EUnetHTA Joint Action 3 2016-2020

Continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) as personal, standalone systems in patients with diabetes mellitus treated with insulin

Project ID: ***OTJA08***

Project description and planning

Agency for Quality and Accreditation in Health Care and Social Welfare (AAZ), Croatia

Main Association of Austrian Social Security Institutions (HVB)

The Norwegian Institute of Public Health (NIPHNO)

Version Log

Version number	Date	Modification	Reason for the modification
V1	11/12/2017	1st version of draft project plan	
V2	19/01/2018	2nd version of draft project plan	After comments received from dedicated reviewers
V3	07/02/2018	Revised draft project plan	After comments received from external experts and f2f scoping meeting with manufacturers
V4	12/02/2018	Revised draft project plan	After SABA e-meeting/discussion with co-authors and dedicated reviewers
V5	28/02/2018	Final version	After fact check by manufacturers

Abbreviations and Glossary [1-9]

CGM system: continuous glucose monitoring system
Error Grid (Clarke, Parkes) plots: related to device accuracy
CSII: continuous subcutaneous insulin infusion
CSII + CGM: non-enabled continuous subcutaneous insulin infusion and stand-alone continuous glucose monitoring
CSII + SMBG: non-enabled continuous subcutaneous insulin infusion with self-monitoring of blood glucose by capillary blood testing
FGM system: flash glucose monitoring system (called also iCGM: intermittently viewed continuous glucose monitoring) - provides the current glucose value plus retrospective glucose data for a specified time period upon "scanning"

HbA1c: glycated haemoglobin
Impaired awareness of hypoglycaemia: when people with diabetes, usually type 1 diabetes mellitus, are frequently unable to notice when they have low blood sugar

MARD scores: Mean Absolute Relative Difference related to device accuracy
MDII: Multiple daily insulin injections
MDII + CGM: multiple daily insulin injections with continuous monitoring of blood glucose
MDII + SMBG: multiple daily insulin injections with self-monitoring of blood glucose by capillary blood testing

Reference standard: the best currently available diagnostic test, against which the index test is compared
rtCGM: real-time CGM: provides real-time numerical and graphical information about the current glucose level, glucose trends, and the direction/rate of change of glucose

SMBG: Self-monitoring blood glucose
SAP: sensor-augmented (or enabled) insulin pump or CGM-enabled insulin pumps: Sensor enabled (or augmented) insulin pump systems compatible (connected) with specific CGM system - sensor data display on pump; Sensor-integrated pump: sensor data display on pump and pump acts on sensor data (suspends insulin at pre-set sensor threshold or suspend insulin in advance of pre-set sensor threshold)

T1DM: type 1 diabetes mellitus
T2DM: type 2 diabetes mellitus
Time spent in the target glucose range: Time in range

Classifications of hypoglycaemia, based on clinical evaluation [1,2]:
Level 1: a hypoglycaemia alert glucose value of 70–54 mg/dL (3.9–3.0 mmol/L) with or without symptoms. This should be considered an alert that the individual may be at risk for developing hypoglycaemia and should work to minimize the time spent in this range to reduce the risk of developing more clinically significant hypoglycaemia.
Level 2: a glucose level of 54 mg/dL (3.0 mmol/L) with our without symptoms. This should be considered ***clinically significant hypoglycaemia*** requiring immediate attention.

Level 3: severe hypoglycaemia: This denotes cognitive impairment requiring external assistance for recovery but is not defined by a specific glucose value.

Hypoglycaemia should be quantified in the following ways [1,2]:
As the percentage of CGM values that are below a given threshold (70 mg/dL [3.9 mmol/L] or 54 mg/dL [3.0 mmol/L]) or the number of minutes or hours below these thresholds and as the number of hypoglycaemic events that occur over the given CGM reporting period.

A hypoglycaemic event [1,2]:
Beginning of a CGM event readings below the threshold for at least 15 min is considered an event. For example at least 15min, 54 mg/dL (3.0 mmol/L) to define a clinically significant (level 2) hypoglycaemic event.
End of a CGM event: readings for 15 min at 70 mg/dL (3.9 mmol/L).
A second hypoglycaemic event outcome of prolonged hypoglycaemia is considered when CGM levels are 54 mg/dL (3.0 mmol/L) for consecutive 120 min or more.

Time in range (TIR) [1,2] generally refers to the time spent in an individual's target glucose range (usually 70–180 mg/dL [3.9–10 mmol/L] but occasionally 70–140mg/dL [3.9–7.8mmol/L]). TIR measurements add valuable information to assess the level of current glycaemic control in addition to what is known from the HbA1c. It is also necessary to quantitate the times below and above target range, using a few severity thresholds for each level:
Percentage of time in level 2 hypoglycaemic range (54 mg/dL [3.0 mmol/L]).
Percentage of time in level 1 hypoglycaemic range (70–54 mg/dL [3.9–3.0 mmol/L]).
Percentage of time in target range: 70–180 mg/dL (3.9–10.0 mmol/L) (default); 70–140 mg/dL (3.9–7.8 mmol/L)(secondary);
Percentage of time in level 1 hyperglycaemic range (180 mg/dL [10.0mmol/L]).
Percentage of time in level 2 hyperglycaemic range (250 mg/dL [13.9mmol/L]).
Episodes of hypoglycaemia and hyperglycaemia

