Assessment element tables for HTA Core Model Application for Diagnostic Technologies (2.0)

Contents

1 Health Problem and Current Use of the Technology

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
A0001	Utilisation	For which health conditions and for what purposes is the technology used?	All relevant conditions and populations should be included. This question is especially relevant when there are multiple potential target conditions and populations for which the technology is used, and multiple intended uses, both indicated and other. There may also be differing views about the appropriate use of the technology that it is essential to	Critical	Complete	Yes	Sources: HTAs, guidelines, reviews, clinician consultation, developers/manufacturers. Method: A descriptive summary.			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}

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			highlight. Describe the differences in the use of the technology for the various indications and how it might act differently in different patient groups. Point out e.g. if certain populations should be excluded from using the technology, or if they require e.g. a different dosage. Certain technologies may be primarily indicated for second-line use but also used for first-line treatment.							
A0007	Target Population	What is the target population in this current assessment of the technology?	Relevant for all assessments: both safety and effectiveness depend largely on the subpopulation towards which the intervention is targeted. The technology may be used for all patients with the condition, or only those in the early stages, or at a specific severity level, or for those at moderate risk of having the condition. Personalised medicine divides the target population into even smaller units when targeting the intervention to specific subgroups based on e.g. genetic profile. Use the target population defined in the scope of the project, and consider adding further details and description of who defined the selected subgroups and why.	Critical	None	Yes	Sources: HTAs, guidelines, reviews, developers/manufacturers. Method: A descriptive summary.			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0002	Target Condition	What is the disease or health condition in the scope of this assessment?	Relevant for all assessments. Especially when effectiveness depends on the subtype, stage or severity of the disease. Use the target condition and ICD codes defined in the scope of the project and consider adding details such as: description of anatomical site, disease aetiology and pathophysiology, types of disease or classification according to origin, severity, stages, or risk level, and different manifestations of the condition. The following properties of the target	Critical	Complete	Yes	Sources: text books, HTAs, guidelines, epidemiological reviews or studies, WHO documents, disease registers. Method: A descriptive summary.			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}

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			condition are defined in separate assessment elements: risk factors (A0003), natural course (A0004), symptoms (A0005), and burden of disease including prevalence and incidence (A0006).							
A0003	Target Condition	What are the known risk factors for the disease or health condition?	Describing risk factors is especially important when they suggest possibilities for primary and secondary prevention. This information may affect the choice of comparator or the appraisal of the overall value of the technology under assessment. The risk factors for acquiring the condition, and the risk factors for relapses or worsening of the condition should be reported here, separately. The prevalence of the various risk factors might differ in different geographic areas and among different sub-populations.	Important	Partial	Yes	Sources: text books, HTAs, guidelines, epidemiological reviews or studies. Method: Systematic review is generally not required. A descriptive summary is sufficient.			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0004	Target Condition	What is the natural course of the disease or health condition?	This assessment element should provide information on the prognosis and course of the condition when untreated. This information is relevant for appraising the overall value of the technology. A technology targeted to cure a life-threatening condition has a different significance from a technology intended to alleviate the symptoms of self-limiting conditions. It may also guide the assessment of the predicted value or effectiveness of the technology, as technologies may work differently at different stages or severity grades of the disease, and there may be a relationship between earlier intervention and better prognosis. This element should also provide information on the time lag between the onset of disease and the symptoms or other findings that	Critical	Complete	Yes	Sources: text books, HTAs, guidelines, epidemiological reviews or studies. Method: A descriptive summary.			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}

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			eventually trigger the need of diagnostics and care.							
A0005	Target Condition	What are the symptoms and burden of disease for the patient at different stages of the disease?	This issue is especially relevant when the patient or individual is expected to undergo a substantial change in pain, disability, psychosocial issues, or other determinants of quality of life. This element should describe the patient's relevant symptoms before intervention with the technology, their severity and whether they are persistent, intermittent, or undulating. Patients' perceptions of the burden of the disease are not always in line with the clinical seriousness of the disease or its societal burden.	Critical	Complete	Yes	Sources: text books, HTAs, quality of life studies, qualitative patient perception studies. Method: A descriptive summary.			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0006	Target Condition	What are the consequences of the disease or the health condition for the society (i.e. the burden of the disease)?	Prevalence and incidence of the disease that is prevented or treated by using the technology; disease-specific mortality and disability, life years lost., and/or disability-adjusted life years, quality of life, QALYs.	Critical	Partial	Yes	Sources: text books, HTAs, registries and national statistics, WHO incidence, mortality and survival databases.http://www.who.int/cancerc/resources/incidences/en / Method: A descriptive summary			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0009	Target Condition	What aspects of the consequences / burden of disease are targeted by the technology?	The technology can affect only some aspects (e.g. mortality) and leave other aspects (e.g. quality of life) untouched. The application of the diagnostic technology may target only one aspect of the burden of disease, eg. disability but not mortality. Or mortality but not symptomatology	Critical	Complete	Yes	Deductive models (based on the natural history of the disease, test target and treatment target; epidemiological studies (if sufficient testing has been done).	B0002		
A0011	Utilisation	How much is the technology utilised currently and in the future?	Provide national estimates for current and future utilisation rates, for both the technology under assessment and its comparators. Variations in utilisation reflect market access, sales figures, actual usage in hospital level and adherence to the use of the technology	Critical	None	Yes	National statistics, surveys, technology and procedure registers, disease management studies, utilisation studies, manufacturer sales data	G0009 G0010		Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}

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			by both professionals and patients. Data on current and previous utilisation reflect the phase of the technology (experimental, emerging, established or obsolete). This also has implications for the availability of evidence and the level of uncertainties.							
A0012	Utilisation	What kind of variations in use are there across countries/regions/settings?	This information can be useful for decision-makers to understand regional variations in their own country and also understand the situation in comparison with other countries.	Important	Partial	Yes	National statistics, surveys, disease management studies, manufacturer sales data, utilisation reviews, audits, studies on praxis-variation. Own primary analysis of: Disease register, procedure register, device register, administrative data (DRG, dicharge databases, reimbursement claims database).	G0009 G0010		Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0023	Target Population	How many people belong to the target population?	This information can be used to give an idea of the resource requirements in general for implementing the technology. Estimates of likely relevant increases or decreases in the size of the target population in the future should also be included.	Critical	None	Yes	Sources: text books, HTAs, national registries, statistics, systematic reviews. Method: A descriptive summary.			Burls 2000 {1}, Velasco 2002 {25}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0017	Current Management of the Condition	What are the differences in the management for different stages of the disease or health condition?	Identification of practice variations due to the differences in the forms, stages or severity of the disease. May be useful to understand the proper place of technology in the health care delivery process. Different stages of disease may call for different therapeutic procedures (for example aortic insufficiency is first treated with medication and at a certain point of cardiac structural changes an operation is	Important	Partial	Yes	Surveys, utilisation reviews, clinical guidelines, recommendations. If such information is lacking: expert surveys / expert interviews			Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}

