Biodegradable stents for benign refractory or recurrent esophageal stenosis

Project ID: WP5-SB-14

Project description and planning

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[Version 5 / 12 January 2015]

Contents:

A. VERSION LOG

Version number	Date	Name (Initials)	Modification	Reason for the modification
V1	09/04/2014	II	First version of draft project plan	Draft sent to co-authors
V2	14/04/2014	II	Second version of draft project plan	Draft sent to dedicated reviewers
V3	09/05/2014	II	Third version of draft project plan	Draft for public consultation
V4	13/06/2014	II	Fourth version of project plan	Incorporation of public consultation comments
V5	12/01/2015	II	Fifth version of project plan	The pilot was suspended because of the upcoming publication of the first randomized trial

B. PROJECT PLAN

1.0 PARTICIPANTS

Table 1. Project participants

#	Agency	Role in the project	Individual's expertise	Country
1.	ISCIII - Instituto de Salud Carlos III – "Carlos III" Institute for Health	Author(s)	Medicine, Pharmacy, Health Technology Assessment	Spain
2.	SAGEM - General Directorate of Health Research Ministry of Health	Co-Author(s)	Medicine, Healthcare Management, Health Technology Assessment	Turkey
3.	VASPVT- State Health Care Accreditation Agency	Reviewer	Healthcare management, Health Technology Assessment of medical devices	Lithuania
4.	Slovak Ministry of Health	Reviewer	Medicine, Pharmacy, Health Technology Assessment	Slovakia
5.	LBI-HTA - Ludwig Boltzmann Institute for HTA	Reviewer	Hospital interventions	Austria
6.	Spanish Society of Digestive Endoscopy, Virgen de La Luz Hospital	External Reviewer	Gastroenterologist, Gastro-intestinal endoscopy	Spain
7.	TBC	Medical Editor		
8.	LBI-HTA - Ludwig Boltzmann Institute for HTA	Project coordinator	Project management	Austria

1.1 PROJECT STAKEHOLDERS

Table 2. Project stakeholders

Organisation	Contact (name, e-mail, tel)	Comments
ELLA-CS	ELLA-CS, Milady Horakove 504. 500 06 Hradec Kralove 6. Czech Republic. Tel: +420 495 279 111. E-mail: info@ellacs.eu	The biodegradable stent SX-ELLA Esophageal Stent™ is the only biodegradable stent identified with CE mark (CE-1014).

2.0 PROJECT INTRODUCTION/ RATIONALE

Project introduction/ rationale
The rational for this pilot assessment report is to test the capacity of national HTA bodies to collaboratively produce structured rapid core HTA information on pharmaceuticals (strand A) and other medical technologies, such as medical devices, surgical interventions or diagnostics (strand B). In addition, the application (translation) of those collaboratively produced HTAs in the national contexts will be tested.

3.0 PROJECT SCOPE AND OBJECTIVES

	List of project objectives	Indicator (and target)
1.	To test the capacity of national HTA bodies to collaboratively produce structured rapid core HTA	Production of 1 pilot rapid assessment according to the research question (see Table 3)
2.	To test the application of these collaboratively produced rapid assessments into a national/local context	Production of ≥1 national/local report per pilot rapid assessment
3.	To compile a pilot rapid assessment of "biodegradable stents for benign esophageal strictures"	Production of a pilot rapid assessment on biodegradable stents for benign refractory esophageal stenosis. The technology is under evaluation for inclusion in the list of reimbursed services of the "Common Health Care Services Portfolio of the Spanish Healthcare System".

This pilot rapid assessment addresses the research question whether the use of biodegradable stents for benign refractory or recurrent esophageal stenosis is more effective and/or safer than self-expanded metal or plastic stents or esophageal dilation.

