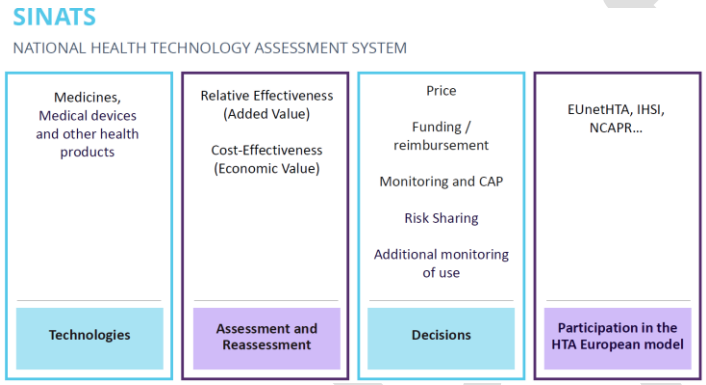
Within the first three years of full implementation (2015–2018), assessments demonstrated increased methodological clarity, explicit therapeutic value judgements, and widespread

use of cost-minimization analyses for technologies without demonstrated added value, an important principle also applied to medical devices.

Impact and System Maturity

By introducing SiNATS, Portugal significantly modernized, centralized, and standardized HTA processes for medical devices. Stakeholders reported improvements in efficiency, transparency, and system sustainability, although areas such as coordination across the Ministry of Health and monitoring of real-world effectiveness continue to require strengthening.

Since 2015, SiNATS has been the foundation for Portugal's HTA of medical devices, ensuring that new technologies entering the health system demonstrate clinical value, economic justification, and affordability. Managed by INFARMED, the system aligns Portugal with European HTA standards and supports rational, equitable access to innovation while maintaining sustainability of the SNS.



1.4.2 AGENAS

In Italy, HTA for medical devices is a structured, multi-dimensional process coordinated at national level by AGENAS (Agenzia Nazionale per i Servizi Sanitari Regionali). AGENAS operates under the mandate of the Ministry of Health and supports Regions and Autonomous Provinces in evidence-based decision-making related to the adoption, reimbursement, procurement, and appropriate use of medical devices within the Italian National Health Service (Servizio Sanitario Nazionale, SSN). The Italian HTA framework for medical devices aligns with European methodological standards, in particular the EUnetHTA Core Model (version 3.0), and is progressively integrated with the requirements of Regulation (EU) 2021/2282 on Health Technology Assessment. Within this context, AGENAS acts as a technical-scientific body responsible for producing standardized HTA assessment documents based on transparent, reproducible, and policy-relevant methodologies. The draft protocol (see Annex 1) represents the standard HTA research protocol template used by AGENAS for the assessment of medical devices. It defines the structure, domains, research questions, and analytical methods that guide the entire assessment process.

Objectives and Scope of AGENAS

The primary objective of the AGENAS HTA process is to inform policy and managerial decisions regarding medical devices by evaluating their clinical value, safety, economic sustainability, organizational impact, and broader ethical, social, and legal implications.

Each HTA assessment is conducted in response to a formal mandate, typically issued by national or regional institutions. The mandate defines the policy needs and is translated into:

- Policy questions, reflecting decision-making requirements (e.g. adoption, disinvestment, prioritization);
- Research questions, analytically framed to generate evidence capable of addressing those policy questions.

The assessment explicitly considers comparative technologies, current clinical practice, and potential alternatives, ensuring relevance to real-world healthcare pathways in the SSN.

Methodological Framework

AGENAS HTA assessments are grounded in:

- The EUnetHTA 3.0 Core Model, ensuring harmonization with European HTA standards.
- Methodological guidance developed under EU Regulation 2021/2282, particularly for clinical domains (safety and effectiveness).
- Additional European Commission methodological documents, referenced in the protocol appendices.

This framework ensures methodological rigor, transparency, and consistency across assessments, while allowing flexibility depending on the nature and maturity of the technology.

HTA Domains

The AGENAS HTA process is organized into nine core domains, each addressing a specific dimension of value and impact:

1. Clinical problem and current use of technology (CUR)
2. Description and technical characteristics of the technology (TEC)
3. Safety (SAF)
4. Clinical effectiveness (EFF)
5. Economic aspects (ECO)
6. Organizational aspects (ORG)
7. Ethical aspects (ETH)

8. Social and patient aspects (SOC)
9. Legal aspects (LEG)

Not all domains are necessarily included in every assessment; domain selection is driven by the mandate and decision context.

Clinical Problem and Current Use (CUR)

This domain contextualizes the technology within the healthcare system by describing:

- Epidemiology of the target condition (incidence, prevalence, mortality);
- Clinical and socio-economic burden of disease;
- Current patterns of technology use within the SSN;
- Available alternatives and existing standards of care; and
- Unmet medical needs and geographical variations in access.

Evidence is gathered through guideline analysis, epidemiological data, administrative databases (e.g. discharge records, consumption data), literature review, and expert consultation.

Technology Description and Technical Characteristics (TEC)

This domain provides a detailed technical overview of the medical device, including:

- Mechanism of action and intended use;
- Technological features and materials;
- Regulatory status and conformity documentation; and
- Requirements for installation, use, and maintenance.

Information sources include manufacturer documentation, regulatory databases, technical data sheets, and structured questionnaires to producers or distributors.

Safety and Clinical Effectiveness (SAF & EFF)

Safety and effectiveness are evaluated through a systematic review of the scientific literature, structured around clearly defined PICOD(s) (Population, Intervention, Comparator, Outcomes, Design).

Key methodological steps include:

- Definition of clinically relevant outcomes based on guidelines and expert input;
- Comprehensive literature searches across predefined databases and timeframes;
- Study selection, data extraction, and critical appraisal; and
- Quality assessment of evidence and synthesis of results.