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			preferred). Provide an overview of other treatment alternatives. Likewise diagnostic or monitoring methods used for various diseases may vary depending on the stage of disease..							
A0018	Current Management of the Condition	What are the other typical or common alternatives to the current technology?	Provide an overview of other treatment alternatives. Focus primarily on those used within professional health care delivery. Consider including technologies that people may commonly seek or use even if these wouldn't be commonly provided in professional health care (e.g. technologies for self-testing or self-treatment, or alternative medicine).	Critical	Partial	Yes	Clinical guidelines, recommendations, systematic reviews	B0001		Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0024	Current Management of the Condition	How is the disease or health condition currently diagnosed according to published guidelines and in practice?	The effectiveness of an intervention may vary in differently diagnosed populations. A sensitive test tends to have low specificity such that there are several people who do not have the condition among the test-positive population. The effectiveness of an intervention in that population may be lower than in a population examined with a less sensitive test (but with more true positive cases). It is important to point out possible discrepancies between guidelines and actual practice.	Critical	Partial	Yes	Sources: Clinical guidelines and published utilisation reviews; in the absence of these, clinical experts survey. See Appendix 1. Method: Systematic review of clinical guidelines. Quality appraisal of guidelines can be done using e.g. AGREE II Instrument. For practice mapping, a pragmatic review or listing of available information is sufficient. Flowcharts are illustrative in reporting diagnostic pathways.			Burls 2000 {1}, Velasco 2002 {25}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0025	Current Management of the Condition	How is the disease or health condition currently managed according to published guidelines and	It is important to describe whether the technology is an add-on or a replacement for the existing management options, and what the other evidence-based alternatives are. Are there differences in the treatment of diseases at their different stages? Identification of practice variations may imply differences in the quality of health care. Deviation from	Critical	Partial	Yes	Sources: Clinical guidelines and published utilisation reviews; in the absence of these clinical experts survey. See Appendix 1. Method: Systematic review of clinical guidelines. Quality appraisal of guidelines can be done using e.g. AGREE II Instrument. For practice			

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		in practice?	evidence-based guidelines may suggest over/under use of the technology.				mapping, a pragmatic review or listing of available information is sufficient. Flowcharts are illustrative in reporting management pathways.			
G0009	Utilisation	Who decides which people are eligible for the technology and on what basis?	Provide information on who are the key actors in deciding on the use of the technology. Do most important decisions take place on the national level (e.g. population screening) or for example by individual professionals (e.g. surgical method for a specific disease)? How is the decision made; are there some documented criteria? Information about the possible variations in the decision level and criteria has ethical implications. This issue is related to the issue of work processes (G0001)	Critical	Partial	Yes	Literature search, guidelines, documents of hospitals, own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory).	A0011 A0012 :B0016, D0 021, F0012, I0012, H0012		Kristensen 2007 {24} {14}
B0003	Utilisation	What is the phase of development and implementation of the technology and the comparator(s) ?	Most technologies will be introduced at approximately the same time in several countries. This information is relevant for the assessment while the evidence base may change rapidly for technologies that are at an earlier stage in their development. It is also important to establish whether new versions of the technology with substantial improvements are expected in the near future. For end users it is useful to know if new versions or adaptations of the technology are expected in the near future. Describe the following aspects:	Critical	Partial	Yes	Manufacturers´ sites and effectiveness studies, HTAs, guidelines, published literature including reviews, textbooks, introduction sections of research articles, grey literature, hand-searches and conference proceedings.	A0020 A0021 A0011 A0019 A0020 F0001		Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24} Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002

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			- Is the technology an innovation? -When was it developed? -Is the technology only partially innovative (i.e. a modification of an existing technology), and in that case, is it possible to specify the degree of innovation the technology may represent? -When was the technology introduced into healthcare? -Is the technology an already established one, but now used in a different way, for instance for a new indication? -Is it experimental, emerging, established in use or obsolete (implementation level)? - Is the technology field changing rapidly -How does this technology differ from its predecessors (other technologies used for similar purposes)? -Are there new aspects that may need to be considered when applying it? -Is there evidence that the technology works (or is used) outside its current indication area or produces incidental findings that can have consequences relevant to effectiveness, safety, organisational, social and ethical domains.							

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F0001	Utilisation	Is the technology a new, innovative mode of care, an add-on to or modification of a standard mode of care or replacement of a standard mode of care?	Explain how the possible use / non-use of the technology would affect the current treatment process and practices. How substantial is the change to current practices? Notice that the technology may be in a different phase of utilisation for different health conditions or purposes of use.	Critical	Partial	Yes	Horizon scanning databases, ongoing research databases, information from manufacturers.			Mitcham 2004 {26}
A0020	Regulatory Status	What is the marketing authorisation status of the technology?	There are both international and national market authorisation systems. An overview of the status with regard to key processes, e.g. CE marking, EMA/FDA approval is recommended. Also information on national data and an analysis of possible discrepancies can be highly useful. Imaging devices may require approval. Substances needed for obtaining images may require additional approval (e.g. radiotracers). In some cases the approval for primary screening is different to that for clinical use (FDA recently licensed tests explicitly for screening), but in most cases approval is obtained for diagnostic use and the test is proposed for screening without any other formal approval.	Critical	Complete	Yes	CE-Approval, EMA, FDA, national authorities. Manufacturers should be contacted in order to identify which steps have they taken/ are they planning to take concerning market approval	I0015 B0002		Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}
A0021	Regulatory Status	What is the reimbursement status of the technology across countries?	Information on national reimbursement status from different countries for the technology as well as the comparators, including key dates and anticipated licensing timeframe should be listed here. Notice that reimbursement status may differ for different purposes: e.g.	Important	Complete	Yes	Appendix 1 of REA model = List of websites of national agencies with information on reimbursement, EVIDENT database.	I0012 B0002		Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24}

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			treatment vs. prevention. Information on full coverage, co-payments, coverage under special circumstances/conditional coverage is useful.							