Table 3. Project Scope: PICO

Description	Project scope
Population	*Indications:* • *Benign refractory or recurrent esophageal stenosis* *Contraindications:* • *Inability to pass the 9.4 mm (28 F) delivery system through the stricture.* • *Benign stricture in the upper part of esophagus too close to the cricopharyngeal muscle.* • *Patients with benign strictures due to previously performed laryngectomy.* *Rationale:* *Benign esophageal stenosis can be caused by a wide range of disorders as the following: achalasia, anastomotic radiation, sclerotherapy, or medication induced strictures. Refractory and recurrent esophageal stenosis can be defined as an anatomical restriction of the esophageal lumen that results in the clinical symptom of dysphagia in the absence of endoscopic evidence of inflammation, after either inability to successfully dilate the stenosis to a diameter of 14 mm over 5 sessions at 2 weekly intervals (refractory) or after the inability to maintain satisfactory luminal diameter for 4 weeks once the target diameter of 14 mm has been achieved (recurrent) (Kochman et al. 2005) (Sharma et al 2010). Esophageal stenoses due to malignant processes are not included among the indications of CE mark for SX-ELLA Esophageal StentTM, which is the only identified biodegradable stent having CE mark.* *ICD-10 codes: Oesophagus obstruction (K22.2), achalasia of cardia (K22.0), dyskinesia of esophagus (K22.4)*

	Mesh-terms: Esophageal Stenosis; Esophageal Achalasia; Constriction, Pathologic; Esophageal Spasm, Diffuse *Intended use of the technology: Treatment*
Intervention	*Esophageal Biodegradable Stent.* *SX-ELLA Stent Esophageal Degradable™ is the only identified esophageal biodegradable stent having CE mark currently. The CE mark (CE-1014) was provided by ELEKTROTECHNICKY ZU in 2007. The stent has been designed for esophagus stenosis, made of poly-dioxanone, and is available in several sizes.* *Biodegradable stents are placed in the esophageal tract to maintain lumen patency. After approximately two-four months they degrade. Biodegradable stents' integrity and radial force should be maintained for 6 – 8 weeks following implantation. The stent has a dual "flared ends" design in order to reduce migration rates. The stent is made of polydioxanone, which is a degradable polymer.* *Insertion method is by means of endoscopic and/or fluoroscopic guidance. First a guide-wire is passed through the stricture and dilatation is performed to allow passage of the stent delivery apparatus. Then the stent is deployed. The stent has radiopaque markers at both ends in order to warrant an accurate stent positioning. Sometimes proton-pump inhibitors are prescribed to avoid rapid stent degradation.* *MeSH-terms: Stents; Bioprosthesis; Absorbable Implants; Dilatation; Prosthesis Implantation; Prosthesis Failure; Device Removal*
Comparison	*Comparators:* • *Self-Expanding Metal Stents (SEMS)* • *Self-Expanding Plastic Stents (SEPS)* • *Esophageal dilation (balloon dilation, bougie dilation)* *Rationale: Benign esophageal stenoses are initially treated by endoscopic dilation using push or balloons dilators. Temporary CSEMS and SEPS placement was suggested as a treatment for refractory or recurrent esophageal stenoses to prolong the dilatory effect (Van Boeckel 2013). Biodegradable stents could have advantages over the above mentioned treatments because of a potential reduction in adverse events, complications and number of interventions.*
Outcomes	*Primary effectiveness outcomes:*

	• *Reduction in dysphagia (dysphagia score: Mellow and Pinkas 1985)* • *Number of dilations per patient* • *Number of patients dysphagia free or remaining dysphagia after intervention* *Secondary effectiveness outcomes:* • *Time to recurrent significant dysphagia* • *Time to dilation of recurrent stricture* • *Esophageal lumen patency* • *Reduction of pain* • *Mortality (overall and disease related mortality)* • *Health related quality of life* • *Time to re-intervention (dilation, because of stent migration, because of disease worsening, other surgical or endoscopic interventions).* *Safety outcomes:* • *Adverse events and Serious Adverse Events during follow-up* • *Technical failure of the intervention* • *Intervention-associated adverse events (during and after intervention)* • *Unexpected procedures because of the intervention (removals, re-interventions)* • *Procedure-related mortality*
Study design	*Exclusions:* • *Studies with less than ten patients* • *Retrospective case series with non-consecutive enrolment* • *Studies with less than six weeks of follow-up* • *Congress Abstracts*
Languages	*English, Spanish, French, Turkish, German, Italian, Portuguese*