European clinical guidelines and stakeholder input may complement published evidence, particularly for innovative or rapidly evolving technologies.

Economic Aspects (ECO)

The economic domain assesses the financial implications of adopting the technology, focusing on both efficiency and affordability.

Analyses may include:

- Review of existing economic evaluations;
- Cost-effectiveness or cost-utility modeling, where appropriate; and
- Budget impact analysis from the SSN perspective.

Economic inputs are derived from tariffs, DRGs, published literature, and healthcare utilization data. The analysis explicitly links costs to outcomes defined in the clinical domains.

Organizational Aspects (ORG)

This domain evaluates how the technology affects healthcare organization, including:

- Staffing and training requirements;
- Infrastructure and workflow changes;
- Impact on care pathways and service delivery models.

Methods include literature reviews, administrative data analysis, stakeholder consultations, and the use of logic or process diagrams to model organizational changes.

Ethical Aspects (ETH)

The ethical assessment examines whether the technology respects fundamental ethical principles, such as:

- Human dignity and patient autonomy;
- Equity and fairness in access;
- Transparency and informed consent; and
- Appropriate management of conflicts of interest.

Evidence is gathered through ethical literature, regulatory documents, expert consultation, and qualitative methods involving clinicians, patients, and civil society representatives.

Social and Patient Aspects (SOC)

This domain focuses on the impact of the technology on:

- Patient quality of life;

- Caregiver burden;
- Social acceptability and perception;
- Patient involvement in decision-making; and
- Potential inequalities in access or outcomes.

Both qualitative and quantitative data are used, including patient-reported outcomes, interviews, questionnaires, and input from patient associations.

Legal Aspects (LEG)

The legal domain assesses compliance with applicable national and European regulations, covering:

- Medical device safety and liability;
- Data protection and privacy;
- Professional responsibility;
- Informed consent; and
- Regulatory barriers to adoption.

The analysis is based on legal texts, policy documents, case law, and consultation with legal and regulatory experts.

Reporting and Outputs

Each domain addresses predefined assessment elements, ensuring completeness and consistency across HTA reports. Results are synthesized into a structured HTA assessment document, designed to support decisions at national and regional level.

Appendices document search strategies, methodological choices, and supplementary analyses, enhancing transparency and reproducibility. The AGENAS HTA process for medical devices represents a comprehensive, methodologically robust framework that balances clinical evidence, economic sustainability, organizational feasibility, and societal values. By aligning national assessments with European standards and explicitly addressing policy-relevant questions, AGENAS plays a central role in promoting equitable, efficient, and evidence-based innovation within the Italian National Health Service.

1.4.3 Recommendations for Greece

In developing a fit-for-purpose HTA framework for medical devices, Greece should draw systematically on the established methods and procedural experience of both AGENAS and INFARMED. These agencies provide complementary models: AGENAS offers a comprehensive, methodologically robust approach aligned with European cooperation, while INFARMED demonstrates how proportionality and administrative efficiency can be embedded within device assessments. Leveraging these experiences would allow Greece to avoid

duplicative development efforts, accelerate institutional learning, and ensure early alignment with European best practice for medical device HTA.

For the clinical assessment component, Greece should adapt the methods and processes used by AGENAS, particularly those recently updated from EUnetHTA methodologies to ensure consistency with the EU Health Technology Assessment Regulation (EUHTAR). AGENAS's structured approach to defining PICO elements, assessing clinical effectiveness and safety, and transparently grading evidence is especially relevant for medical devices, where randomized controlled trials are often limited. Adopting these approaches, while allowing flexibility for device-specific evidence profiles, would support methodological credibility and facilitate future joint or collaborative assessments at EU level.

In parallel, Greece should adapt AGENAS's established processes and templates for economic evaluation and for the assessment of organizational, ethical, and societal dimensions. These templates provide a pragmatic structure for capturing budget impact, resource use, and system-level implications, which are particularly important for devices that may require changes in infrastructure, training, or care pathways. Tailoring these tools to the Greek health system context would promote consistency across assessments while ensuring that local cost structures, service delivery models, and policy priorities are adequately reflected.

Given the central role of real-world evidence (RWE) in the assessment of medical devices, Greece should also adapt existing methods guidance (currently for medicinal products), notably HAS's methodological recommendations on the use of RWE for devices. Such guidance is especially relevant where pre-market evidence is immature or where iterative innovation leads to evolving clinical performance. Embedding clear expectations around the generation, appraisal, and use of RWE, both at the time of initial assessment and post-adoption, would strengthen decision-making while supporting managed entry or conditional reimbursement approaches where appropriate.

Finally, Greece should consider adapting INFARMED's simplified and rapid assessment pathway for medical devices as a proportional response to lower-risk or lower-impact technologies. A tiered assessment model, with the option of expedited reviews based on predefined criteria, would help manage workload, reduce time to decision, and allocate analytical resources more efficiently. Such an approach would be particularly valuable in a resource-constrained setting, enabling the HTA system to remain responsive while preserving more intensive assessments for high-impact or high-uncertainty technologies.

1.5 Situation analysis of medical devices in Greece

As part of the situation analysis to understand the HTA landscape of Greece conducted by WHO Europe in 2024[15], it was determined that though there was legal basis for a

[15] The health technology assessment landscape in Greece: situation analysis and alignment

comprehensive HTA to be also conducted for medical devices in Greece, this was not actually happening in practice.