CONTENTS

List of tables

1 Project organisation

1.1 Participants

Table 1-1: Project participants

	Agency	Role in the project	Country	Distribution of work
Assessment team				
1.	Agency for Quality and Accreditation in Health Care and Social Welfare (AAZ)	Author	Croatia	Develop first draft of the project plan; Perform the literature search; Carry out the assessment: select and answer assessment elements (of all four domains TEC, CUR, EFF and SAF), fill in the checklist on potential "ethical, organisational, patient and social and legal aspects" of the HTA Core Model ® for rapid REA; Send "draft versions" to reviewers for comments, compile feedback from reviewers and incorporate relevant changes to the draft; Prepare all draft versions and the final assessment including an executive summary.
2.	Main Association of Austrian Social Security Institutions (HVB)	Co-Author	Austria	Review the project plan draft; Support the production of TEC and CUR domains and quality check all steps of their production (data, information, sources); Contribute in answering questions related to potential ethical, organisational, patient and social and legal aspects if needed. Approve/endorse conclusions drawn as well as all draft versions and the final assessment including the executive summary.
3.	The Norwegian Institute of Public Health (NIPHNO)	Co-Author	Norway	Review the project plan draft; Support the production of EFF and SAF domains and quality check all steps of their production; Contribute in data extraction, quality check and approve all assessment steps (data extraction, assessment of risk of bias, data analyses and evidence syntheses); Review drafts of EFF and SAF assessments, propose amendments where necessary and provide written feedback. Contribute in answering questions related to potential ethical, organisational, patient and social and legal aspects if needed; Approve/endorse conclusions drawn as well as all draft versions and the final assessment including the executive summary.
4.	Agency for Health Quality and Assessment of Catalonia (AQUAS)	Dedicated Reviewer	Spain	Thorough review of 1st draft report incl. studies + results
5.	Healthcare Improvement Scotland (HIS)	Dedicated Reviewer	Scotland	Thorough review of 1st draft report incl. studies + results
6.	Regione Emilia-Romagna (RER)	Dedicated Reviewer	Italy	Thorough review of 1st draft report incl. studies + results
7.	Administração Central do Sistema de Saúde (ACSS)	Observer	Portugal	Observe the process (as a dedicated reviewer, but without providing feedback)
8.	Agency for Health Technology Assessment and Tariff System (AOTMiT)	Observer	Poland	Observe the process (as a dedicated reviewer, but without providing feedback)
Contributors				
9.	Institute of Cardiovascular and Medical Sciences BHF Glasgow Cardiovascular Research	External expert	Scotland	Take part in the scoping of the project and the review of the assessment prior to publication

	Centre University of Glasgow			
10.	Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Trondheim	External expert	Norway	Take part in the scoping of the project and the review of the assessment prior to publication
11.	Rogor Editing	Medical Editor	Croatia	Text editing
12.	Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA)	Project Manager	Austria	Central project management

Abbreviations: TEC: Description and technical characteristics of technology; CUR: Health problem and current use of technology; EFF: Clinical Effectiveness; SAF: Safety

1.2 Project stakeholders

Table 1-2: Project stakeholders

Organisation	Role in the project
Abbott Diabetes Care	Manufacturer
Dexcom, Inc.	Manufacturer
Medtronic	Manufacturer
Nemaura Medical Inc.	Manufacturer
Senseonic Incorporated	Manufacturer
International Diabetes Federation European Region, Brussels	Patient group representative
Diabetes Scotland, Scotland	Patient group representative
Croatian Diabetes Association or Zagreb Diabetes Association	Patients for Focus group
The International Association of Mutual Benefit Societies (AIM), Brussels	Payer

1.3 Milestones and Deliverables

Table 1-3: Milestones and Deliverables

Milestones/Deliverables	Start date	End date
Project duration	20/11/2017	
Scoping phase	20/11/2017	21/02/2018
Kick-off e-meeting with the assessment team		23/11/2017
Internal Scoping e-meeting with the assessment team		13/12/2017
Send the request for the completion of the Submission file template to manufacturers		15/12/2017
Identification of manufacturers, external experts, patients	20/11/2017	31/12/2017
Scoping and development of draft Project Plan incl. preliminary PICO	20/11/2017	28/12/2017
Consultation of draft Project Plan with dedicated reviewers	28/12/2017	15/01/2018
Consultation of draft Project Plan with external experts	22/01/2018	29/01/2018
Scoping f2f meeting with manufacturers in Vienna/Austria		01-02/02/2018
Fact check by manufacturers	12/02/2018	19/02/2018
Contact patient organisations - organise and perform focus groups, send and get back patient input template	28/12/2017	23/02/2018
Amendment of draft Project Plan & final Project Plan available		28/02/2018

Completion of Submission file template by manufacturer(s) + Clarifying further questions concerning draft Submission file)		14/02/2018
Assessment phase		
Writing first draft rapid assessment	23/02/2018	04/04/2018
Review by dedicated reviewer(s)	05/04/2018	18/04/2018
Writing second draft rapid assessment	19/04/2018	08/05/2018
Review by ≥ 2 external clinical experts	09/05/2018	23/05/2018
Fact check by manufacturers	09/05/2018	29/05/2018
Writing third draft rapid assessment	24/05/2018	11/06/2018
Medical editing	12/06/2018	19/06/2018
Writing of fourth version of rapid assessment	20/06/2018	26/06/2018
Formatting	27/06/2018	02/07/2018
Final version of rapid assessment		**week** from 02/07/2018

2 Project Outline

2.1 Project Objectives

The rationale of this assessment is to collaboratively produce structured (rapid) core HTA information on other technologies. In addition, the aim is to apply those collaboratively produced assessments in the national or regional context.

Table 2-1: Project objectives

	List of project objectives	Indicator (and target)
1.	To jointly produce a health technology assessment that is fit for purpose, of high quality, of timely availability, and which includes all brands of health technologies available on the market (in use).	Production of 1 (rapid) relative effectiveness assessment.
2.	To apply this collaboratively produced assessment into local (e.g. regional or national) context.	Production of ≥2 local (e.g. national or regional) reports based on the jointly produced assessment.

