EUnetHTA 21

Project Plan

ASSESSMENT OF HIGH-RISK MEDICAL DEVICES

D4.7.1 SYNTHESIS OF NATIONAL REQUIREMENTS

D4.7.2 FRAMEWORK FOR THE ASSESSMENT OF HIGH-RISK MEDICAL DEVICES AND IN-VITRO-DIAGNOSTICS

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DOCUMENT HISTORY AND CONTRIBUTORS

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Participants

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The work in EUnetHTA 21 is a collaborative effort. While the agencies in the Hands-on Group will be actively writing the deliverable, the entire EUnetHTA 21 consortium is involved in its production throughout various stages. This means that the Committee for Scientific Consistency and Quality (CSCQ) will review and discuss several drafts of the deliverable prior to validation. Afterwards the Consortium Executive Board (CEB) will endorse the final deliverable prior to publication. For further information on stakeholder involvement in this deliverable, please see section 3.2.

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LIST OF ABBREVIATIONS

AIHTA	Austrian Institute for Health Technology Assessment
CA	Collaborative Assessment
CEB	Consortium Executive Board
CSCQ	Committee for Scientific Consistency and Quality
EU	European Union
EUDAMED	European database on medical devices
EUnetHTA	European Network of Health Technology Assessment
HAS	Haute Autorité de Santé
HCP	Healthcare Professional
HOG	Hands-on group
HRQoL	Health Related Quality of Life
HTA	Health Technology Assessment
HTD	Health Technology Developer
IVD	In-vitro Diagnostic
JA3	Joint Action 3 of EUnetHTA 2016-2021
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
MD	Medical Device
MDCG	Medical device Coordination Group
NRS	Non-randomised Studies
OT	Other Technologies
REA	Relative Effectiveness Assessment
SOP	Standard Operating Procedure
TISP	Topic identification, selection and prioritisation

1 INTRODUCTION

In the technical offer submitted on 04/05/2021, deliverables for the production of at least 2 joint clinical assessments (JCA) or collaborative assessments (CA) of high-risk medical devices (MD) or in-vitro diagnostics (IVD) have been defined. Upstream of the production, revision of JA3 methodological guidance and templates as well as development of new systems to identify relevant high-risk MD and to further collaborate with regulatory bodies are planned.

This Project Plan describes the objectives, approach and timelines for deliverables D4.7.1 Synthesis of national requirements and D4.7.2. Framework for the Assessment of high-risk Medical Devices and In-Vitro-Diagnostics.

2 BACKGROUND

- Timing and place of reimbursement decision-making on high-risk medical devices and in-vitro diagnostics vary among European countries and are more decentralised in most of them (often via tertiary hospitals for class IIb and III devices or via selective contracts for digital monitoring or class D IVD) compared to pharmaceutical products. Therefore, the related pathways, procedures and evidence requirements are less pre-defined than those of pharmaceutical products;

- The implementation of the regulations (EU) 2017/745 on medical devices (MD) and 2017/746 on in vitro diagnostic (IVD) medical devices has set the basis for a more centralised approach for MD risk class IIB and III and IVD risk class D. In the next few years, the EU regulation on HTA should also drive toward the joint assessment of individual high-risk MDs and class D IVDs early in the lifecycle based on dossier submitted by health technology developers (HTD);

- In JA3, 27 JCA/CA of MD or diagnostics were conducted covering a wide range of technologies, of which only 9 risk class IIB and III MD and 5 risk class D IVD. Most evaluations were collaborative assessments conducted by few agencies on multiple techniques and technologies for indication groups in a late stage of implementation;

- Therefore, there is a need to adapt the existing procedural framework to include early joint assessment of individual high-risk MDs and IVD. The framework should include adapted methods and procedures for the assessment of relevant technologies once they have been identified (see D4.7.4). It should also include detailed and precise information on requirements for the assessments as well as a reliable, transparent process for stakeholder involvement.