1.5.1 Scope and legal framework

In Greece, medical devices are not formally currently covered by the national Health Technology Assessment (HTA) system. The HTA framework established in 2018 under Law 4512/2018 though does not exclusively apply to medicinal products, medical devices, diagnostic tests, medical procedures, and population-level interventions are currently outside the HTA assessment and appraisal process. As a result, there is no formal HTA-based evaluation of the clinical or economic value of medical devices for reimbursement or coverage decisions.

1.5.2 Governance and institutional responsibilities

Medical devices fall under a separate governance and negotiation pathway. Pricing and reimbursement decisions for medical devices are handled by the Negotiation Committee for the Reimbursement of Health Services, Medical Technology Products and Materials, which operates within the National Organization for the Provision of Health Services (EOPYY). This committee:

- Is distinct from the HTA Committee responsible for medicines
- Negotiates prices and contractual terms only
- Does not conduct HTA-type assessments of clinical effectiveness, comparative value, or cost–effectiveness.

One of its subcommittees (five members) negotiates prices for medical devices that are either already on the market or imported via ad hoc decisions (e.g., ministerial decrees). Negotiations may consider factors such as geographical availability and delivery timelines, but not clinical value or comparative effectiveness.

1.5.3 Market authorization and regulatory oversight

The National Evaluation Centre of Quality and Technology in Health oversees the certification and conformity assessment of medical devices in line with European medical device directives. This body focuses exclusively on regulatory compliance and market access requirements, rather than HTA domains such as therapeutic added value, cost–effectiveness, or broader health system impact.

1.5.4 Absence of HTA for medical devices

There are no governance structures in Greece responsible for HTA assessment or appraisal of:

- Medical devices
- Diagnostic tests
- Medical procedures

This is also the case for population-level health interventions.

As a result, decisions on reimbursement and procurement of medical devices are largely price-driven and fragmented, with limited formal assessment of value for patients or the health system.

1.5.5 Capacity and data limitations

The situation analysis highlighted minimal technical, organizational, and methodological capacity for conducting HTA on medical devices in the existing landscape in 2024 in Greece. Existing HTA expertise and infrastructure were overwhelmingly oriented toward medicines, with little familiarity with device-specific assessment challenges, such as learning curves, organizational impacts, or real-world evidence generation.

1.5.6 Future outlook and EU HTA regulation

As noted in section 1.2, the EU Regulation on Health Technology Assessment (EU HTAR 2021/2282) introduces JCAs and JSCs for medical devices, which will become mandatory at EU level from January 2026 onwards for selected, prioritized devices and in-vitro diagnostic medical devices. This creates an important future obligation for Greece to develop technical and institutional capacity to use, interpret, and implement device-related JCA and JSC outputs in national decision-making.

At present, medical devices in Greece are regulated and reimbursed without HTA-based evaluation, relying primarily on price negotiations and regulatory conformity assessments. With EU-level HTA for medical devices on the horizon, Greece faces a critical need to establish HTA governance, methodology, data access, and capacity specific to medical devices to ensure evidence-based and transparent decision-making in the coming years.

1.5.7 Local Greek mapping

In addition to the formal situational analysis conducted by WHO Europe, which primarily focused on medical products, a local mapping by the Ministry of Health of Greece was also done at the end of 2025 and early 2026.

Methods

Study design and analytical approach

This study employs an informal desk-based situational analysis to examine how medical devices (MDs) and in vitro diagnostics (IVDs) are reimbursed and procured in Greece. The analysis focuses on institutional arrangements, decision-making pathways, and procedural rules, rather than on the clinical or economic evaluation of individual technologies.

This methodological approach is appropriate given the governance context of medical devices in Greece. Unlike pharmaceuticals, MDs and IVDs are not subject to a formalized health technology assessment (HTA) framework, and there are no publicly available assessment reports or standardized evaluation criteria guiding reimbursement decisions. Instead, access decisions are shaped through legislation, administrative regulations, procurement mechanisms, and negotiation procedures, which constitute the primary sources of decision-making authority.

Situational analysis is a recognized method in health policy and health systems research for examining such contexts, particularly where policy processes are fragmented, evolving, or only partially documented in academic literature (World Health Organization, 2015; OECD & European Observatory on Health Systems and Policies, 2017). For medical devices specifically, previous research highlights that reimbursement decisions are frequently embedded in procurement and administrative processes rather than formal HTA outputs, making desk-based policy analysis the most appropriate methodological choice (Sorenson et al., 2015; Drummond et al., 2017).

Scope and focus of the analysis

The analysis is organized around the medical device decision pathway, rather than around individual products. It examines three main stages:

1. Regulatory entry, including requirements for market access and compliance
2. Inpatient access, which is primarily determined through procurement and tendering mechanisms
3. Outpatient reimbursement, which is governed through the EOPYY benefits framework, registries, and negotiation procedures.

This pathway-based structure reflects the fragmented governance of medical devices in Greece and allows the study to identify how forms of "assessment" are applied implicitly, in the absence of a formal HTA process.

Data sources

Legislative and institutional documents

The core evidence base for the situational analysis consisted of legislation and official institutional documentation, including laws, ministerial decisions, reimbursement regulations, procurement rules, and formal descriptions of institutional responsibilities. These sources were prioritized because they define the formal rules, mandates, and procedures governing medical device reimbursement and procurement in Greece.

The use of legislative and policy documents as primary data is consistent with established methodological guidance for situational analysis and health system mapping, particularly in settings where formal evaluation outputs are absent or limited (World Health Organization, 2015).

Academic and grey literature

Exploratory searches of academic and grey literature (including Google Scholar) were conducted to identify publications relevant to medical device reimbursement in Greece. However, this process

yielded very limited results, which were largely descriptive and generic and did not provide detailed analysis of reimbursement pathways or decision-making criteria.