2 Description and technical characteristics of technology

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
A0022	Other	Who manufactures the technology?		Important	Partial	Yes	Manufacturers´ information, clinical guidelines, legislation, HTAs, approving authority, National or local judgement.	Related to Organisational domain		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0012	Training and information needed to use the technology	What kind of qualification and quality assurance processes are needed for the use or maintenance of the technology?	Differentiate between the users who are. 1. applying the technology (could be different from those interpreting results) 2. interpreting the results and make clinical decisions. 3. taking care of service and maintenance. Describe what type of training materials (writing and/or translation, other adaptation) and the characteristics of the personal training (individual and/or group sessions, number and length of sessions, number and qualifications of trainers) and if regular or frequent standardisation or quality checks are required (E.g. CME points). Provide an estimate to what extent the training and quality assurance measures may affect the efficacy and safety of the technology.	Critical	Partial	Yes	Manufacturers´ sites, approving authority, published literature including handbooks, textbooks, reviews, HTA-reports, interviews with specialists and clinical experts, as well as grey literature, hand-searches and conference proceedings. Research studies and national or local judgement can be used.	G0003 C0020 C0062 C0063 E0001 E0002 G0006		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0013	Training and information	What kind of training and	Describe what type of training materials (writing and/or translation, other	Important	Partial	Yes	Manufacturer, effectiveness studies, observational studies,	G0003 C0020		Liberati A. et al. 1997; Busse R. et

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	needed to use the technology	information is needed for the personnel/carer using this technology?	adaptation) and the characteristics of the personal training (individual and/or group sessions, number and length of sessions, number and qualifications of trainers); if the technology requires a specific skill that is developed over a period of time using the technology (learning curve), an estimate should be provided of the number of patients a professional needs to treat (as a basis or per year) in order to reach an acceptable minimum standard. Provide an estimate to what extent the training and quality assurance measures may affect the efficacy and safety of the technology.				applicability studies, clinical experts, user information, HTA-reports. National or local judgement.	C0062 C0063 I0008 F0006		al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0014	Training and information needed to use the technology	What kind of training and information should be provided for the patient who uses the technology, or for his family?	Describe what type of training materials should be provided (writing and/or translation, other adaptation) by whom, and the characteristics of the personal training (individual and/or group sessions, number and length of sessions, number and qualifications of trainers) and if the informed consent regarding the risk/benefits of participation is required.	Important	Partial	Yes	Manufacturer data, effectiveness studies, observational studies, applicability studies, clinical experts, user information, patient organisations, HTA-reports. National or local judgement	C0001 C0003 C0005 C0007 C0062 F0004 F0006 G0004 H0003 H0007 H0008 I0002		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0015	Training and information needed to use the technology	What information of the technology should be provided for patients outside the target group and the general public?	Describe what type of information materials should be provided (writing and/or translation, other adaptation) and if the informed consent for participating is required?	Critical	Partial	Yes	Manufacturer data, effectiveness studies, observational studies, applicability studies, clinical experts, user information, patient organisations, HTA-reports, discussion forums in web, as well as grey literature, hand-searches and conference proceedings, National or local judgement	F0005 F0011 G0004 H0002 H0007 H0008 I0002 I0008		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002

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B0001	Features of the technology	What is this technology and the comparator(s) ?	This is relevant in all assessments. Use the descriptions of the technology and comparator(s) defined in that scope and elaborate them here in more detail. Technology may include a single device, a questionnaire, imaging or sequence of technologies. The HTA may address one or several similar technologies. Describe separately for the technology and the comparator: the type of device, technique, procedure or therapy; its biological rationale and mechanism of action, and also, describe how the technology differs from its predecessors, and the various current modifications or different manufacturers' products, especially if the dissimilarities affect performance.	Critical	Partial	Yes	Manufacturers´ sites, published literature including reviews, textbooks, introduction sections of research articles, effectiveness studies, clinical experts, studies in basic science, HTA-reports.	A0022 A0018 F0001		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0002	Features of the technology	What is the approved indication and claimed benefit of the technology and the comparator(s) ?	This issue is especially relevant in new technologies with uncertain expectations and claims of benefit. Describe the following aspects: -How is it expected to be an improvement over previous /existing technologies used for the same health problem? -The expressed objectives for the implementation of the technology in health care; what are the claimed objectives e.g. increased safety, health benefit, accuracy or patient compliance, and whether it is intended to replace or to supplement existing technologies. Is the technology licensed as a mono-intervention, or in addition to current	Important	Complete	Yes	Manufacturers´ sites, HTAs, effectiveness studies, clinical experts, published literature including reviews, introduction sections of research articles, grey literature, hand-searches and conference proceedings, consulting clinical professionals, lay journals and websites.	A0001 A0009 C0008		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002

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			interventions (which should be specified) Are there stopping rules for use of the technology? Is there evidence that the technology works (or is used) outside its current indication area, or produces incidental findings that can have consequences relevant to effectiveness, safety, organisational, social and ethical domains? This information may explain the choice of comparator(s) and outcomes for the assessment and helps in appraising the overall results.							
B0003	Features of the technology	What is the phase of development and implementation of the technology and the comparator(s)?	Most technologies will be introduced at approximately the same time in several countries. This information is relevant for the assessment while the evidence base may change rapidly for technologies that are at an earlier stage in their development. It is also important to establish whether new versions of the technology with substantial improvements are expected in the near future. For end users it is useful to know if new versions or adaptations of the technology are expected in the near future. Describe the following aspects: - Is the technology an innovation? -When was it developed? -Is the technology only partially innovative (i.e. a modification of an existing technology), and in that case, is it possible to specify the degree of innovation the technology may	Critical	Partial	Yes	Manufacturers´ sites and effectiveness studies, HTAs, guidelines, published literature including reviews, textbooks, introduction sections of research articles, grey literature, hand-searches and conference proceedings.	A0020 A0021 A0011 A0019 A0020 F0001		Burls 2000 {1}, Busse 2002 {2}, Liberati 1997 {3}, Imaz-Iglesia 1999, Kristensen 2007 {24} Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002