The purpose of this project is first to collectively produce a rapid core HTA on continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) systems using the EUnetHTA HTA Core Model® for Relative Effectiveness Assessment (REA) [10,11] and next, to initiate the local productions based on this assessment.
Different definitions and/or category names are currently being used for continuous glucose monitoring (CGM) systems and flash glucose monitoring (FGM) systems in the published literature. FGM, for instance, may be described as a separate entity from CGM between a traditional blood glucose meter and a continuous glucose monitoring (CGM) system, or as special case of CGM or subset of CGM or intermittently viewed CGM (iCGM) or “flash” CGM/ [1,2,4,6,9]. Authors have therefore decided to use definitions according their specific “Instruction for Use” documents – “Indication for use” sections, and thus are referring to them as flash glucose monitoring (FGM) system and continuous glucose monitoring (CGM) systems.
We will address the research question whether the use of continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems: *adjunctive*: cannot be used to make treatment decision without confirmatory finger-stick testing or *non-adjunctive*: can be used to make treatment decision without confirmatory finger-stick testing) in patients with diabetes mellitus /type 1 and type 2 (DM1 and DM2) including adults and children, gestational DM/ treated with insulin,

either through insulin pump therapy or multiple daily insulin injections (MDII), is more effective and/or safer than using self-monitoring blood glucose (SMBG) medical devices. The relative effectiveness and safety of CGM and FGM will be assessed against each other also (head-to-head). Potential ethical, organisational, patient and social and legal aspects will be addressed if relevant.

This topic was chosen based on the initial request from the Croatian national payer organisation who commissioned AAZ to do an HTA on continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices in patients with diabetes. The topic is highly relevant as many of these glucose monitoring devices have become available on the market. As they allow continuous evaluation of glycaemic control, providing trends and fluctuations of interstitial glucose levels over time, they may affect adherence to self-monitoring and quality of life. Therefore, their potential benefit would seem particularly relevant in children, patients with poorly controlled diabetes, pregnant women, and patients with hypoglycaemia unawareness. In light of these potential clinical and quality of life benefits, the number of brands on the market, the high costs of purchase and further use, and differences among countries in implementation status and use, many EUnetHTA partners have communicated their interest in this assessment. In addition, obviously many stakeholders may benefit from this report.

2.2 Project Method and Scope

2.2.1 Approach and Method

Table 2-2: Project approach and method

Project approach and method
The selection of assessment elements will be based on the EUnetHTA Core Model® Application for Rapid Relative Effectiveness (REA) Assessments (4.2) [11]. The Checklist for potential ethical, organisational, patient and social and legal aspects of the HTA Core Model® for rapid REA will be filled in as well. Additionally, further assessment elements from the EUnetHTA Core Model® domains: ethical analysis, organisational aspects, patients and social aspects, legal aspects will be included if deemed relevant (3.0) [10]. The selected issues (generic questions) will be translated into actual research questions (answerable questions). For Description and technical characteristics of technology (TEC) and Health problem and current use of technology (CUR) domains no quality assessment tool will be used, but multiple sources will be used in order to validate individual, possibly biased, sources. We will perform descriptive analyses of information from the various sources explored. The completed part of EUnetHTA submission file from the manufacturer will be used as starting point. The Medical Devices Evidence Submission template will be sent to all relevant manufacturers of the technology. Manufacturers will be asked to submit non-confidential evidence, focusing on the technical characteristics and current use of the technology. The documentation provided will be used in addition to the literature identified by the literature search. For assessment elements from other domains (Ethical-ETH, Organisational-ORG, Patient and social-SOC, Legal-LEG) if deemed relevant: Hand search, internet-search, contacting manufacturers (part of manufacturer submission file). No quality assessment tool will be used, but multiple sources will be used in order to validate individual, possibly biased, sources. We will perform descriptive analyses of information from the various sources explored. The quality of the included systematic reviews (SRs) will be assessed using the AMSTAR tool [12].The results from the included SRs will be included according to the methodology suggested by Whitlock 2008 [13] and Robinson 2014 [14] on how to integrate existing SRs into new SRs. As

described by Robinson et al., we may answer our research questions through four different approaches: (1) Use the existing SR(s)' list of included studies as a quality check for our literature search and screening strategy (Scan References); (2) Use the existing SR(s) to completely or partially provide the body of included studies for one or more research questions of our assessment ("Use Existing Search"); (3) Use the data abstraction, risk of bias assessments, and/or analyses from existing SRs for one or more research questions of our assessment ("Use Data Abstraction/Syntheses"), and (4) Use the existing SR(s), including conclusions, to fully or partially answer one or more research questions of our REA ("Use Complete Review").
For new primary studies identified, the risk of bias of included RCTs will be evaluated independently by two researchers. Study and outcomes validity and level of evidence will be assessed according to the EUnetHTA guidelines [15]. We will use The Cochrane Risk of Bias Tool both on study and outcome levels, and GRADE (Grading of Recommendations, Assessment, Development and Evaluation) to assess the quality of the body of evidence [16-18]. Relevant subgroup analyses will be done especially for the most important outcomes, and new meta-analyses of RCTs will be performed where possible. Indirect comparisons (through network meta-analysis) will be performed when appropriate.

Patient involvement methods: Two different methods will be used in this assessment, one involving individual patients and second involving patient organisations.

Focus group (with individual patients) will be held in Croatia – one for adults and one for children with informal caregivers. Patients will be recruited through the Croatian Diabetes Association or Zagreb Diabetes Association, Croatia. To minimise the risk of last minute cancelation, all participants will receive a written confirmation of the invitation of the Focus group (by email), including an information and Consent form. All participants will receive a reminder (by phone or by email) one or two days before the Focus group. Four to five-hours meeting is planned and four flip-overs will be used with predefined questions related to impact of condition; experience with currently available medical devices; experiences with, and expectations of, the medical devices being assessed; and additional information which patients believe would be helpful to the HTA researchers. The entire Focus group discussion will be recorded and transcriptions will be made in Croatian language. Written notes will be taken as well and patient answers will be written on flip-overs. No ethical approval is necessary for the focus group in Croatia but patients and informal caregivers (parents) need to sign Informed consent form.