4.0 PROJECT APPROACH AND METHOD

Table 4a. Project approach and method

Project approach and method
The selection of assessment elements will be primarily based on the EUnetHTA Core Model Application for Pharmaceuticals (2.0). Additionally, assessment elements from other EUnetHTA Core Model Applications (for medical and surgical interventions, for diagnostic technologies or for screening) have been screened and were included if deemed relevant. A systematic review will be performed in order to obtain information of the selected assessment elements. The following sources of information will be used to obtain information: • Biomedical literature databases (Pubmed, Embase) • The Cochrane Library and Centre for Reviews and Dissemination. • Clinical trials registries will be assessed for registered ongoing clinical trials or observational studies: ClinicalTrials.gov, ISRCTN, metaRegister of Controlled Trials (mRCT) and International Clinical Trials Registry Platform (ICTRP). • Request to manufacturers. In addition the bibliographic search will be complemented by hand-search. Relevant articles or documents will be selected by two researchers independently, resolving disagreements by consensus. Articles or documents will be included or excluded according to the Population-Intervention-Control-Outcome (PICO)-scheme described earlier. In cases where questions within the domains “Health problem and current use of technology” and “Description and technical characteristics of technology” and “Safety” cannot be answered using the information retrieved from the basic systematic literature search described above, additional searches within specific information sources (e.g. databases for clinical guidelines, registries etc.) and, if needed, hand searching will be performed. The quality of the studies will be analysed by using the Cochrane risk of bias tool for randomized controlled trials (Higgins 2011) and the Institute for Health Economics checklist (Moga 2012) for case-series. From the selected studies, study characteristics, results concerning efficacy/effectiveness and safety will be extracted into a data extraction table covering the elements described in the table below. The GRADE-instrument will be used to describe evidence of efficacy and safety domains (GRADE 2004). All reporting of clinical effectiveness and safety data will be done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA Statement 2012). From the selected studies, study characteristics, results concerning efficacy/effectiveness and safety will be extracted into a data extraction table covering the following elements (see subsequent table). Since we do not expect a sufficient number of homogeneous RCTs we will not carry out a quantitative meta-analysis. Responsibilities and distribution of work between author (ISCIII) and co-author (SAGEM). ISCIII’s specific tasks are to: • Develop the first draft the project plan

- Involve clinical expert(s)
- Develop a scientific process plan with specific tasks to be carried out, time frames and deadlines of milestones and deliverables (below)
- Perform the basic literature search
- Carry out the assessment of “Safety” and “Clinical effectiveness” of the pilot
- Perform assessments of ethical and organisational aspects if needed
- Review assessments of the co-author
- Send “final versions” to reviewers, compile feedback from reviewers and stakeholders as well as changes made according reviewers and stakeholders’ comments
- Compile all domains into a final report and write a final summary of the review

SAGEM’s specific tasks are to:

- Review draft project plan
- Prepare the “Health problem and current use of the technology” and “Description and technical characteristics” domains of the review, which includes performing additional searches if needed
- Review assessments of the author
- Review final version of the pilot

Table 4b. Preliminary Evidence

Preliminary evidence table
Author, year, reference number
Country
Sponsor
Intervention/product
Comparator
Study design
Number of patients
Inclusion criteria
Patient characteristics: age, sex
Author Disclosure (Conflict of interest)
Follow-up (months)
Loss-to-follow-up, n (%)
Outcomes
Effectiveness
Reduction in dysphagia (dysphagia score)
Number of dilations per patient
Number of patients dysphagia free or remaining dysphagia after intervention
Time to recurrent significant dysphagia
Time to dilation of recurrent stricture
Esophageal lumen patency (time with patency, change in patency)
Reduction of pain)

Time to re-intervention
Health Related Quality of life
Overall mortality
Disease-related mortality
Safety
Adverse events (AE) in n (%) of patients
Description of AE in n (%) of patients
Serious adverse events (SAE) in n (%) of patients
Description of SEA in n (%) of patients
Intervention-associated adverse events
Unexpected interventions because of the intervention (removals, re-interventions)
Procedure-related mortality

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 assessments elements contained in the document "Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals". Additionally, assessment elements from other EUnetHTA Core Model Applications (for medical and surgical interventions, for diagnostic technologies or for screening available at 'HTA Core Model® Applications 2.0') have been screened and included/merged with the existing questions if deemed relevant.