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			represent? -When was the technology introduced into healthcare? -Is the technology an already established one, but now used in a different way, for instance for a new indication? -Is it experimental, emerging, established in use or obsolete (implementation level)? - Is the technology field changing rapidly -How does this technology differ from its predecessors (other technologies used for similar purposes)? -Are there new aspects that may need to be considered when applying it? -Is there evidence that the technology works (or is used) outside its current indication area or produces incidental findings that can have consequences relevant to effectiveness, safety, organisational, social and ethical domains.							
B0004	Features of the technology	Who performs or administers the technology and the comparator(s) ?	Describe the following aspects: -Which professionals (nurses, doctors, and other professionals) apply and make decisions about starting or stopping the use of the technology? -Do the patients themselves, or their	Critical	Partial	Yes	Clinical guidelines, professionals' consensus statements, HTAs, manufacturers´ websites, introduction sections of research articles, interviews with clinical professionals or patients.	Current Use		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002

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			carers, administer the technology? -Who can select the patients, make referrals, decide to initiate the use of the technology, or interpret the outcome? -Are there certain criteria (skills, function, training requirements) for the patients or professionals who will administer the technology?				Manufacturer, effectiveness studies, clinical experts, legislation. National or local judgement, as well as grey literature, hand-searches and conference proceedings can be also used.			
B0005	Features of the technology	In what context and level of care are the technology and the comparator used?	Describe the level of care in which the technology is used: self care, primary care, secondary and tertiary care. If secondary or tertiary care, describe whether it is intended to be used in the outpatient or inpatient setting. Its role in the management pathway can be as a replacement, an add-on or for triage	Critical	Partial	Yes	Manufacturers´ information, clinical guidelines, professionals' consensus statements, HTAs, manufacturers´ websites, introduction sections of research articles, interviews with clinical professionals or patients. Manufacturer, effectiveness studies, clinical experts, legislation. National or local judgement, as well as grey literature, hand-searches and conference proceedings can be also used.	A0012 A0025 G001 G0005		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0018	Features of the technology	Are the reference values or cut-off points clearly established?	Are conflicting /varying definitions of an abnormal finding likely to affect the interpretation of the results? (please describe them)	Important	Partial	Yes	Manufacturers´ sites, published literature including reviews, textbooks, handbooks, introduction sections of research articles, interviews with specialists, as well as grey literature, hand-searches and conference proceedings.			Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0007	Investments and tools required to	What material investments are needed to	Devices, machinery, computer programs, etc. Those parts of the technology that need to be purchased (and often	Important	Partial	Yes	Manufacturers´ sites, published literature including reviews, textbooks, handbooks,	E0001 E0002 G0006		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen

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	use the technology	use the technology?	installed) by an organisation in order to use the technology. Includes need for back-up investment to cover for breakdowns in use.				introduction sections of research articles, interviews with specialists, clinical experts, user information. National or local judgement, as well as grey literature, hand-searches and conference proceedings.	G0003?		FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0008	Investments and tools required to use the technology	What kind of special premises are needed to use the technology and the comparator(s) ?	Many technologies require purpose-built premises, such as radiation-secured areas, Faraday cages, dressing rooms for the patient, or specific premises for storage and reconstitution of chemotherapy pharmaceuticals equipped with fume cupboards. Typical premises in primary or secondary care may differ markedly from country to country. A clear description of necessary facilities is needed instead of general statement (e.g. to be used in hospitals only)	Important	Partial	Yes	Sources: User information from manufacturer, and market approval authority. HTAs, applicability studies, interviews with clinical experts and hospital managers. Manufacturer, applicability studies, clinical experts, user information. National or local judgement can be also used.	Safety domain, Organisational domain		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0009	Investments and tools required to use the technology	What equipment and supplies are needed to use the technology and the comparator?	Describe all required disposable items necessary for using the technology, such as: syringes, needles, pharmaceuticals and contrast agents, fluids, bandages and tests to identify patients eligible for treatment.	Important	Partial	Yes	Sources: Information from manufacturer, HTAs, applicability studies, interviews with clinical professionals and hospital managers. Manufacturer, applicability studies, clinical experts, user information. National or local judgement can be also used.	E0001 E0002 G0006		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002
B0010	Investments and tools required to use the technology	What kind of data and records are needed to monitor the use of the	Describe the data that needs to be collected about the care process, professionals involved, patients and their health outcomes. These include: e.g. clinical indications, specified populations, prescriber information, inpatient or	Important	Partial	Yes	Sources: Local authorities and legislation, administrative staff, clinical professionals, HTAs, National or local judgement.	G0008		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		technology and the comparator?	outpatient use, test results, review period, and health outcomes. In case of new technologies, EVIDENT database could be consulted.							al. 1997; Busse R. et al. 2002
B0011	Investments and tools required to use the technology	What kind of registers are needed to monitor the use the technology and comparator?	Describe the general importance of having a registry to monitor the use of this particular technology and the comparator. Are there existing registries that should be used, or should a registry be established, to collect the necessary data to monitor safety or true life effectiveness? Provide national examples.	Important	None	No	Sources: Local authorities and legislation, administrative staff, clinical professionals. HTAs, National or local judgement.	G0008 G0003?		Liberati A. et al. 1997; Busse R. et al. 2002; Kristensen FB et al. 2001; Draborg E et al. 2005 Liberati A. et al. 1997; Busse R. et al. 2002

3 Safety

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
C0001	Patient safety	What kind of harms can use of the technology cause to the patient; what are the incidence, severity and duration of harms?	Here one should identify and describe the direct harms of the use and the administration of the technology. User dependent harms are described in C0007, and comparative harms in C0008. Harms are identified in placebo-controlled trials, observational studies, and in registries. It is important to refer to the source and report separately harms identified in spontaneous reporting databases. Harms should be reported per indication or target population . The identified harms should be categorised according to their severity and frequency. The seriousness of harm is typically graded based on events that pose a threat to a patient's life or functioning. Frequency of occurrence for each harm is usually presented in comparison with placebo or no treatment, as percentages	Critical	Complete	Yes	Sources: Placebo controlled trials, observational research, FDA database, safety monitoring databases, observational research, safety monitoring databases, registers, statistics registers, statistics. Method: Systematic review. Results should be presented by risk level (i.e. the product of severity and frequency of harm).	Effectiveness domain D0009; D0003 A0001 A0007 B0001	A0001 A0007 B0001	{ 1, 12, 14, 16, 28, 29, 34, 37 }