Two patient groups will be contacted, one at European level and one at national level. Patient Group Submission template will be sent to International Diabetes Federation European Region, Brussels and Diabetes Scotland, Scotland. Patient Group Submission template is prepared for this assessment by modifying the HTAi Patient Group Submission template for HTA of health interventions (not medicines) [19] and with inclusion of topics and issues from EUnetHTA Core Model® 3.0 related to Patients and Social Domain aspect [10]. This will help in the assessment of the value of health technologies, specifically CGM and FGM medical devices. The form is intended to help patient groups present the range of experiences and views of patients with the disease/condition for which the health intervention is being assessed.

Payer involvement methods: Payer representatives at EU level (The International Association of Mutual Benefit Societies (AIM), Brussels) will be contacted related to reimbursement status of technologies under assessment.

Table 2-3: Planned literature search strategy

Literature search strategy
For Effectiveness (EFF) and Safety (SAF) domains, a systematic literature search, according to the predefined search strategy (without limitations) will be performed according to the Cochrane methodology [16], in standard medical and HTA databases (The Cochrane Central Register of Controlled Trials, The Database of Abstracts of Reviews of Effects, The Health Technology Assessment Database, NHS Economic Evaluation Database, MEDLINE, EMBASE, EBSCO CINAHL). Hand searches (from reference lists of relevant studies) will also be carried out. The following clinical trials registries: ClinicalTrials.gov (http://www.clinicaltrials.gov/), WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx) and EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/) will be searched in as well for registered ongoing clinical trials and observational studies. Relevant references (after duplicates removed) will be screened and assessed for eligibility independently by two reviewers. References will be included or excluded according to the overall research question, Population-Intervention-Control-Outcome (PICO)-scheme (as described in Project Scope) and the predefined inclusion/exclusion criteria, and presented according to the PRISMA Statement [20].

Table 2-4: Plan for data extraction

Planned data extraction
Data extraction related to *Study characteristics* (authors, year of publication, setting, study design, clinical trial identification number/ registry identifier and funding source, objectives, study duration, statistical analysis), *Patient characteristics* (number of participants in the trial, age, sex, diagnosis, time since diagnosis with DM, comorbidities, insulin treatment), *Intervention* (type of medical devices), *Comparators* (type of medical devices), and *Outcomes* related to effectiveness (clinical utility: Mortality; Glycaemic control: change in HbA1c (glycosylated haemoglobin); Incidence of hypoglycaemia (i.e., level 1, 2 and 3 hypoglycaemia); Incidence of hyperglycaemia; Time spent in range; Time spent in hypoglycaemia; Time spent in hyperglycaemia; Quality of life; Patient satisfaction; Hypoglycaemia fear; Incidence of diabetic ketoacidosis (in type 1 diabetes); Incidence of hyperosmolar, hyperglycaemic coma (in type 2 diabetes); Resource utilization related to diabetes mellitus (i.e., number of visits to emergency room, primary care, specialists; hospitalizations); Number of daily finger-sticks tests; Number of calibration; Need of re-calibration; Compliance/adherence: Percentage of time using CGM and Number of sensor scans per day (in FGM system); Safety /Adverse events (AEs) device related, i.e. Pain or discomfort related to glucose monitoring and not related to device, Any AEs, Serious AE (SAE), most frequent AEs and SEAs, Death as SAE, withdrawals due AEs/ will be performed by one researcher on pre-defined extraction tables and double-checked regarding completeness and accuracy by a second researcher. Any differences in extraction results will be discussed to achieve consensus; any disagreements will be resolved by consulting a third researcher. Quantitative synthesis from existing SRs will be used and presented in the Result section when available and appropriate for specific assessment element questions. Organisational, ethical, patient and social, legal aspects will be considered if deemed relevant, please see Checklist for potential ethical, organisational, patient and social and legal aspects in Appendix A.

2.2.2 Project Scope

The EUnetHTA Guidelines, available at http://www.eunethta.eu/eunethta-guidelines, **need to be consulted** throughout the assessment process.

Table 2-5: Project Scope: PICO (please see HTA Core Model® for rapid REA)

Description	Project Scope
Population	Patients with diabetes mellitus (Type 1 or Type 2, including adults and children, gestational DM) treated with insulin (insulin pump therapy or multiple daily injections - MDII) Intended use of the technology: ICD 10 codes: E10, E11, O24.4 Mesh-terms and non-Mesh terms: Diabetes Mellitus, Type 1; Diabetes Mellitus, Type 2; Diabetes, Gestational; Insulin; Injections, Subcutaneous; Insulin Infusion Systems
Intervention **(see table below)**	Continuous glucose monitoring (CGM) systems (real-time) and flash glucose monitoring (FGM) systems as personal, standalone medical devices Mesh-terms and non-Mesh terms: Continuous glucose monitoring; Flash glucose monitoring
Comparison	**Comparisons to the reference standard (SMBG) and head-to-head comparisons** ***Patients on multiple daily insulin injection (MDII)*** MDII + Stand-alone CGM vs MDII +SMBG MDII + Stand-alone FGM vs MDII + SMBG MDII + Stand-alone CGM vs MDII + Stand-alone FGM MDII + Stand-alone CGM vs MDII + Stand-alone CGM ***Patients on insulin pump therapy (CSII)*** CSII + Stand-alone CGM vs CSII + SMBG CSII + Stand-alone FGM vs CSII + SMBG CSII + Stand-alone CGM vs CSII + Stand-alone FGM CSII + Stand-alone CGM vs CSII + Stand-alone CGM CSII + Stand-alone CGM vs sensor-integrated/augmented (enabled) CSII CSII + Stand-alone FGM vs sensor-integrated/augmented (enabled) CSII CSII + SMBG vs sensor-integrated/augmented (enabled) CSII Rationale: Comparators will be selected based on the recommendations from the relevant HTAs, clinical guidelines [1-9] and the EUnetHTA Guidelines [15]. Mesh-terms and non-Mesh terms: Blood Glucose Self-Monitoring; Multiple daily insulin injection; Insulin pump therapy; Continuous glucose monitoring; Flash glucose monitoring; Sensor-integrated/augmented (enabled) pump
Outcomes	COMET database was consulted to identify standardised core outcome sets, without success. **TEC Domain** **Clinical validity:** Device Accuracy