Table 2.1. Existing EUnetHTA documents

Science item	Stated aim
Guidelines	
Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness *(updated 2020)*	To provide an up-to-date and transparent overview of the whole information retrieval process. To provide orientation for systematic searches on clinical effectiveness conducted within the framework of EUnetHTA.
Endpoints used for Relative Effectiveness Assessment: Clinical Endpoints *(updated 2015)*	To describe the common characteristics of clinical endpoints, issues relating to their measurement and presentation, and to briefly outline some of the problems arising when comparing or pooling clinical endpoint data. To provide recommendations for the selection and the interpretation of clinical endpoints in the context of Relative Effectiveness Assessment (REA).
Endpoints used for Relative Effectiveness Assessment Composite endpoints *(updated 2015)*	To describe the advantages and disadvantages of the use of composite endpoints as opposed to single endpoints and offer guidance for assessors about construction, reporting and interpretation of the results of composite endpoints in the context of REA

Science item	Stated aim
Endpoints used in Relative Effectiveness Assessment: Surrogate Endpoints *(updated 2015)*	To provide guidance on when and how surrogate endpoints can be used for REA.
Endpoints used in Relative Effectiveness Assessment: Safety *(updated 2015)*	This guideline focuses on the relative safety assessment performed by the HTA assessors when conducting REA and deals with the following methodological issues: • objectives of HTA assessors • terminology • identification of adverse reactions: sources of information • evaluation of sources of information • synthesis and reporting of results compared to other interventions
Endpoints used for Relative Effectiveness Assessment: Health related quality of life and utility measures *(updated 2015)*	(1) Support assessors in identifying the strengths and weaknesses in the evidence provided and (2) inform researchers about the requirements regarding health-related quality of life (HRQoL) assessment to allow them to anticipate the collection of the required data for REA when developing trial protocols.
Comparators & Comparisons: Criteria for the choice of the most appropriate comparator(s) *(updated 2015)*	To summarise the available literature, the advice provided by existing national guidelines and the information from current national practice on the choice of comparator, and to outline some of the challenges arising when establishing what the comparator for a specific assessment should be. Best practice recommendations for the selection of the most appropriate comparator when completing a REA.
Comparators & Comparisons: Direct and indirect comparisons *(updated 2015, revision concept developed in 2020)*	To describe the main methods of direct, indirect and mixed treatment comparison available in terms of the types of relationship they can model and the assumptions inherent in them. Recommendations regarding the use of direct and indirect comparisons in a REA.
Levels of Evidence - Applicability of evidence for the context of a relative effectiveness assessment *(updated 2015)*	How to assess whether there is a relevant modification of the effect of the results in the clinical studies (e.g., a randomised controlled trial (RCT)) if the intervention is applied to the population of interest in clinical setting?
Internal validity of randomised controlled trials *(updated 2015)*	To provide recommendations for the assessment of the internal validity of RCTs whose purpose is the determination of the relative effectiveness of health care interventions
Internal validity of non-randomised studies (NRS) on interventions *(updated 2015)*	To provide recommendations on the assessment of the internal validity of NRS used for the evaluation of effects of interventions
Meta-analysis of diagnostic test accuracy studies *(updated 2014)*	A review of the available methods for the meta-analysis of diagnostic test accuracy studies. The aim of the guideline is to highlight the circumstances in which it is appropriate to use each of the approaches
Therapeutic medical devices *(updated 2015)*	To provide systematic review methodology advice for evaluating the clinical effectiveness of therapeutic medical devices. The focus is on: 1. Aspects deriving from the incremental development of MD 2. The greater importance of context and user dependence in the evaluation of MD compared to drugs
Companion Guide on Rapid REA Other Technologies (incl. related SOPs and process-related guidance documents)	A comprehensive repository that aims to provide support and guidance for the assessment teams of "Joint Production" (joint and collaborative assessments). The Companion Guide is composed of the Process Flows and Standard Operating Procedures (SOPs).
Report	