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			or risk ratios. Finally, the harms should be grouped by their severity and frequency and ordered so that the severe and/or frequent harms are presented first. If there are many different harms reported in the literature, concentrate on reporting the most serious and the most frequent harms							
C0002	Patient safety	Are the harms related to dosage or frequency of applying the technology?	Information should be included if safe use of the technology is sensitive to even small changes of the dose because this may have implications for the training and organisation of care. The potential for accumulated harm due to repeated dosage or testing should also be considered.	Critical	Complete	Yes	Phase 1 studies for pharmaceuticals, other research articles, HTAs, manufacturers' product data sheets, safety monitoring databases. Method: Systematic review.	A0017 B0001	A0017 B0001	{ 2, 11 }
C0004	Patient safety	How does the frequency or severity of harms change over time or in different settings?	This issue is especially relevant for new or evolving technologies where there are considerable uncertainties in the safety evidence, and in technologies with steep learning curves. How does the safety profile of the technology vary between different generations, approved versions or products? Is there evidence that harms increase or decrease in different organisational settings?	Critical	Partial	Yes	Sources: HTAs, efficacy and safety research articles, articles on learning curve, manufacturers' information. Method: Descriptive summary.	Current use, effectiveness (D0001; D0008; D0009) , costs domains B0004 B0005 B0001	B0004 B0005 B0001	
C0005	Patient safety	Are there susceptible patient groups that are more likely to be harmed through use of the technology?	Typically, people with comorbidities and co-medication, pregnancy, intolerances, or specific genetic profiles, elderly people, children and immunosuppressed patients.	Important	Complete	Yes	HTAs, guidelines, market access authorities, manufacturers' product information, label warnings, safety monitoring databases. Method: Descriptive summary.	Ethical, Effectiveness domain (D0008;D0009) B0016 B0001	B0016 B0001	{ 2, 11 }
C0006	Patient safety	What are the consequences of false positive, false	What are the consequences of false positive, false negative and incidental findings generated by using the	Critical	Partial	Yes	Research articles, manufacturers' product data sheets, safety monitoring	Effectiveness domain D0028, D0027	B0001	Welch G, Schwartz L, Woloshin S. Overdiagnosed: Making people sick

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		negative and incidental findings generated by using the technology from the viewpoint of patient safety?	technology? False negative test results (Type II error) identify sick people incorrectly as healthy with the possible consequence of incorrectly rejected or delayed treatment. Volume of false negative test results can be estimated to be 1- sensitivity of the test. False positive test results (Type I error) identify healthy people incorrectly as sick with the possible consequence of overtreatment. Volume of false positive test results can be estimated to be 1 - specificity of the test. Incidental findings in tests carry major risk of overdiagnosis and overtreatment.				databases Research articles, manufacturers' product data sheets, safety monitoring databases	D0009 D0003 B0001 D0003 E0001 F0001 G0001, G0100		in pursuit of health, Beacon Press, Boston, 2011
C0007	Patient safety	Are there special issues in the use of the technology that may increase the risk of harmful events?	Describe here what is known of the harms caused by the properties or behaviour of professionals, patients or other individuals who apply or maintain the technology. Is there e.g. a noteworthy risk of malfunction of a device, due to deficient user training or personal attitude; or a risk of errors related to reconstitution, dosage, administration, or storage of medicines, that may have serious consequences; or, is there a risk of addiction? Describe what is known of the learning curve, intra- or inter-observer variation in interpretation of outcomes, errors or other user-dependent concerns in the quality of care	Important	Partial	Yes	Sources: Studies on effectiveness, safety and health services research; manufacturers' product data sheets, safety monitoring databases, label warnings. Method: Systematic review	Description and technical characteristics and Organisational domains B0006 B0001 Description	B0006 B0001	{ 2, 11 }
C0008	Patient safety	How safe is the technology in relation to the	Highlight the differences in the most important risks (i.e. the most severe and frequent harms) of the technology and its comparator(s). For harms that are	Critical	Partial	Yes	Research articles, manufacturers' product data sheets, safety monitoring	Current use/ organisational aspects/ costs,	B0001 A0018	

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		comparator(s)?	common to both the technology and the comparator(s), provide information on which has the higher risk of the particular harm. Aspects of individual patients, populations, service delivery & cost effectiveness should be considered.				databases. Other HTA reports or systematic reviews of main comparators. Method: Systematic review.	economic evaluation B0001 A0018 Current use		
C0020	Occupational safety	What kind of occupational harms can occur when using the technology?	Consider if there are possible harms to professional applying the technology: working positions, radiation or infection risks, etc.	Important	Complete	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases	Ethical and Social domains B0012 B0013	B0012 B0013	
C0040	Environmental safety	What kind of risks for public and environment may occur when using the technology?	Several chemical substances or their toxic metabolites are potentially harmful in ecological environments; some of the most recent concerns are endocrine modulators and disruptors and nanoparticles. The statistical risk of radiation at the public level should also be described here.	Optional	Partial	No	Research articles, manufacturers' product data sheets, safety monitoring databases Method: Systematic review.	Ethical and Social domains		
C0060	Safety risk management	How does the safety profile of the technology vary between different generations, approved versions or products?		Important	Complete	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases	Description and Technical Characteristics		
C0061	Safety risk management	Can different organizational settings increase or decrease harms?		Critical	Complete	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases. Descriptive review on a ccuracy and effectiveness research, epidemiological risk research	Current use, Effectiveness (D0009; Organisational B0020 A0012	B0020 A0012	

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
C0062	Safety risk management	How can one reduce safety risks for patients (including technology-, user-, and patient-dependent aspects)?	Is there a requirement for specific training, use of a protocol or available guideline which may reduce the occurrence or severity of the harm. Information on what kind of risk communication is needed for patients, citizens and decision makers may be included.	Critical	Complete	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases	Ethical F0006, Description and technical characteristics B0012, B0014, B0015		
C0063	Safety risk management	How can one reduce safety risks for professionals (including technology-, user-, and patient-dependent aspects)?	Is there a requirement for specific training, use of a protocol or available guideline which may reduce the occurrence or severity of the harm. Information on what kind of risk communication is needed for patients, citizens and decision makers may be included.	Important	Partial	Yes	Research in occupational health and safety research literature	Organisational and Social Domains		
C0064	Safety risk management	How can one reduce safety risks for environment (including technology-, user-, and patient-dependent aspects)	Is there a requirement for specific training, use of a protocol or available guideline which may reduce the occurrence or severity of the harm. Information on what kind of risk communication is needed for patients, citizens and decision makers may be included.	Important	Partial	Yes	Research articles, manufacturers' product data sheets.	Social Domain		