	A combination of the MARD score and Error Grid plots (Clarke Error Grid; Parkes Error Grid) define the accuracy of rtCGM and FGM systems. **EFF Domain** **Clinical utility:** Mortality Glycaemic control: change in HbA1c (glycosylated haemoglobin) Incidence of hypoglycaemia (i.e., level 1, 2 and 3 hypoglycaemia) Incidence of hyperglycaemia Time spent in range Time spent in hypoglycaemia Time spent in hyperglycaemia Quality of life Patient satisfaction Hypoglycaemia fear Incidence of diabetic ketoacidosis (in type 1 diabetes) Incidence of hyperosmolar, hyperglycaemic coma (in type 2 diabetes) Resource utilization related to diabetes mellitus (i.e., number of visits to emergency room, primary care, specialists; hospitalizations) Number of daily finger-sticks tests Number of calibration Need of re-calibration Compliance/adherence: Percentage of time using rtCGM Number of sensor scans per day (in FGM system) *Outcomes for EFF domain* possibly used in meta-analysis will be: Change in HbA1c; Incidence of hypoglycaemia (i.e., level 1, 2 and 3 hypoglycaemia); Incidence of hyperglycaemia; Time spent in range; Time spent in hypoglycaemia; Quality of life **SAF Domain** **Adverse events (AEs)** (device related, i.e. Pain or discomfort related to glucose monitoring and not related to device) /Any AEs, Serious AE (SAE), most frequent AEs and SEAs, Death as SAE, withdrawals due AEs/ *Outcomes for SAF domain* possibly used in meta-analysis will be: Frequency of any AEs and SAE. ***From the Checklist for potential ethical, organisational, patient and social and legal aspects***, if needed. Rationale: Outcomes will be selected based on the recommendations from the relevant HTAs, clinical guidelines [1-9] and the EUnetHTA Guidelines on Clinical and Surrogate Endpoints and Safety [15].
Subgroup Analysis (if possible)	Type 1 DM-Type 2 DM-gestational DM; adults-children; adjunctive*-non-adjunctive**; insulin pump therapy-multiple daily injections (MDII); patients with impaired awareness of hypoglycaemia- patients with awareness of hypoglycaemia

Study design	**Clinical validity:** SR of accuracy studies or primary accuracy studies **Effectiveness:** If suitable evidence syntheses (SRs/HTA reports) are available: • evidence syntheses (SRs/HTA reports) and • primary studies (as described in next bullet) published after the last search date of the latest SR/HTA document If suitable evidence syntheses (SRs/HTA reports) are NOT available: • Randomised controlled trials • Prospective controlled studies, if no RCTs available **Safety:** If suitable evidence syntheses (SRs/HTA reports) are available: • evidence syntheses (SRs/HTA reports) and • primary studies (as described in next bullets) published after the last search date of the latest SR/HTA document If suitable evidence syntheses (SRs/HTA reports) are NOT available: • Randomised controlled trials • Non-randomised controlled trials • Prospective studies with or without a control group • Medical device adverse event registers and • Post marketing surveillance data on device-related adverse events **Organisational, ethical, patient and social, legal aspects:** Qualitative and quantitative studies, reports or opinions (according to the EUnetHTA Core HTA Model® 3.0), if needed [10]. Only English language studies will be included.

*Adjunctive: cannot be used to make treatment decision without confirmatory finger-stick testing **Non-adjunctive: can be used to make treatment decision without confirmatory finger-stick testing
CGM real-time: continuous glucose monitoring; FGM: flash glucose monitoring; CSII: continuous subcutaneous insulin infusion; MDII: multiple daily insulin injections; SMBG: self-monitoring blood glucose; Note: Professional (retrospective) devices will not be included in this assessment.

Stand-alone systems (with approved indications) for measuring interstitial fluid glucose levels: flash or real-time continuous glucose monitoring systems which will be assessed in this Rapid REA include following medical devices:

Flash or real-time continuous glucose monitoring systems	**Indications for use**
The FreeStyle Libre® Flash Glucose Monitoring System, Abbott	Measuring interstitial fluid glucose levels in people (age 4 and older) with diabetes mellitus, including pregnant women. The indication for children (age 4 - 12) is limited to those who are supervised by a caregiver who is at least 18 years of age. The caregiver is responsible for managing or assisting the child to manage the FreeStyle Libre® Flash Glucose Monitoring System and also for interpreting or