The scarcity of peer-reviewed literature reflects the early and evolving nature of medical device reimbursement governance in Greece, as well as the fact that many relevant decisions are not documented in academic outlets. Where relevant, academic and grey literature was therefore used contextually, to support background discussion rather than as a primary analytical source. Given the limited volume and relevance of identified publications, a formal screening or systematic selection process was not applied. This approach is consistent with guidance on the use of grey and non-academic sources in policy research where published evidence is sparse (Paez, 2017).

Key Findings

Regulatory Context

Consistent with the WHO situational assessment, the local mapping confirms that, unlike pharmaceuticals, for which a formal HTA process has existed in Greece since 2018 (Law 4512/2018), there is no dedicated HTA framework for Medical Devices (MDs) and In Vitro Diagnostics (IVDs). The current process relies more on financial considerations and ad hoc processes than on HTA decision-making. Regulation of these technologies relies primarily on EU conformity assessment and national regulatory oversight rather than systematic clinical or economic evaluation. Market entry is conditional on valid CE marking under EU Regulations (EU) 2017/745 and (EU) 2017/746, and registration with the National Organization for Medicines (EOF), which is responsible for ensuring device safety, quality, and post-market surveillance. However, unlike pharmaceuticals, no formal national assessment of comparative clinical effectiveness or cost-effectiveness is required before commercialization in Greece.

Inpatient use and procurement

In practice, the same medical device or diagnostic technology may be used in both inpatient and outpatient care, but reimbursement follows different institutional pathways. The majority of medical devices are adopted through hospital-level device uptake. They are introduced into clinical practice through a combination of centralized and hospital-level procurement processes rather than through a systematic pre-assessment by a dedicated HTA authority. Procurement is carried out either centrally via the National Centralised Health Procurement Authority (EKAPY), which is responsible for strategic planning, national tenders, and contract management for health-system supplies, or locally within the National Health System (ESY) through hospital-level tenders or direct supplier contracts. Provided that devices are CE-marked, their uptake is primarily shaped by procurement procedures, budgetary constraints, and clinical utilization patterns, while tendering decisions generally emphasize price and technical compliance as key award criteria rather than a formal, nationwide HTA-based or value-based assessment framework.

Outpatient Reimbursement

Outpatient medical devices and diagnostics are reimbursed through the National Organisation for Healthcare Services Provision (EOPYY), which administers the statutory benefits package covering medical devices and supplies (e.g., prosthetics and consumables). For a CE-marked product to be reimbursed, it must fall within the scope of the Unified Health Benefits Regulation (EKPY), adopted

through a Joint Ministerial Decision of the Ministers of Health and Finance. EKPY defines the categories of services and products eligible for coverage by EOPYY. However, inclusion in EKPY is primarily administrative and category-based rather than the result of a structured clinical or economic evaluation process, highlighting a broader gap in the systematic assessment of medical technologies outside the pharmaceutical HTA framework.

In the absence of a formally designated HTA body, reimbursement conditions for health services, medical technology products and materials are addressed primarily through the Negotiation Committee for Reimbursement Prices of Health Services, Medical Technology Products and Materials within EOPYY, established under Article 29(4) of Law 3918/2011 and codified in its current form by Article 5 of Law 4931/2022. The statutory role of this body is to negotiate reimbursement prices and contractual terms with providers and suppliers and to submit recommendations to the EOPYY Board. This institutional arrangement differs fundamentally from the pharmaceutical pathway, where reimbursement follows a defined process of clinical and economic evaluation through the HTA Committee and subsequent price negotiation. For medical technologies, negotiation effectively substitutes for structured value assessment, operating without a transparent methodological framework or clearly stated evaluation criteria comparable to those applied to medicines. As a result, decision-making for non-pharmaceutical technologies remains predominantly price-driven and procedurally fragmented, limiting consistency, transparency, and the systematic integration of clinical and economic evidence into reimbursement policy.

The Committee consists of eleven members who are senior experts with experience in the economic organization and functioning of health services, holding university degrees in health sciences, economics, social or legal sciences, with at least two years of relevant professional experience and good knowledge of English, while the Chair is required to hold a postgraduate or doctoral degree in a relevant field and at least ten years of professional experience. The Committee operates through specialized Subcommittees covering Clinics, Diagnostic Centres, Medical Devices and Materials, and Other Health Services, in accordance with Ministerial Decision ΕΑΛΕ/Γ.Π.69310/6.11.2020. It is responsible for negotiating with healthcare providers and suppliers regarding fees, reimbursement prices, contractual terms and financial agreements related to the provision of health services and the use of medical technology equipment already available on the market or introduced through ad-hoc regulatory arrangements.

Manufacturers submit a dossier or application to EOPYY for their device to be included in the reimbursement framework (FEK B’ 4043/21.09.2020). Submitted dossiers undergo technical and economic assessment by the competent Subcommittee before the negotiation process begins. The negotiation process is conducted in accordance with a set of indicative criteria to be taken into account. These include clinical effectiveness, budget impact, innovation, geographical coverage, safety, reliability, efficiency, and the quality of healthcare services (Law 4931/2022). These function mainly as supporting elements within a negotiation procedure and do not constitute a structured or standardized HTA framework for MDs and IVDs. Pricing, therefore, remains the central element of the process rather than value-based methods. By law, price is typically determined through external reference pricing across EU Member States (the average of the three lowest prices for that device in EU Member States) or through negotiated financial terms. These practices may lead to variability in assessment and decision-making.

Operational Challenges

Several practical and structural challenges further affect the process. The Committees responsible for evaluating and negotiating device reimbursement do not operate as permanent or exclusive bodies, as their members participate alongside their main professional duties rather than within a dedicated full-time structure. In practice, this results in limited availability, accumulated workload, and insufficient specialized expertise, despite the requirement to review a broad spectrum of therapeutic areas and highly technical product categories. These conditions contribute to prolonged evaluation timelines and delays in final decision-making, particularly for innovative or complex technologies requiring deeper clinical and economic assessment.