Science item	Stated aim
An analysis of HTA and reimbursement procedures in EUnetHTA partner countries: final report, 2017	This study analyses existing HTA and reimbursement procedures within EUnetHTA partner countries. It identifies how within their existing procedures agencies in these countries can: 1) engage in HTA cooperation; 2) use jointly produced HTA information; and 3) re-use national, regional and local HTA information from other jurisdictions.
SOP	
How to create an SOP (*updated 2018*)	This SOP describes the process of how to create an SOP. It forms part of the body of SOPs establishing EUnetHTA's quality management control system.

3 OBJECTIVE AND METHODS

For all of the objectives below the future EU HTA regulation will serve as the basis and the past JA3 experiences will be taken into account.

The objective of this project is to define the framework for joint clinical assessments of high-risk medical devices and in-vitro diagnostics with a view to foster national uptake of the assessment reports.

This framework should include early assessment (after CE marking) in the life cycle of an individual technology (within the scope of the HTA regulation). This project is composed of two deliverables: the first one will establish a synthesis of national requirements at the European Union level (D4.7.1) and the second will develop the **Framework for the Assessment of high-risk Medical Devices and In-Vitro Diagnostics** (D4.7.2) to complement the existing framework developed during JA3.

3.1 Methods to achieve the objectives

3.1.1 Objective 1: Establish the synthesis of national requirements

The following steps will be taken to achieve the objective and carry out a synthesis of national requirements (D4.7.1.):

- **Review existing documents** (namely "An analysis of HTA and reimbursement procedures in EUnetHTA partner countries: final report"[1], and "Mapping of HTA national organisations, programmes and processes in EU and Norway"[2]) and synthesise relevant information on the national access points, evidence and procedural requirements for the assessment of high-risk medical devices and in-vitro diagnostics among the members of the EUnetHTA 21 consortium and other EUnetHTA members, which have contributed to JCA/CA on MDs during Joint Actions.
- Ensure that this information is up-to-date based on interaction with HTA institutions/relevant bodies and, when needed, gather missing relevant information.
- **Produce an updated overview of the national requirements** for the **assessment of high-risk medical devices and in-vitro diagnostics** at the European Union level.

3.1.2 Objective 2: Develop the Framework for the Assessment of high-risk Medical Devices and In-Vitro Diagnostics (D4.7.2)

The Framework for the Assessment of high-risk Medical Devices and In-Vitro Diagnostics (D4.7.2) will include a guidance, templates and the related SOPs.

[1] An analysis of HTA and reimbursement procedures in EUnetHTA partner countries: final report. EUnetHTA WP7 https://eunethta.sharepoint.com/sites/Archive/NII/Shared%20Documents/D7.1%20Research%20and%20Analysis/WP7%20activity%201%20report/WP7%20Activity%201%20Report.pdf

[2] Mapping of HTA national organisations, programmes and processes in EU and Norway. European Commission, 2017https://ec.europa.eu/health/sites/default/files/technology_assessment/docs/2018_mapping_npc_en.pdf

The following steps will be taken to consensually develop this Framework :

- **Consensually develop a general guidance** for early assessments (JCA) of individual high-risk MD and IVD after CE marking, with general principles, details on processes, work step tasks and responsibilities, timing and points of interaction with stakeholders, and information requirements (submission dossier) from health technology developers. Since there is no existing EUnetHTA SOP for creating a guidance, the development of this Guidance will be based on the general recommendations of the SOP "How to create an SOP" and will take into account the relevant recommendations from the EUnetHTA guideline "Therapeutic medical devices";
- **Actively participate in the development of templates** (submission dossier for HTD and assessment report) planned in the tender to **ensure they are adapted** to any kind of OT assessment;
- **Check whether existing procedures** (SOPs) developed during JA3 for OT assessment are still adapted or need to be adapted. Consensually develop new SOPs, where relevant;
- **Monitor other new methodological guidelines** planned in the tender to **ensure they are adapted** to any kind of OT assessment.