4 Clinical Effectiveness

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
D0011	Function	What is the effect of the technology on	International classification of function proposes the following categories for body functions: mental, sensory and pain,	Critical	Partial	Yes	Trials and observational studies with functioning as an outcome. The instruments for outcome	H0005 E0005 F0101		ICF http://apps.who.int/classifications/icfbro

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		patients' body functions	voice and speech, cardiac, respiratory and immune functions, genitourinary and reproductive functions, movement-related, and skin functions. Report the results both in absolute terms and relative to the comparator.				reporting should be validated			wser
D0012	Health-related Quality of life	What is the effect of the technology on generic health-related quality of life?	Health related quality of life (HRQL) is typically measured with self- or interviewer-administered questionnaires to measure cross-sectional differences in quality of life between patients at a point in time (discriminative instruments) or longitudinal changes in HRQL within patients during a period of time (evaluative instruments). Two basic approaches to quality-of-life measurement are available: generic instruments that provide a summary of HRQL; and specific instruments that focus on problems associated with single disease states, patient groups, or areas of function. Generic instruments include health profiles and instruments that generate health utilities. Each approach has its strengths and weaknesses and may be suitable for different circumstances. See also •Methodological guideline for REA of pharmaceuticals: Health-related quality of life and utility measures. http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Health-related%20quality%20of%20life.pdf	Critical	Partial	Yes	Trials, observational and qualitative studies	H0005 E0005		EMEA 2005, FDA 2009, Chassany 2002, Terwee 2007, Revicki 2008, Puhan 2006
D0013	Health-related Quality of life	What is the effect of the technology on disease specific quality of life?	Health related quality of life (HRQL) is typically measured with self- or interviewer-administered questionnaires to measure cross-sectional differences in quality of life between patients at a point in time (discriminative instruments) or	Critical	Partial	Yes	Trials, observational and qualitative studies	H0005 E0005		EMEA 2005, FDA 2009, Chassany 2002, Terwee 2007, Revicki 2008, Puhan 2006

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			longitudinal changes in HRQL within patients during a period of time (evaluative instruments). Two basic approaches to quality-of-life measurement are available: generic instruments that provide a summary of HRQL; and specific instruments that focus on problems associated with single disease states, patient groups, or areas of function. Each approach has its strengths and weaknesses and may be suitable for different circumstances.See also •Methodological guideline for REA of pharmaceuticals: Health-related quality of life. http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Health-related%20quality%20of%20life.pdf							
D0014	Function	What is the effect of the technology on work ability?	Describe the effects of the intervention on sick leave, absenteeism, presenteeism, return-to-work, retirement and other relevant outcomes describing working ability	Critical	Partial	Yes	Trials and other studies with return-to-work or work ability outcomes reported.	H0005 E0001		Fit for Work Europe website. Available at: www.fitforworkeurope.eu European Commission (2007). Together for Health: A Strategic Approach for the EU 2008-2013. Available at http://ec.europa.eu/health-eu/doc/whitepaper_en.pdf
D0015	Function	What is the effect of the technology on return to	Discharge to the living conditions in which patients lived before admission is one of the most important treatment goals particularly for elderly patients.	Critical	Partial	Yes	Trials and observational studies using one of the several evaluation tools, such as the Katz ADL scale, the Lawton	H0005		

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		previous living conditions?	Implications for family members and carers should be considered too.				IADL scale or the Bristol Activities of Daily Living Scale. Health care service providers may use ADL evaluations in their practice, using models such as the Roper-Logan-Tierney model of nursing, and the resident-centered models, such as the Program of All-Inclusive Care for the Elderly (PACE).			
D0016	Function	How does use of the technology affect activities of daily living?	Activities of Daily Living (ADL) is used in rehabilitation as an umbrella term relating to self care, comprising those activities or tasks that people undertake routinely in their every day life. The activities can be subdivided into personal care and domestic and community activities. Report the results both in absolute terms and relative to the comparator. For further information see guideline Health-related quality of life and utility measures http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Health-related%20quality%20of%20life.pdf, and guideline: Endpoints used for relative effectiveness assessment of pharmaceuticals, clinical endpoints http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Clinical%20endpoints.pdf	Critical	Partial	Yes	Trials and observational studiesreporting ADL outcomes	H0005		
D0024	Test-treatment chain	Is there an effective treatment for the condition the test is detecting?	The effectiveness or clinical utility of a test usually requires that an effective treatment for the target condition exists and is available to the patients.	Critical	Partial	Yes	Trials, observational studies	F0001		
D0029	Benefit-	What are the	This question integrates all benefits and	Critical	Partial	Yes	Trials, observational studies,	A0007,	A0007,	

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
	harm balance	overall benefits and harms of the technology in health outcomes?	harms concerning mortality, morbidity, QoL and further patient relevant outcomes, also considering the amount of false positive and false negative test results. There is no common quantitative summary measure, and even qualitatively a balanced and meaningful presentation is difficult to reach. The integration of information across domains into the benefit-harm-balance is essential. This issue provides input for ETH (F0010) andECO (E0005) to calculate the incremental effectiveness of the new technology. Information from SAF is needed for this issue: all harms to the patient are listed in outcomes and units which are comparable to the outcomes in EFF domain representing benefits. In diagnostic and screening technologies the problem of overdiagnosis and overtreatment should be covered, as well as the benefits and harms of subsequent diagnostic testing and treatments in patients with true positive test result in a prior diagnostic or screening test.				modelling studies	A0011, C0001, C0003, C0004, C0005, C0006, C0007, C0061, E0005, F0001, F0011	A0011, C0001, C0003, C0004, C0005, C0006, C0007, C0061,	
D0030	Quality of life	Does the knowledge of the test result affect the patient's non-health-related quality of life?	Test result may alleviate or trigger or worsen symptoms as well as improve or worsen the quality of life, although there is no effectiveness to the primary outcome.	Important	Partial	Yes	Qualitative research, observational studies, trials	H0005, H0006 F0001, F0003	H0006	
D0001	Mortality	What is the expected beneficial effect of the intervention	Mortality is the preferred, objective endpoint for assessments of life-threatening conditions. Overall mortality refers to all-cause mortality. It is expressed either as mortality rates	Critical	Partial	Yes	Systematic reviews of trials, trials, both placebo- controlled and with active control. In the absence of head to head trials, studies with indirect comparison	E0005 F0001		Hochman 2011, Black 2002