In more complex cases, EOPYY may seek technical support from the National Evaluation Centre of Quality and Technology in Health (E.K.A.P.T.Y. S.A.). However, the role of E.K.A.P.T.Y. is advisory and does not substitute for HTA, as the institution is not equipped or mandated to evaluate therapeutic value, comparative effectiveness, or cost-effectiveness, nor to inform reimbursement decisions. E.K.A.P.T.Y. operates primarily as an independent certification and conformity-assessment body for quality systems and medical products under the supervision of the Ministry of Health. Although it was initially associated with the evaluation of MDs and IVDs, it focuses on regulatory compliance and technical standards rather than health technology assessment.

Implications

Overall, coverage decisions for medical devices and IVDs are distributed across multiple procedural pathways and are determined mainly through administrative and financial negotiation mechanisms rather than through a unified value-assessment framework. There is no transparent HTA pathway for non-pharmaceutical technologies, no published assessment reports, no formal scoring methodology, and no explicit criteria systematically linking reimbursement to therapeutic benefit. Adoption and reimbursement, therefore, continue to follow parallel inpatient procurement and outpatient reimbursement routes, without a single national framework for evaluating clinical and economic value comparable to that applied to pharmaceuticals. This structural fragmentation remains a central limitation of the current system and a key policy gap.

This structural configuration has direct implications for the efficiency, equity, and sustainability of the health system. Without a transparent and methodologically defined assessment process, resource allocation decisions cannot be consistently linked to demonstrated clinical benefit or economic value. This creates uncertainty for providers, variability in patient access, and limited predictability for manufacturers, while also constraining the ability of the system to prioritize high-value innovation within existing budgetary pressures.

2.1 Proposed draft plan

2.1.1 Methods for Greece for HTA of medical devices and in-vitro diagnostics

Under Regulation (EU) 2021/2282 and its implementing acts, the European Union has established common methods for JCAs and JSCs for selected high-risk medical devices (Classes IIb and III) and in vitro diagnostic medical devices (Class D).

While the overarching HTA principles apply across health technologies, the Methods and Procedural Guidance Subgroup of the HTA Coordination Group (HTA CG) explicitly

differentiates expectations for medical devices (MDs) and in vitro diagnostic medical devices (IVDs) as compared with medicinal products, reflecting their distinct development cycles, evidentiary bases, and regulatory frameworks.

Timing and flexibility

Given the staged market entry and post-market evidence generation typical of MDs and IVDs, the HTA CG allows greater flexibility in timing and content of JSCs and JCAs. Medicinal product procedures follow more standardized and tightly sequenced timelines, mirroring regulatory processes.

Overall, the HTA CG's methods and procedural guidance reflect a deliberate adaptation of EU-level HTA tools to the specific scientific, clinical, and regulatory characteristics of medical devices and in vitro diagnostics, while maintaining methodological consistency and transparency across health technology categories.

Proposed methods, scope and focus for JCAs

JCAs focus exclusively on the comparative clinical effectiveness and safety of a technology versus relevant alternatives, based on a jointly defined PICO and standardized evidence requirements. The assessment is conducted by EU Member State assessors with input from patients, clinical experts, and notified bodies, and results in a structured JCA report and summary report. While the JCA outcomes are mandatory to be considered at national level, they do not cover economic, organizational or reimbursement decisions, which remain within Member State competence.

Nature of clinical evidence

For MDs and IVDs, the HTA CG acknowledges that evidence packages are often more heterogeneous and iterative than for medicines. JCAs therefore place greater emphasis on non-randomized studies, registries, real-world evidence, and post-market clinical follow-up data, whereas medicinal product JCAs generally rely on pivotal randomized controlled trials conducted pre-authorization.

Comparator and outcome selection

For devices and IVDs, comparators and outcomes are expected to reflect current clinical practice, diagnostic pathways, and technology-assisted procedures, which may vary across Member States and evolve rapidly. In contrast, medicinal product assessments typically rely on well-defined pharmacological comparators and standardized clinical endpoints established in regulatory trials.

Lifecycle and incremental innovation

The HTA CG explicitly accounts for the incremental and version-based innovation characteristic of MDs and IVDs. JCAs may therefore address a technology family or platform and consider evidence generation as an ongoing process. For medicinal products,

assessments focus on a fixed active substance and indication at the time of marketing authorization.

Proposed methods, scope and focus of JSCs

JSCs are an optional, pre-market support mechanism allowing medical device and IVD developers to seek coordinated EU-level advice on evidence generation plans before clinical investigations are finalized. JSCs aim to improve the relevance, quality and acceptability of future evidence for JCAs by aligning study design, comparators and outcome selection with HTA expectations. Consultations are conducted using standardized briefing document templates and may be HTA-only or parallel (e.g. with expert panels). Requests are submitted via the EU HTA IT Platform during defined windows in the annual work programme of the HTA Coordination Group, ensuring transparency and predictability of the process.

JSCs for MDs and IVDs place particular emphasis on study design choices for clinical investigations, selection of performance and clinical outcome measures, and integration of real-world evidence. For medicinal products, JSCs primarily focus on confirmatory trial design, comparative effectiveness, and endpoint justification for regulatory and HTA alignment.

Interaction with regulatory assessment

For MDs and IVDs, JCA methodologies are closely coordinated with MDR/IVDR conformity assessments, including structured interaction with expert panels and notified bodies. This differs from medicinal products, where JCAs are closely aligned with the EMA marketing authorization dossier and timelines.