	assisting the child to interpret FreeStyle Libre® readings. It is designed to replace blood glucose testing in the self-management of diabetes with the exceptions listed below. Under the following circumstances, use a blood glucose meter to check the current glucose readings from the FreeStyle Libre® Flash Glucose Monitoring System Sensor: During times of rapidly changing glucose levels, interstitial glucose levels as measured by the Sensor and reported as current may not accurately reflect blood glucose levels. When glucose levels are falling rapidly, glucose readings from the Sensor may be higher than blood glucose levels. Conversely when glucose levels are rising rapidly, glucose readings from the Sensor may be lower than blood glucose levels. In order to confirm hypoglycaemia or impending hypoglycaemia as reported by the Sensor. If symptoms do not match the FreeStyle Libre® Flash Glucose Monitoring System reading.
The FreeStyle Navigator II® Continuous Glucose Monitoring System, Abbott	For continually measuring interstitial fluid glucose levels in people (age 6 and older) with diabetes mellitus. The indication for children (age 6 - 17) is limited to those who are supervised by a caregiver who is at least 18 years of age. The caregiver is responsible for managing or assisting the child to manage the FreeStyle Navigator II® System and also for interpreting or assisting the child to interpret FreeStyle Navigator II® readings. The FreeStyle Navigator II® Continuous Glucose Monitoring System is designed to replace blood glucose testing in the self-management of diabetes with the exceptions listed below. Under the following circumstances, use a blood glucose meter to check the current glucose readings from the FreeStyle Navigator II® Continuous Glucose Monitoring System Sensor: During times of rapidly changing glucose levels, interstitial glucose levels as measured by the Sensor and reported as current may not accurately reflect blood glucose levels. When glucose levels are falling rapidly, glucose readings from the Sensor may be higher than blood glucose levels. Conversely when glucose levels are rising rapidly, glucose readings from the Sensor may be lower than blood glucose levels. In order to confirm hypoglycaemia or impending hypoglycaemia as reported by the Sensor. If symptoms do not match the FreeStyle Navigator II® Continuous Glucose Monitoring System reading.
G4 PLATINUM® Continuous Glucose Monitoring System, Dexcom	For detecting trends and tracking patterns in persons (age 2 and older) with diabetes. The system is intended for use by patients at home and in healthcare facilities. The Dexcom G4 PLATINUM® System is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices. The Dexcom G4 PLATINUM® System aids in the detection of episodes of hyperglycaemia and hypoglycaemia, facilitating both acute and long-term therapy adjustments, which may minimize these excursions. Interpretation of the Dexcom G4 PLATINUM® System results should be based on the trends and patterns seen with several sequential readings over time.
G5 Mobile® Continuous Glucose Monitoring System, Dexcom	For the management of diabetes in persons age 2 years and older. The Dexcom G5 Mobile® CGM System is designed to replace fingerstick blood glucose testing for diabetes treatment decisions. Interpretation of the Dexcom G5 Mobile® CGM System results should be based on the glucose trends and several sequential readings over time. The Dexcom G5 Mobile® CGM System is intended for use by patients at home and in healthcare facilities.
Guardian Connect® Continuous Glucose Monitoring system, Medtronic	For continuous monitoring of glucose levels in the interstitial fluid under the skin, in persons with diabetes mellitus
	The Guardian Connect® app (CSS7200): intended for continuous or periodic monitoring of glucose levels in the interstitial fluid under the skin, in persons with diabetes mellitus. The Guardian Connect® app is intended for use with a compatible consumer mobile electronic device. It allows users to track patterns in glucose concentrations and to possibly identify episodes of low and high glucose. The Guardian Connect® app displays alerts if a glucose level reaches, falls below, or rises above set values. Sensor glucose values displayed on the screen are not intended to be used directly for making therapy adjustments, but rather to provide an indication of when a meter blood glucose measurement may be required.
	Guardian Connect® transmitter (MMT-7821): for single-patient or multiple-patient use as a component of select Medtronic CGM systems
	Enlite™ sensor (MMT-7008): intended for use with Medtronic Diabetes (Medtronic) glucose sensing systems to continuously monitor glucose levels in persons with diabetes
	CareLink™ Connect feature: intended to work with the Guardian Connect® CGM system. The CareLink™ Connect feature is intended to provide a secondary display of continuous glucose monitoring on a supported consumer electronic device for users of a Guardian Connect® CGM system and their designated care partners. The CareLink™ Connect feature is not intended to replace the real-time display of continuous glucose monitoring. All therapy decisions should be based on blood glucose measurements obtained from a blood glucose meter. The CareLink™ Connect feature is not intended to analyze or modify the continuous glucose monitoring data that it receives. Nor is it intended to control any function of the continuous glucose monitoring system to which it is connected.
Eversense® Continuous Glucose	For continually measuring interstitial fluid glucose levels in adults (18 years and

Monitoring system, Senseonics, Incorporated	older) with diabetes for the operating life of the sensor. The system is intended to: Aid in the management of diabetes. Provide real-time glucose readings. Provide glucose trend information. Provide alerts for the detection and prediction of episodes of low blood glucose (hypoglycaemia) and high blood glucose (hyperglycaemia). Historical data from the system can be interpreted to aid in providing therapy adjustments. These adjustments should be based on patterns and trends seen over time. The system is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home blood glucose monitoring devices.
Eversense® XL Continuous Glucose Monitoring system, Senseonics, Incorporated	For continually measuring interstitial fluid glucose levels in adults (18 years and older) with diabetes for the operating life of the sensor. The system is intended to: Aid in the management of diabetes; Provide real-time glucose readings; Provide glucose trend information; Provide alerts for the detection and prediction of episodes of low blood glucose (hypoglycaemia) and high blood glucose (hyperglycaemia). Historical data from the system can be interpreted to aid in providing therapy adjustments. These adjustments should be based on patterns and trends seen over time. The system is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home blood glucose monitoring devices.
SugarBEAT® Continuous Glucose Monitoring system, Nemaura Medical Inc.	CE Mark and Instruction for use documents are not available.

Source: Instructions for use documents

Sensor integrated and sensor augmented (or enabled) insulin pump systems compatible (connected) with specific CGM systems (with approved indications), which will be used as comparators in head-to-head analysis (if clinical studies are available) are listed below:

Sensor integrated and sensor enabled (or augmented) insulin pump systems compatible (connected) with specific CGM system	**Indication for use**
MiniMed Paradigm Veo® system, integrated with MiniLink® transmitter and Enlite Glucose Sensor, Medtronic	For the continuous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. In addition, the pump system is indicated for continuous or periodic monitoring of glucose levels in the fluid under the skin, and possible low and high blood glucose episodes.
MiniMed 640G® system, integrated with Guardian 2 Link transmitter and Enlite Glucose Sensor, Medtronic	For the continuous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. In addition, the system is indicated for continuous or periodic monitoring of glucose levels in the fluid under the skin, and detecting possible low and high glucose episodes.
t:slim X2 Insulin Pump Compatible with Dexcom G5® CGM, Tandem Diabetes Care, Inc.	For the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The t:slim X2 Insulin Pump can be used solely for continuous insulin delivery and as part of the t:slim X2 System to receive and display continuous glucose measurements from the Dexcom G5 Mobile® Sensor and Transmitter. The t:slim X2 System also includes continuous glucose monitoring (CGM) indicated for the management of diabetes. The Dexcom G5 Mobile® CGM is designed to replace fingerstick blood glucose testing for diabetes treatment decisions.
Omnipod, Compatible with Dexcom G5® CGM, Insulet	The only tubeless insulin pump on the market; It consists of a Personal Diabetes Manager (PDM) with integrated blood glucose meter and the “pod,” which delivers insulin; CGM’s provide real-time glucose readings every five minutes for people with type 1 or type 2 diabetes, and many Podders™ count on the Dexcom CGM to provide glucose readings throughout the day and night, including the speed and direction of glucose trends