Table 5. Assessment elements and translating research questions

ID	Domain	Topic	Issue	Relevance in this assessment Yes/No	Reason for non-relevance/ Preliminary research question(s)	Source of assessment element
Health Problem and Current Use of the Technology						
A0002	Health Problem and Current Use of the Technology	Target Condition	What is the disease or health condition in the scope of this assessment?	Yes	What is benign refractory or recurrent esophageal stenosis?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0003	Health Problem and Current Use of the Technology	Target Condition	What are the known risk factors for the condition?	Yes	What are the known risk factors for the refractory or recurrent esophageal stenosis?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0004	Health Problem and Current Use of the Technology	Target Condition	What is the natural course of the condition?	Yes	What is the natural course of benign refractory or recurrent esophageal stenosis?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0005	Health	Target	What is the burden of	Yes	What is the burden of benign refractory or	Model for Rapid Relative

	Problem and Current Use of the Technology	Condition	disease for the patient?		recurrent esophageal stenosis for the patient in terms of mortality, morbidity and quality of life measures?	Effectiveness Assessment of Pharmaceuticals
A0006	Health Problem and Current Use of the Technology	Target Condition	What is the burden of the disease for society?	No	Benign esophageal stenosis is not a frequent disease such to need mentioning on the burden for society	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0007	Health Problem and Current Use of the Technology	Target Population	What is the target population in this assessment?	Yes	What is the target population for biodegradable esophageal stents?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0023	Health Problem and Current Use of the Technology	Target Population	How many people belong to the target population?	No	Benign esophageal stenosis is not a frequent disease and there is not a standardized mode of management globally, nationally even locally so the market and budget effect can vary widely. This element will be addressed in element A0001	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0001	Health Problem and Current Use of the Technology	Utilisation	For which health conditions and populations, and for what purposes is the technology used?	Yes	For which health conditions and populations, and for what purposes are the biodegradable esophageal stents used?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0011	Health Problem and Current Use of the Technology	Utilisation	How much are the technologies utilised?	Yes	How much are the biodegradable esophageal stents utilized?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0024	Health Problem and Current Use of the Technology	Current Management of the Condition	How is the health condition currently diagnosed according to published guidelines and in practice?	Yes	How is the benign refractory or recurrent esophageal stenosis currently diagnosed according to published guidelines and in practice?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0025	Health Problem and Current Use of the Technology	Current Management of the Condition	How is the health condition currently managed according to published guidelines and in practice?	Yes	How is the benign refractory or recurrent esophageal stenosis currently managed according to published guidelines and in practice?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0020	Health Problem and Current Use of the Technology	Regulatory Status	What is the marketing authorisation status of the technology?	Yes	What is the marketing authorization status of the biodegradable esophageal stents?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
A0021	Health Problem and Current Use	Regulatory Status	What is the reimbursement status of the technology?	Yes	What is the reimbursement status of the biodegradable esophageal stents?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals

	of the Technology					
Description and technical characteristics of technology						
B0001	Description and technical characteristics of technology	Features of the technology	What is the technology and the comparator(s)?	Yes	What is biodegradable esophageal stent and the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
B0002	Description and technical characteristics of technology	Features of the technology	What is the approved indication and claimed benefit of the technology and the comparator(s)?	Yes	What is the approved indication and claimed benefit of biodegradable esophageal stent and the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
B0003	Description and technical characteristics of technology	Features of the technology	What is the phase of development and implementation of the technology and the comparator(s)?	No	These devices have still a short life-cycle.	
B0004	Description and technical characteristics of technology	Features of the technology	Who performs or administers the technology and the comparator(s)?	Yes	Who implant the biodegradable esophageal stents and the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
B0005	Description and technical characteristics of technology	Features of the technology	In what context and level of care are the technology and the comparator used?	Yes	In what context and level of care are biodegradable esophageal stents and the comparators used?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
B0008	Description and technical characteristics of technology	Investments and tools required to use the technology	What kind of special premises are needed to use the technology and the comparator(s)?	Yes	What kind of special premises are needed to use biodegradable esophageal stents and the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
B0009	Description and technical characteristics of technology	Investments and tools required to use the technology	What supplies are needed to use the technology and the comparator?	Yes	What supplies are needed to use biodegradable esophageal stents and the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
B0010	Description and technical characteristics of technology	Investments and tools required to use the technology	What kind of data and records are needed to monitor the use of the technology and the comparator?	Yes	What kind of data and records are needed to monitor the use of biodegradable esophageal stents and the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
B0011	Description and technical characteristics of technology	Investments and tools required to use the technology	What kind of registry is needed to monitor the use of the technology and comparator?	Yes	What kind of registry is needed to monitor the use of biodegradable esophageal stents and comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
Safety						
C0001	Safety	Patient safety	What kind of harms can use of the technology	Yes	What are the adverse events in patients with a biodegradable stent?	Model for Rapid Relative Effectiveness Assessment of

			cause to the patient?			Pharmaceuticals
C0002	Safety	Patient safety	What is the dose relationship of the harms?	No	There is no gradation of technology use.	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
C0004	Safety	Patient safety	How does the frequency or severity of harms change over time or in different settings?	Yes	How does the frequency or severity of harms change over time or in different settings?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
C0005	Safety	Patient safety	What are the susceptible patient groups that are more likely to be harmed?	Yes	Are there any susceptible patient groups more likely to be harmed?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
C0007	Safety	Patient safety	What are the user-dependent harms?	Yes	Can adverse events be caused by the behaviour of patients, professionals or manufacturers?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
C0008	Safety	Patient safety	How safe is the technology in relation to the comparator?	Yes	How safe is the biodegradable esophageal stent in relation to the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
C0040	Safety	Environmental safety	What kind of harms are there for public and environment?	No	The stent is made of Polydioxanone, which is a polymer degradable by hydrolysis, and mainly excreted in urine, the remainder being eliminated by digestive or exhaled as CO2.	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
Clinical effectiveness						
D0001	Clinical effectiveness	Mortality	What is the expected beneficial effect of the intervention on overall mortality?	Yes	What is the expected beneficial effect of the biodegradable esophageal stents on overall mortality?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0002	Clinical effectiveness	Mortality	What is the expected beneficial effect on the disease-specific mortality?	Yes	What is the expected beneficial effect of biodegradable esophageal stents on the disease-specific mortality?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0003	Clinical effectiveness	Mortality	What is the effect of the technology on the mortality due to causes other than the target disease?	Yes	What is the expected beneficial effect of biodegradable esophageal stents on the mortality due to causes other than the target disease?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0005	Clinical effectiveness	Morbidity	How does the technology affect symptoms and findings?	Yes	How do biodegradable esophageal stents affect symptoms and findings in relation to the comparators ?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0006	Clinical effectiveness	Morbidity	How does the technology affect progression of disease?	No	Addressed in D0005	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0010	Clinical effectiveness	Change-in management	How does the technology modify the need for hospitalization?	Yes	How does biodegradable esophageal stents modify the need for hospitalization?	Model for Medical and Surgical Interventions (2.0)
D0011	Clinical effectiveness	Function	What is the effect of the technology on patients' body functions?	Yes	What is the effect of the biodegradable esophageal stents on digestive functions?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals

D0016	Clinical effectiveness	Function	How does the use of technology affect activities of daily living?	No	Addressed in D0011	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0012	Clinical effectiveness	Health-related quality of life	What is the effect of the technology on generic health-related quality of life?	Yes	What is the effect of the biodegradable stents on generic health-related quality of life in relation to the comparators ?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0013	Clinical effectiveness	Health-related quality of life	What is the effect of the technology on disease-specific quality of life?	Yes	What is the effect of the biodegradable esophageal stents on disease-specific quality of life in relation to the comparators?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0017	Clinical effectiveness	Patient satisfaction	Was the use of the technology worthwhile?	Yes	Were patients satisfied overall with biodegradable esophageal stents?	Model for Rapid Relative Effectiveness Assessment of Pharmaceuticals
D0023	Clinical effectiveness	Change-in management	How does the technology modify the need for other technologies and use of resources?	Yes	How does biodegradable esophageal stents modify the need for other technologies and use of resources?	Model for Medical and Surgical Interventions (2.0)

Checklist for potential ethical, organisational, social and legal aspects

The following checklist should be considered in order to determine whether there are specific ethical, organisational, social and legal aspects which also need to be addressed. Since the assessment is comparative in nature, only new issues should be dealt with, which arise from a difference between the technology to be assessed and its major comparator(s). Already known problems/issues with regard to ethical, organisational, social and legal aspects which are common to the technology to be assessed and its comparator(s) will, as a rule, not be addressed, as it is not to be expected that the addition of a new technology will lead to changes.
If a question is answered with 'yes', further analysis of these issues may be warranted. If they are answered with no, the domains need not be dealt with further.

Table 6. Checklist for potential ethical, organisational, social and legal aspects.

1. Ethical	
1.1. Does the introduction of the new technology and its potential use/nonuse instead of the defined, existing comparator(s) give rise to any new ethical issues?	No
1.2. Does comparing the new technology to the defined, existing comparators point to any differences which may be ethically relevant?	No
2. Organisational	
2.1. Does the introduction of the new technology and its potential use/nonuse instead of the defined, existing comparators require organisational changes?	No
2.2. Does comparing the new technology to the defined, existing comparators point to any differences which may be organisationally relevant?	No
3. **Social**:	
3.1. Does the introduction of the new technology and its potential use/nonuse instead of the defined, existing comparator(s) give rise to any new social issues?	No

3.2. Does comparing the new technology to the defined, existing comparators point to any differences which may be socially relevant?	No
4. **Legal**:	
4.1. Does the introduction of the new technology and its potential use/nonuse 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 comparators point to any differences which may be legally relevant?	No

5.0 ORGANISATION OF THE WORK

5.1 MILESTONES AND DELIVERABLE(S)

Table 7. Milestones and Deliverables

Milestones/Deliverables	**Start date**	**End date**
Project duration	**17/03/2014**	**27/11/2014**
Scoping phase	**17/03/2014**	**13/06/2014**
Consultation of draft Project Plan with co-authors	04/04/2014	11/04/2014
Consultation of draft Project Plan with dedicated reviewers	14/04/2014	28/04/2014
Second draft of Project Plan available	28/04/2014	09/05/2014
Consultation of draft Project Plan (public consultation including WP5 SAG, manufacturer(s), Stakeholder Forum)	12/05/2014	02/06/2014
Final Project Plan	02/06/2014	13/06/2014
Assessment phase	**16/06/2014**	**05/06/2015**
First draft available	16/06/2014	01/08/2014
Review by dedicated reviewers	04/08/2014	19/08/2014
Postponed due to ongoing publication of RCT	03/09/2014	06/01/2015
Establish new timelines	06/01/2015	19/01/2015
Second draft available	19/01/2015	13/02/2015
2nd review by dedicated reviewers	16/02/2015	27/02/2015
3rd draft available	02/03/2015	13/03/2015
Medical editing	16/03/2013	27/03/2015
4th draft available	30/03/2015	10/04/2015
Review by ≥ 1 external clinical expert, WP5 Strand B members, manufacturer(s) and by other potential stakeholders	13/04/2015	04/05/2015
5th draft available	05/05/2015	22/05/2015
Formatting	25/05/2015	29/05/2015
Final pilot rapid assessment		Week from 01/06/2015 –

		05/06/2015
Local reports		

5.2 MEETINGS

Besides face-to-face meetings mentioned in the Work Plan of WP5, no further face-to-face meetings are planned for this specific project.
Up to 4 e-meetings may be scheduled for this pilot rapid assessment (see section 6.0), if considered necessary.