Digital health technologies including AI

HTA for digital health technologies (DHTs), including AI-enabled tools is a rapidly evolving field where methods are still emerging and not yet harmonized. Traditional HTA approaches struggle to capture the dynamic, data-driven, and adaptive nature of digital and AI technologies, leading to fragmented and incomplete assessments. Recent EU and OECD initiatives, such as the EDiHTA and ASSESS-DHT Horizon Europe projects and the OECD's 2025 review, highlight ongoing efforts to develop fit-for-purpose frameworks that address lifecycle evaluation, real-world performance, data governance, cybersecurity, and ethical considerations. Together, these initiatives illustrate that HTA methods for digital health are still under active development, with countries and international bodies converging on new, more flexible and collaborative models to support responsible, evidence-based adoption of digital and AI health technologies. These are summarized in **section 1.3** in this document and Greece will need to follow these projects in the coming months and years to finalize their recommendations accordingly once they are all complete.

Economic assessment and other considerations

Apart from the clinical assessment, which is regulated and mandated by the JCA, the economic assessment and other considerations need to also be done at the national level.

The current methods guidance for economic assessment and other considerations for medicinal products needs to be reviewed and adapted to the Greek setting for MDs and IVDs as has been done by AGENAS in Italy, refer to the **section 1.4.2** and **Annex 1** of this document.

2.1.2 Proposed process guidance for Greece for HTA of medical devices and in-vitro diagnostics

The Methods and Procedural Guidance Subgroup of the HTA Coordination Group have acknowledged that processes for HTA for medical devices and in-vitro diagnostics do need to be different to those for medicinal products. The Methods and Procedural Guidance Subgroup developed new guidance in light of that, which was at the end of 2025, adopted by the HTA Coordination Group. This is a package of guidance documents to support implementation from 2026 and the details are available in **section 1.2** of this document.

These include guidance on selecting eligible devices for JCA (defining high-risk MD and IVD eligibility, a formal three-step selection process, and criteria such as unmet medical need, first-in-class status, and potential system impact); procedural guidance for JCAs, detailing scoping, dossier submission, assessment, endorsement, publication, and updates; methodological Q&A, clarifying PICO handling, evidence gaps, indirect comparisons, subgroup analyses, and dossier completeness; and technical guidance on completing the JCA dossier template, specifying structure, versioning, confidentiality handling, evidence standards, and mandatory documentation for MDs and IVDs. Together, these documents translate the Regulation into a predictable, transparent, and methodologically rigorous system for joint EU clinical assessment of high-risk medical technologies. Greece will have to follow these implementing acts and procedures.

In the end, the EU HTAR (EU) 2021/2282 establishes a harmonized EU-wide framework for joint HTAs, extending for the first time to high-risk MDs and in vitro diagnostics (IVDs). Central to the framework are JCAs, which evaluate comparative clinical effectiveness and safety at EU level, and JSCs, which provide early advice to developers on evidence generation. Developers submit a single evidence dossier at EU level, and Member States must give due consideration to the JCA outcomes in national HTA processes, while retaining full competence for economic, organizational, and reimbursement decisions. The overarching objective is to reduce duplication, align methodologies, and support faster and more consistent patient access to innovation across the EU.

Two key implementing regulations adopted in 2025 operationalize this system for devices and IVDs. Commission Implementing Regulation (EU) 2025/117 establishes the procedural framework for JSCs, setting out structured early dialogue between developers, HTA bodies, regulators, clinicians, and patients. It defines consultation windows, documentation requirements, timelines, and allows parallel advice with regulatory bodies (e.g. notified bodies or EMA-linked processes) to align clinical development, regulatory approval, and HTA evidence needs. Commission Implementing Regulation (EU) 2025/2086 lays down detailed

procedural rules for JCAs, including standardized templates, timelines, governance arrangements, and interaction mechanisms. JCAs focus strictly on clinical domains (effectiveness, safety, patient-relevant outcomes) and are conducted through a single EU dossier, assessed by appointed assessors under the HTA Coordination Group, with transparent endorsement and publication processes.

In addition, as noted in **section 1.2.8**, changes are also proposed to the wider medical devices and in-vitro diagnostic medical devices regulation. Over the past decade, the EU has overhauled its medical device regulatory system through the Medical Devices Regulation (EU) 2017/745 (MDR) and the In Vitro Diagnostic Regulation (EU) 2017/746 (IVDR), replacing earlier directives with a stricter, lifecycle-based framework that strengthens clinical evidence requirements, post-market surveillance, traceability, and notified body oversight, and became applicable in 2021 and 2022 respectively.

While these reforms significantly improved patient safety and transparency, their implementation exposed challenges such as notified body capacity constraints and risks to device availability, prompting transitional extensions, removal of sell-off deadlines, and phased deployment of EUDAMED. In response to sustained concerns, the Commission proposed in December 2025 (COM(2025) 1023) a targeted "second-generation" revision of MDR/IVDR to rebalance the system by simplifying requirements, reducing administrative burden, particularly for SMEs and well-established technologies, introducing more flexible clinical evidence rules, potentially down-classifying certain devices, and easing post-market obligations, while maintaining high safety standards and ensuring long-term sustainability, supply security, and readiness for innovation, subject to approval by the European Parliament and Council.

2.1.3 Proposed roll-out

The draft HTA methods and process guidance for medicinal products went through a thorough stakeholder consultation and review with patient organizations and industry organizations in Greece and a similar structured formal consultation would also be recommended for the HTA methods and processes for MDs and IVDs.

In addition, the draft HTA methods and processes for medicinal products were only finalized along with the input that came through the pilot process, which provided the key insights into the practical elements of implementing the guidance. Once again, a similar process would be recommended for MDs and IVDs.