Source: Instructions for use documents

3 Communication and collaboration

Table 3-1: Communication

Communication Type	Description	Date	Format	Participants/ Distribution
Scoping	To internally discuss and reach consensus on the scoping.	23/11/2017	E-meeting	Author(s), co-author(s), dedicated reviewers, observers, project manager
	To discuss the preliminary PICO and draft project plan with manufacturer(s) – optional	01-02/02/2018	*Face to face or e-meeting*	*Author(s), co-author(s), manufacturer(s), project manager*
		13/12/2017	*Additional e-meetings may be planned whenever needed*	*Author(s), Co-author(s), dedicated reviewer(s), project manager*
Feedback on draft submission file (optional)	*To point out the requirements for the final submission file by manufacturers*	*14/02/2018*	*E-mail*	*Author(s), project manager, manufacturers*
First draft of the rapid assessment	*To discuss comments of dedicated reviewers*	*26/04/2018*	*E-meetings may be planned*	*Author(s), co-author(s), dedicated reviewers*
Second draft of the rapid assessment	*To discuss comments from ≥ 2 external clinical experts and manufacturers*	*30/05/2018*	*E-meetings may be planned*	*Author(s), co-author(s), dedicated reviewers; external experts, manufacturers*

3.1 Dissemination plan

The final rapid assessment will be published on the EUnetHTA website: http://www.eunethta.eu/joint-assessments.

All stakeholders and contributors are informed about the publication of the final assessment by the project manager.

3.2 Collaboration with stakeholders

Collaboration with manufacturers

There will be a review of the preliminary PICO and a fact check of the 2nd draft project plan and the 2nd draft assessment by the manufacturers. The manufacturers will fill in certain modules of the Submission file templates and will be contacted with regard to questions, if necessary. Scoping f2f meetings were held on Feb 1-2, 2018.

Collaboration with other stakeholders

Collaboration with other stakeholders is planned – Patients representatives (Focus group will be held in Croatia and Patient Group Submission template will be sent to International Diabetes Federation European Region, Brussels and Diabetes Scotland, Scotland) and Payer representatives at EU level (The International Association of Mutual Benefit Societies (AIM), Brussels, related to reimbursement status of technologies under assessment).

3.3 Collaboration with EUnetHTA WPs

For the individual rapid assessment, some collaboration with other WPs is planned: WP7 [Implementation] will be informed on the project, in order to prepare activities to improve national uptake of the final assessment. Feedback on the WP4 REA process will be asked from the involved parties by WP6 [Quality Management], and this information will be processed by WP6 to improve the quality of the process and output.

3.4 Conflict of interest and confidentiality management

Conflicts of interest will be handled according to the EUnetHTA Conflict of Interest Policy. All individuals participating in this project will sign the standardised EUnetHTA "Declaration of Interest and Confidentiality Undertaking" (DOICU) statement.

Authors, co-authors and dedicated reviewers who declare a specific conflict of interest will be excluded from the whole work under this specific topic. However they still may be included in other assessments.

For external experts, patients or other stakeholders involved, conflict of interest declarations are collected regarding the topic. External experts or patients who declare a specific conflict of interest will be excluded from parts of or the whole work under this specific topic. However they still may be included in other assessments.

Manufacturers will sign a Confidentiality Undertaking (CU) form regarding the specific project.

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5 Appendix A

5.1 Selected Assessment Elements

The table shows the assessment elements and the translated research questions that will be addressed in the assessment. They are based on the assessment elements contained in the 'Model for Rapid Relative Effectiveness Assessment'. Additionally, assessment elements from other HTA Core Model Applications (for medical and surgical interventions, for diagnostic technologies or for screening) have been screened and included/ merged with the existing questions if deemed relevant.

Table 5-1: Selected Assessment Elements

ID	Topic	Topic Issue	Relevance in this assessment	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
Description and technical characteristics of technology					
B0001	Features of the technology and comparators	What is the technology and the comparator(s)?	Yes	M	What are the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) and the comparators medical devices?
A0020	Regulatory Status	For which indications has the technology received marketing authorisation or CE marking? [This assessment element can be placed either in the TEC OR in the CUR domain]	Yes	M	For which indications has the technology- the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) received CE marking?
B0002	Features of the technology and comparators	What is the claimed benefit of the technology in relation to the comparator(s)?	Yes	M	What is the claimed benefit of the technology - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) in relation to the comparator(s)medical devices?
B0003	Features of the technology	What is the phase of development and implementation of the technology and the comparator(s)?	Yes	NM	What is the phase of development and implementation of the technology - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) and the comparator(s) medical devices?
B0004	Features of the technology	Who administers the technology and the comparator(s) and in what context and level of care are they provided?	Yes	M	Who administers the technology - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) and the comparator(s) medical devices and in what context and level of care are they provided?
B0008	Investments and tools required to use the technology	What kind of special premises are needed to use the technology and the comparator(s)?	Yes	NM	What kind of special premises are needed to use the technology - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) and the comparator(s) medical devices?
B0009	Investments and tools required to use the	What equipment and supplies are needed to use the technology and the comparator(s)?	Yes	NM	What equipment and supplies are needed to use the technology - the continuous glucose monitoring (CGM real-time) and flash glucose