6.0 COMMUNICATION

Table 8. Communication

Communication Type	Description	Date	Format	Participants/ Distribution
Draft Project Plan with timelines	Introduction of pilot team members, first discussion on scope of pilot assessment	27/03/2014	e-meeting	Author(s), Co-author(s), dedicated reviewers, Coordinating Team
Draft Project Plan with timelines	Review of methods and assessment elements chosen, discussion of time-lines	14/04/2014	E-mail	Author(s), Co-author(s), dedicated reviewers, Coordinating Team
Final Project Plan	Review of methods and assessment elements chosen, discussion of time-lines considering comments from Stakeholder Advisory Group, public, manufacturer	13/06/2014	E-mail	Author(s), Co-author(s), dedicated reviewers, Coordinating Team
First draft of the pilot assessment	To be reviewed by dedicated reviewers	01/08/2014	E-mail	Dedicated reviewers
	To discuss comments of dedicated reviewers (optional)	01/09/2014-12/09/2014	E-Mail	Author(s), co-author(s), dedicated reviewers
Second draft of the assessement	To be reviewed by dedicated reviewers	16/02/2015-27/02/2015	E-Mail	Author(s), co-author(s), dedicated reviewers
Third draft of the pilot assessment	Medical editing by external editor	16/03/2015-27/03/2015	E-mail	Medical Editor
Fourth draft of the assessment	To be consulted with ≥1 clinical expert, WP5 members, manufacturer(s), other potential stakeholders	13/04/2015-04/05/2015	E-Mail	≥1 clinical expert, WP5 members, manufacturer, other potential stakeholders

6.1 DISSEMINATION PLAN

The final pilot rapid assessment will be distributed as laid-out in the Work Plan of WP5.

7.0 COLLABORATION WITH STAKEHOLDERS

A public consultation of the draft Project Plan will be conducted. The draft Project Plan will be made publicly available on the EUnetHTA website for a period of 15 days. The WP5 SAG, the Stakeholder Forum as well as the manufacturer(s) will be invited to comment on the draft Project Plan for this pilot rapid assessment.

In addition, the manufacturer will be asked for further information (e.g. CE mark, on-going studies, available evidence, reimbursement status).

8.0 COLLABORATION WITH EUnetHTA WPs

For the individual pilot rapid assessment, no collaboration with other WPs is planned.

9.0 RESOURCE PLANNING

9.1 HUMAN RESOURCES

Table 9. Human resources

Role	**Total number of person days**	**Source**	
		Staff of participating organisations	**Subcontracting**
Author	60 person days	60 person days	-
Co-Author	30 person days	30 person days	-
Reviewer	3 person days each	3 person days each	-
External reviewer	3 person days	-	3 person days
Medical Editor	5 person days	-	5 person days
Layout	4 person days	-	4 person days

10.0 CONFLICT OF INTEREST MANAGEMENT

Conflicts of interest will be handled according to EUnetHTA JA2 Conflict of Interest Policy. As conflict of interest may be topic dependent, conflict of interest declarations will be collected from authors and reviewers involved in a specific pilot assessments. Authors and reviewers who declare a conflict of interest will be excluded from parts of, or the whole work under this specific topic. However, they may still be included in other pilots.
If external experts are involved in WP5 a conflict of interest declarations will be collected from them regarding the topic. External experts who declare a conflict of interest will be excluded from parts of, or the whole work under this specific topic. However, they may still be included in other pilots.

11.0 EXPECTED OUTCOME(S)

Project outcome(s)
The capacity of national HTA bodies to collaboratively produce structured rapid core HTA and the translation into local reports will have been proven. Redundancies will have been reduced and therefore efficiency gains achieved. Applicability of the HTA Core Model for rapid REAs to other technologies will have been elicited and the Model accordingly adapted.

C. REFERENCES

1. GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004;328(7454):1490.

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