Stakeholder consultation of draft guidance Q2-Q3 2026

The methods guidance for HTA for MDs and IVDs is as recommended by the Methods and Procedural Guidance Subgroup of the HTA CG, i.e. most elements remain the same as per medicinal products but with certain specific considerations due to the specifications of the type of technologies. These are summarized in **section 2.1.1** in this document. The key learnings from other European agencies (AGENAS and INFARMED from Italy and Portugal

respectively, see **sections 1.4.1 and 1.4.2**) also provide a good basis for practical implementation of these methods in practice. The key recommendations for Greece to take forward in practice are summarized in **section 1.4.3**.

In addition, the regulations and procedural elements that the HTA process for MDs and IVDs need to follow are summarized in **section 1.2** and for implementation in Greece in **section 2.1.2.** These proposed methods and procedures need to be implemented keeping in mind the Greek context and therefore the following is recommended:

- a dedicated detailed workshop with national stakeholders and international experts including scientific advisors;
- formal written consultation with national stakeholders and international experts including scientific advisors;
- deliberative meetings with different stakeholders to understand their comments and views;
- updating the draft methods and process guidance documents to incorporate the feedback received to be used for a pilot in 2027.

Governance structure Q3-Q4 2026

To ensure sustainability of the HTA for MDs and IVDs a dedicated structure, unit or team needs to be put into place that can lead and work with the Ministry of Health of Greece to finalize the methods and process guidance documents with the input from all relevant stakeholders.

They will also then be responsible for supporting the European level work and the national pilots going forward.

Providing input to JSCs and JCAs for MDs and IVDs at the European level Q3-Q4 2026

The requests for providing input into JSCs and JCAs for MDs and IVDs will likely start in of Q3 and through to Q4 and onwards. There needs to be a mechanism to provide input to JSCs so evidence requirements for Greece as well as input to PICOs and then draft assessments for JCAs.

Once the methods and processes are finalized and a governance structure is established then Greece should focus on initially in 2026, contributing to JSCs and JCAs led by other lead assessor and co-assessor teams, to understand and learn the methods and procedures involved.

Integrating EU-level JCAs into national procedures Q4 2026 and Q1-Q2 2027

The first JCA for a MD or an IVD may be published by the end of 2026 but more likely in Q1 or Q2 of 2027. The governance structure established will then have to imbed the European level HTA into national procedures in terms of economic assessment and other considerations as well adapting from the agreed methods and procedures for medicinal products and learning

from the example of AGENAS. This will enable evidence-informed and HTA guided reimbursement and procurement policies for MDs and IVDs.

Full national HTAs for MDs and IVDs Q3-Q4 2027

The EU HTAR only will conduct JCAs for selected MDs and IVDs in line with **the section 1.2.3** of this document. So majority of the MDs and IVDs will not go through a formal HTA process, but Greece can capitalize on this establishment and identify other MDs and IVDs that would benefit from a structured HTA process, that will not be selected or considered at a EU level.

Once the methods, processes and the governance structure are established, then they can be used for national HTAs for other MDs and IVDs of value or interest to Greece. It would be recommended that the two-type of HTA format as is done by INFARMED in Portugal is considered also for Greece, where there is a rapid pathway as well as a full formal HTA pathway (similar to the full European assessment) depending upon the type of technology being considered, as described in **section 1.4.1** in this document.

Co-assessor or lead assessors Q1 2028 onwards

If all the other elements of the plan are followed and implemented successfully then by the start of 2028, Greece can also submit itself as a co-assessor or in the future a lead-assessor for the assessments of MDs and IVDs.

3.0 Annex 1 DRAFT HTA Assessment protocol, translated in English from AGENAS

[Report Title]

HTA assessment document

Research protocol

Index

Introduction

[Describe the general purpose of the report, specifying the technology being evaluated and the regulatory and institutional context in which it is being prepared (agreement with which institutions, etc.)]

Technology

[Brief description of the technology being reported, including its clinical scope and purpose .]

Goals

[Define the specific objectives of the HTA report, explicitly stating the (possible) comparative technology on which the evaluation will be based.]

Policy Questions:

[Please report the policy questions received in a list:

- *Policy question 1;*
- *Policy question 2;*
- *….]*

Research questions:

[Formulate and report the research questions according to the decision-making needs (policy questions) expressed in the mandate received in the form of a list:

- *Research Question 1;*
- *Research question 2;*
- *...]*

Methods

The methodology of this report is based on the **EUnetHTA 3.0 Core Model** (and related Assessments Elements), integrated, in terms of safety and efficacy domains, by the guidelines and methodological documents developed within the scope of the application of **Regulation (EU) 2021/2282,** the references of which can be consulted in *Appendix 1*.

The following evaluation domains were selected for this report:

[Please indicate the HTA domains identified for the report, among the following

- *clinical problem and current use of technology (CUR);*
- *description and technical characteristics of the technology (TEC);*
- *safety (SAF);*
- *clinical effectiveness (EFF);*
- *economic aspects (ECO);*
- *organizational aspects (ORG);*
- *ethical aspects (ETH);*

- *social and patient aspects (SOC);*
- *legal aspects (LEG).]*

The following section presents the methods that will be used in each domain.

Clinical problem and current use of technology (CUR)

[This domain describes the pathology (incidence, prevalence, mortality, social and economic burden related to the disease), the analysis of the current use of the technology in the NHS, the identification of available alternatives and current clinical practices, the highlighting of any critical issues or unmet needs, the detection of geographical variations in access or use of the technology]

***Assessments** in a table **Elements** which is intended to be answered in this domain.*

Please enter the methods used to gather the above information and subsequent analysis methods used for this domain (e.g., analysis of guidelines, scientific literature, and epidemiological evidence; consultation with clinical experts and stakeholders; analysis of information flows (e.g., SDO, RDM, consumption data); conducting interviews with clinicians, other.)