ID	Topic	Topic Issue	Relevance in this assessment	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
	technology				monitoring (FGM) medical devices (as personal, standalone systems) and the comparator(s) medical devices?
A0021	Regulatory Status	What is the reimbursement status of the technology? [This assessment element can be placed either in the TEC OR in the CUR domain]	Yes	NM	What is the reimbursement status of the technology - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems)?
Health problem and current use of technology					
A0002	Target Condition	What is the disease or health condition in the scope of this assessment?	Yes	M	What is the diabetes mellitus (Type 1 and Type 2, gestational DM)?
A0003	Target Condition	What are the known risk factors for the disease or health condition?	No	NM	
A0004	Target Condition	What is the natural course of the disease or health condition?	Yes	M	What is the natural course of the diabetes mellitus?
A0005	Target Condition	What are the symptoms and the burden of disease or health condition for the patient?	Yes	M	What are the symptoms and the burden of diabetes mellitus for the patient?
A0006	Target Condition	What are the consequences of the disease or health condition for the society?	Yes	NM	What are the consequences of the diabetes mellitus for the society?
A0024	Current Management of the Condition	How is the disease or health condition currently diagnosed according to published guidelines and in practice?	Yes	M	How the diabetes mellitus is currently diagnosed according to published guidelines and in practice?
A0025	Current Management of the Condition	How is the disease or health condition currently managed according to published guidelines and in practice?	Yes	M	How the diabetes mellitus is currently managed according to published guidelines and in practice?
A0007	Target Population	What is the target population in this assessment?	Yes	M	What is the target population in this assessment?
A0023	Target Population	How many people belong to the target population?	Yes	M	How many people belong to the target population?
A0011	Utilisation	How much are the technologies utilised?	Yes	M (NM for diagnostics)	How much are the technologies - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) utilised?
Clinical effectiveness					
D0001	Mortality	What is the expected beneficial effect of the intervention on mortality?	Yes	M	What is the expected beneficial effect of the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) on mortality?
D0005	Morbidity	How does the technology affect symptoms and findings	Yes	M	How does the ccontinuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical

ID	Topic	Topic Issue	Relevance in this assessment	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
		(severity, frequency) of the disease or health condition?			devices (as personal, standalone systems) affect symptoms and findings (severity, frequency) of the diabetes mellitus?
D0006	Morbidity	How does the technology affect progression (or recurrence) of the disease or health condition?	Yes	M	How does the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) affect progression of the diabetes mellitus?
D0011	Function	What is the effect of the technology on patients' body functions?	Yes	M	What is the effect of the ccontinuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) on patients' body functions?
D0016	Function	How does the use of technology affect activities of daily living?	Yes	NM	How does the use of the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) affect activities of daily living?
D0012	Health-related quality of life	What is the effect of the technology on generic health-related quality of life?	Yes	M	What is the effect of the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) on generic health-related quality of life?
D0013	Health-related quality of life	What is the effect of the technology on disease-specific quality of life?	Yes	M	What is the effect of the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) on disease-specific quality of life?
D0017	Patient satisfaction	Were patients satisfied with the technology?	Yes	NM	Were patients satisfied with the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems)?
Safety					
C0008	Patient safety	How safe is the technology in relation to the comparator(s)?	Yes	M	How safe is the technology - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) in relation to the comparator(s)?
C0002	Patient safety	Are the harms related to dosage or frequency of applying the technology?	No	NM	
C0004	Patient safety	How does the frequency or severity of harms change over time or in different settings?	Yes	M	How does the frequency or severity of harms change over time or in different settings?
C0005	Patient safety	What are the susceptible patient groups that are more likely to be harmed through the use of the technology?	Yes	M	What are the susceptible patient groups that are more likely to be harmed through the use of the technology - the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems)?
C0007	Patient safety	Are the technology and comparator(s) associated with user-dependent harms?	No	NM	
B0010	Safety risk management	What kind of data/records and/or	Yes	M for medical devices	What kind of data/records and/or registry is needed to monitor the use

ID	Topic	Topic Issue	Relevance in this assessment	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
		registry is needed to monitor the use of the technology and the comparator(s)?		NM for screening and diagnostics	of the technology- the continuous glucose monitoring (CGM real-time) and flash glucose monitoring (FGM) medical devices (as personal, standalone systems) and the comparator(s)?

5.2 Checklist for potential ethical, organisational, patient and social and legal aspects

1. Ethical	
1.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new ethical issues?	**Yes**
Questions related to equity could be important to take into consideration. Could potential inequalities prevent access to the technology? And more specifically, are there factors that could prevent a group or person from gaining access to the technology? If so, is it possible to influence these factors or manage the utilisation of the technology in a way that gives equal access to those in equal need? *Questions related to supportive actions and information could be important to focus on. Is there any specific information or any support patients (or decision-makers?) should seek to decide upon adopting the technology? Are there any particular challenges related to the use of the technology that the patient and/or care-givers need to be aware of? Is there clear and sufficient information available to understand the technology and possible risk related to unappropriated use?*	
1.2. Does comparing the new technology to the defined, existing comparators point to any differences that may be ethically relevant?	**No**
2. Organisational	
2.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) require organisational changes?	**Yes**
Questions related to the involvement of patients and caregivers as well as proper education and training could be important to raise. What kind of involvement of patients/participants and/or caregivers is the most suited? And, what kinds of co-operation and communication of activities are needed?	
2.2. Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be organisationally relevant?	**No**
3. Social	
3.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new social issues?	**Yes**
Questions related to patients' perspectives and perceptions as well as their expectations from using the technology could be important to discuss. This includes any positive or negative experiences that	

may arise as a consequence of using the technology (i.e., worries, satisfaction, stigmatisation, social status…). *A new technology may allow patients to return to work, however since the technology possibly can be seen or alarm sound can be heard by co-workers, it may lead to undesired attention from the surroundings.*	
3.2. Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be socially relevant?	**No**
4. Legal	
4.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any legal issues?	**No**
4.2. Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be legally relevant?	**No**