This framework will serve as a specification of the general rules laid down in the HTA regulation.

The guidance will be sent for comment to the broader EUnetHTA group; if the guidance will be officially applied in the forthcoming years, it might require formal approval by the EUnetHTA community. Within the tender project the Framework for the Assessment of high-risk medical devices and IVD (within the scope of the HTA regulation) will be piloted in JCA. The guidance will be discussed with regulatory bodies in the context of the interaction with MDR/IVDR regulator (Medical Device Coordination Group, MDCG) workplan (D7.4.2 MDCG-EUnetHTA).

There will be close collaboration with the hands-on group (HOG) on D4.7.3 (EUDAMED data reporting template) and D4.7.4. (Guidance for EUDAMED-based topic identification, selection and prioritisation (TISP) process) – the same organisations (AIHTA and HAS) are part of these groups, which will facilitate the work. There will also be close collaboration with the HOG on D5.1. JCA/CA Submission dossier template and D5.2. JCA/CA Report template.

Furthermore, the hands-on group working on the production of JCA/CA for medical devices (D5.4.1.) will be kept informed.

3.2 Stakeholder inclusion

EUnetHTA 21 Stakeholder Pool is composed of HTA bodies (HTAb) outside of EUnetHTA 21 consortium, as well as stakeholder groups on patients, health technology developers (HTD), healthcare professionals (HCP), payers, and regulatory agencies from the EU/EEA countries.

Non-consortium HTAb (i.e. those not part of the EUnetHTA 21 consortium) who will be involved in the future subgroups of the HTA Regulation, should participate in the development of this project in order to ensure the deliverables are applicable to all European HTAb. They should be consulted at the beginning of the project. Additionally, they will be invited to review, at the same time as the Committee for Scientific Consistency and Quality (CSCQ), the 1st draft of the deliverable and the pre-final draft that will be submitted for public consultation.

In addition, the Hands-on Group (HOG) will consult specifically HTD to collect their point of view on the general guidance for early assessments of individual high risk MD and IVD. Furthermore, the HOG aims to consult on a regular basis relevant regulatory bodies during development of the deliverables.

Other members of the EUnetHTA 21 Stakeholder pool will also be involved in this project. Their involvement will include, at minimum, participation in an informational kick-off meeting and regular stakeholder fora. They will also be invited to contribute to the work through public consultation.

4 ORGANISATION OF THE WORK

4.1 Mode of collaboration and frequency of meetings

The work will be distributed evenly between the agencies of the HOG. All HOG members will review each other's work prior to review by the CSCQ. The HOG will appoint one agency to interact with the three CSCQ configurations and the CEB.

The HOG will have meetings/email updates when needed, but at least monthly meetings, to update each other on the progress. In addition, the HOG will also have regular meetings with the relevant other HOGs, namely the HOGs on D7.4.2 (MDCG-EUnetHTA), D4.7.3 (EUDAMED data reporting template), D4.7.4 (Guidance for EUDAMED-based Topic identification, selection and prioritisation (TISP) process), D7.1.1 – Guidance for the interaction between HTD and HTA (for JCA and JSC), D5.1. JCA/CA Submission dossier template and D5.2. JCA/CA Report template. The HOG working on the production of JCA/CA for medical devices (D5.4.1.) will be kept informed.

4.2 Timelines

Table 4.1. Timetable

Milestones	Start date	End date
Project duration	28/09/2021	29/07/2022
1st Draft deliverable	28/09/2021	26/01/2022
Public consultation	02/05/2022	31/05/2022
Validate final version deliverable (CSCQ)	12/07/2022	
Endorsement final version deliverable (CEB)	27/07/2022	
Estimated finalisation date of the deliverable *	29/07/2022	

*publication date may fluctuate depending on the outcome of the Consortium Executive Board endorsement