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		on overall mortality?	(incidence in given population, at given time point and usually risk standardised), or survival (number of people alive for a given period after an intervention). Several methods are used to adjust mortality rates and survival curves, e.g. relative survival (observed versus expected survival), which can be quite misleading; and hazard ratio (derived from a statistical method comparing the median survivals in the two groups). Note that progression-free survival is not a mortality endpoint; it describes the time from the beginning of an intervention until a patient shows signs of disease progression. Consider separately absolute mortality (compared to placebo or waiting list) and mortality relative to the comparator. See also Methodological guideline for REA of pharmaceuticals: Endpoints used for relative effectiveness assessment of pharmaceuticals, clinical endpoints http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Clinical%20endpoints.pdf In diagnostic and screening technologies this issue refers to the expected beneficial effect of the test-treatment-chain,				(see Methodological guideline for REA of pharmaceuticals: Direct and indirect comparison, http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Direct%20and%20indirect%20comparisons.pdf). If these are not available, non-controlled studies and respective systematic reviews. Health care register data. Modelling studies.			
D0002	Mortality	What is the expected beneficial effect on the disease-specific mortality?	Disease-specific mortality is a proportion of the all-cause mortality. It should be noted that even if a given treatment reduces one type of death, it could increase the risk of dying from another cause, to an equal or greater extent. Disease-specific mortality is typically presented as rates and as age- and risk-adjusted measures such as hazard ratio. It is a frequently used endpoint in	Critical	Partial	Yes	Systematic reviews of trials, trials, both placebo- controlled and with active control. In the absence of head to head trials, studies with indirect comparison (see Methodological guideline for REA of pharmaceuticals: Direct and indirect comparison, http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Dir	E0005 F0001		Hochman 2011, Black 2002

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			screening trials, where it is considered to be subject to bias. Consider separately absolute mortality (compared with placebo or waiting list) and mortality relative to the comparator. See also Methodological guideline for REA of pharmaceuticals: Endpoints used for relative effectiveness assessment of pharmaceuticals, clinical endpoints http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Clinical%20endpoints.pdf In diagnostic and screening technologies this issue refers to the expected beneficial effect of the test-treatment-chain,				ect%20and%20indirect%20comparisons.pdf). If these are not available, non-controlled studies and respective systematic reviews. Health care register data. Modelling studies.			
D0003	Mortality	What is the effect of the technology on the mortality due to causes other than the target disease?	This issue includes all unintended, either positive or negative effects of the technology on mortality. There may be e.g. decrease of mortality of another disease observed or suspected; or increased mortality due to accidents or hazardous medical interventions after false positive or incidental test results. In diagnostic and screening technologies this issue refers to the effect of the test-treatment-chain,	Critical	Partial	Yes	Systematic reviews of trials, trials, both placebo- controlled and with active control. In the absence of head to head trials, studies with indirect comparison (see Methodological guideline for REA of pharmaceuticals: Direct and indirect comparison, http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Direct%20and%20indirect%20comparisons.pdf). If these are not available, non-controlled studies and respective systematic reviews. Health care register data. Modelling studies.	C0001 E0005 C0006		
D0026	Morbidity	How does the technology modify the effectiveness of subsequent interventions?	Different tests may detect slightly different subpopulations as test positive. Results from further diagnostic testing and the effectiveness of subsequent interventions can be different in test A positive compared to test B positive. E.g. treatment may work differently in screening-identified cases than in cases	Important	Partial	Yes	Trials, observational studies, accuracy studies			

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			that are diagnosed at regular physician's appointment							
D0010	Change-in management	How does the technology modify the need for hospitalization ?	Consider also changes at different levels of care e.g. ward instead of intensive care.	Important	Partial	Yes	Trials, observational studies	E0001 G0001		
D0020	Change-in management	Does use of the test lead to improved detection of the condition?	Although the test is reliable, the information it provides does not necessarily affect clinical decision making. If it does not change sufficiently the pre-test probability the added value of the information may be low. E.g there may be routine preoperative lab tests that nobody uses in decision making. Moreover, users´ ability to make a correct diagnosis may depend on their knowledge and ability to interpret the results.	Important	Partial	Yes	Trials, accuracy studies, before-after studies, interrupted time series, change-in management studies	G0001		Guyatt GH, Tugwell PX, Feeny DH, Haynes RB, Drummond M. A framework for clinical evaluation of diagnostic technologies. CMAJ 1986 Mar 15;134(6):587-594.
D0021	Change-in management	How does use of the test change physicians' management decisions?	There may be technology-related or non-related factors that might influence the physicians' perceptions, ability and attitude to decision making. Management decisions mean both testing and treatment decisions.	Important	Partial	Yes	Change-in-management studies, qualitative research	G0001, G0008, G0009		Guyatt GH, Tugwell PX, Feeny DH, Haynes RB, Drummond M. A framework for clinical evaluation of diagnostic technologies. CMAJ 1986 Mar 15;134(6):587-594.
D0022	Change-in management	Does the test detect other potential health conditions that can impact the subsequent management	Management decisions mean both testing and treatment decisions. Notice issue C0006 which deals also with incidental findings.	Important	Partial	Yes	Trials, accuracy studies	F0003		Guyatt GH, Tugwell PX, Feeny DH, Haynes RB, Drummond M. A framework for clinical evaluation of diagnostic technologies. CMAJ 1986 Mar