Description and technical characteristics of the technology (TEC)

[This domain describes the technical characteristics of the technology, how it works, and the regulatory documentation.]

***Assessments** in a table **Elements** that are intended to be answered in this domain.*

Enter the methods used to retrieve information for this domain. For example:

- *Analysis of technical data sheets, user manuals, manufacturer documentation;*
- *Consultation of national and international regulatory databases;*
  Administration of technical questionnaires to producers or distributors (material attached in the Appendix)]

Clinical Safety and Efficacy (SAF and EFF)

[In this domain, an evaluation of the scientific literature is performed to assess the safety and clinical efficacy of the technology.

***Assessments** in a table **Elements** which is intended to be answered in this domain.*

Please include the methods, detailing the PICOD(s) (study design) and the resulting search strategy (to be attached in the Appendix) for the selection of existing literature, indicating the databases, the publication period of the searched literature, the process of screening, extraction, data analysis and synthesis of the included studies and the method for assessing the quality of the studies (to be attached in the Appendix). Indicate any methods of analysis of the outcomes obtained.

The PICO can be developed based on the mandate received, for example using:

▪ *European clinical guidelines relevant to the therapeutic area, providing guidance on the natural history of the disease, available alternatives and relevant outcomes;*

▪ *Alternative reference documents, if specific European guidelines are not available for the declared therapeutic indication/ intended use;*

▪ *Contributions from patients, clinical experts and/or other relevant experts .*

Economic aspects (ECO)

This domain analyzes the economic and budgetary impact of technology on the healthcare system.

Specify the PICO models for this domain especially in terms of outcomes , illustrate the research strategy (to be attached in the Appendix) and then explain the economic analysis methods applied:

- *Analysis of existing economic studies (attach search strategy).*
- *Modeling economic , where applicable (e.g. cost-effectiveness, budget impact).*
- *Sources: healthcare rates, DRGs, economic literature, consumer data.*

***Assessments** in a table **Elements** that are intended to be answered in this domain.]*

Organizational aspects (ORG)

[This domain analyzes the impact of technology on resources (e.g., staff training), organizational structures, and processes. Specify the PICO models for this domain, especially in terms of outcomes , illustrate the research strategy (to be attached in the Appendix), and then explain the methods applied for organizational analysis and with reference to which aspects (e.g., the impact of technology on resources, structures, and organizational processes).

- *Literature review;*
- *Consultation with stakeholders and healthcare personnel;*

- *Administrative data;*
- *Use of logic diagrams or process diagrams (attached in the Appendix).*

***Assessments** in a table **Elements** that are intended to be answered in this domain.]*

Ethical Aspects (ETH)

This domain analyzes the ethical implications of the introduction and use of health technology. The ethical principles involved are evaluated, such as respect for human dignity, patient autonomy, equitable access to care, and distributive justice. Potential conflicts of interest and aspects related to transparency and informed consent are also considered.

***Assessments** in a table **Elements** that are intended to be answered in this domain.*

Enter the methods used to retrieve information for this domain, for example:

- *Analysis of specific ethical and bioethical literature;*
- *Review of national and international regulatory and ethical documents;*
- *Consultation of experts in medical ethics and bioethics;*
- *Administration of questionnaires or interviews to clinicians, patients and stakeholders;*
- *Workshops or focus groups with patients and representatives of civil society.*

Social and Patient Aspects (SOC)

This domain assesses the impact of technology on the quality of life of patients and their families, also considering broader social effects such as social perception of the technology, acceptability, social support, patient participation in decision-making, and any disparities in access or use of the technology. The effects on caregivers and the community are also considered.

***Assessments** in a table **Elements** that are intended to be answered in this domain.*

Enter the methods used to retrieve information for this domain, such as:

- *Review of the scientific literature on quality of life and social impact;*
- *Interviews and questionnaires administered to patients, caregivers, and representatives of patient associations;*
- *Analysis of qualitative and quantitative data collected through observational studies or trials;*
- *Consultation of experts in social sciences and public health;*
- *Focus groups and workshops with social stakeholders .]*

Legal Aspects (LEG)

This domain analyzes the regulatory and legal framework applicable to the use of the technology, including regulations regarding medical device safety, privacy and personal data protection, professional liability, informed consent, and compliance with national and European regulations. Any legal or regulatory barriers that may impact the adoption of the technology are assessed.

***Assessments** in a table **Elements** that are intended to be answered in this domain.*

Enter the methods used to retrieve information for this domain, for example:

- *Regulatory and legislative analysis at national and European level;*
- *Review of legal literature and policy documents;*
- *Consultation with legal and regulatory experts;*
- *Case law analysis and legal guidelines;*
- *Interviews with healthcare professionals and managers regarding legal and compliance issues.*

Appendix 1: Documents methodological

Practical Guideline for Quantitative Evidence Synthesis: Direct and Indirect Comparisons - European Commission

Methodological Guideline for Quantitative Evidence Synthesis: Direct and Indirect Comparisons - European Commission

https://health.ec.europa.eu/publications/guidance-reporting-requirements-multiplicity-issues-and-subgroup-sensitivity-and-post-hoc-analyses_en

https://health.ec.europa.eu/publications/guidance-outcomes-joint-clinical-assessments_en

https://health.ec.europa.eu/publications/guidance-validity-clinical-studies-joint-clinical-assessments_en

Appendix 2. Research Strategy – EFF SAF

Appendix 3. Research Strategy – ECO

Appendix 4. Search Strategy – ORG