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		decisions?								15;134(6):587-594.
D0023	Change-in management	How does the technology modify the need for other technologies and use of resources?	New (less invasive) interventions can reduce the need for surgical interventions. Some treatments require ongoing monitoring and healthcare visits including hospitalisation.	Important	Partial	Yes	Trials and pharmaco-economic studies, guidelines on utilization of resources. Observational studies, statistics	B0013 E0001 F0003 G0001, G0003, G0004, G0007	G0001,G0003,G0007	
D0017	Patient satisfaction	Was the use of the technology worthwhile?	Describe patients' overall perception of the value of the intervention and their satisfaction with the treatment. See also Methodological guideline for REA of pharmaceuticals: Endpoints used for relative effectiveness assessment of pharmaceuticals, clinical endpoints http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Clinical%20endpoints.pdf	Critical	Partial	Yes	Surveys, qualitative research, observational studies, trials	H0006 F0001, F0011	H0006	
D0018	Patient satisfaction	Is the patient willing to use the technology again?	Differences in acceptability may predict the overall uptake of the technology and would impact on the overall effectiveness.	Important	Partial	Yes	Qualitative research, observational studies, trials	H0006	H0006	
D0032	Morbidity	How does the test-treatment intervention modify the magnitude and frequency of morbidity?	A more accurate replacement test could improve treatment and effectiveness. A satisfactory triage test may decrease the number of adverse outcomes from another test. An add-on test may increase sensitivity so that more patients receive proper treatment and thus improved outcomes.	Critical	Partial	Yes	Accuracy and other observational studies, trials, qualitative research	H0005		
C0006	Patient safety	What are the consequences of false positive, false negative and incidental findings generated by	What are the consequences of false positive, false negative and incidental findings generated by using the technology? False negative test results (Type II error) identify sick people incorrectly as healthy	Critical	Partial	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases Research articles, manufacturers' product data	Effectiveness domain D0028, D0027 D0009 D0003 B0001 D0003	B0001	Welch G, Schwartz L, Woloshin S. Overdiagnosed: Making people sick in pursuit of health, Beacon Press, Boston, 2011

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		using the technology from the viewpoint of patient safety?	with the possible consequence of incorrectly rejected or delayed treatment. Volume of false negative test results can be estimated to be 1- sensitivity of the test. False positive test results (Type I error) identify healthy people incorrectly as sick with the possible consequence of overtreatment. Volume of false positive test results can be estimated to be 1 - specificity of the test. Incidental findings in tests carry major risk of overdiagnosis and overtreatment.				sheets, safety monitoring databases	E0001 F0001 G0001, G0100		
D1001	Test accuracy	What is the accuracy of the test against reference standard?	Accuracy in terms of sensitivity and specificity, and other measures such as likelihood ratios, pre-test probabilities, SDORs, AUC or Q*.	Critical	Complete	Yes	Accuracy studies			
D1002	Test accuracy	How does the test compare to other optional tests in terms of accuracy measures?	Consider also how does the technology compare to other development stages of the same technology?	Critical	Complete	Yes	Accuracy studies			
D1003	Test accuracy	What is the reference standard and how likely does it classify the target condition correctly?	Consider also the situation when there is no proper reference standard.	Important	Partial	Yes	Accuracy studies			Rutjes AWS, Reitsma JB, Coomarasamy A, Khan KS, Bossuyt PMM. Evaluation of diagnostic tests when there is no gold standard. A review of methods. Health Technol Assess 2007;11(50).

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
D1004	Test accuracy	What are the requirements for accuracy in the context the technology will be used?	Discuss what could be an estimate for acceptable number of false negative and false positive test results in different situations e.g. in replacement/ triage/ add-on situations, and in life threatening / harmless conditions.	Critical	Partial	Yes	Descriptive ethical literature, expert advice, prevalence data, modelling studies, calculations	F0017		
D1005	Test accuracy	What is the optimal threshold value in this context?	Sensitivity and specificity vary according to the threshold value. Optimal combination of sensitivity and specificity defines optimal threshold value. The optimum depends on the consequences of the test results. E.g. whether it does more harm to overlook a case or to treat someone unnecessarily.	Critical	Partial	Yes	Screening studies with varying thresholds, accuracy studies with varying thresholds, modelling studies	F0017		
D1006	Test accuracy	Does the test reliably rule in or rule out the target condition?	This question is relevant in e.g triage situation where the aim of the test is to rule out a severe condition in patients to avoid further testing which may be more harmful and expensive.	Critical	Partial	Yes	Accuracy studies, modelling studies	C0001 F0017		
D1007	Test accuracy	How does test accuracy vary in different settings?	How do patient spectrum, disease prevalence, disease severity, and properties of the technology itself affect the accuracy of the test? This may have implications on how frequently a test needs to be repeated, optimal age range for a screening programme and adjustments in different populations.	Important	Partial	Yes	Accuracy studies in different settings, descriptive literature, expert advice	B0005,	B0005	
D1008	Test accuracy	What is known about the intra- and inter-observer variation in test interpretation?	This is especially relevant in tests with subjective assessments, such as most imaging tests.	Important	Partial	Yes	Accuracy studies, trials, observational studies			
D1019	Test accuracy	Is there evidence that the replacing test is more	If there is effective treatment for a condition, then a new diagnostic technology with similar sensitivity but greater safety or specificity may be seen	Important	Partial	Yes	Accuracy studies, trials, observational studies	C0001 F0001	C0001	Lord SJ, Irwig L, Simes RJ. When is measuring sensitivity and

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		specific or safer than the old one?	as improved effectiveness.							specificity sufficient to evaluate a diagnostic test, and when do we need randomized trials? Ann.Intern.Med. 2006 Jun 6;144(11):850-855.

5 Costs and economic evaluation

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
E0001	Resource utilization	What types of resources are used when delivering the assessed technology and its comparators (resource-use identification)?	Report the resource items taken into account for each technology, as well as the sources of information used when identifying these and the reasons for their inclusion. Providing the results in tabular form is recommended.	Critical	Partial	Yes	Health-care registers and databases, RCT's with resource utilization data, reimbursement databases, micro-level costing studies/ABC-costing studies. Data may be available from different registers, and sources e.g., on sick leave, sickness allowance, patient administration systems/ clinical databases, earlier studies, cost diaries.	A0011, A0017, A0024, A0025 B0007, B0008, B0009 D0010, D0014, D0023 F0012 G0001, G0003, G0004, G0005, G0006, G0007 H0003, H0010	A0017, A0024, A0025 B0007, B0008, B0009 D0010, D0023 G0001	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al. {57}; Husereau et al. {51}.
E0002	Resource utilization	What amounts of resources are used when delivering the assessed	Report the parameters required to estimate overall costs (E0009). Include the appropriate values, ranges, probability distributions as well as all references used. Providing the results in	Critical	Partial	Yes	Health-care registers and databases, RCT's with resource utilization data, reimbursement databases, micro-level costing studies/ABC-costing studies	E0001	E0001	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al.

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		technology and its comparators (resource-use measurement)?	tabular form is recommended. Report the approach(es) and data source(s) used to measure resource use associated with the technologies.							{57}; Husereau et al. {51}.
E0009	Resource utilization	What were the measured and/or estimated costs of the assessed technology and its comparator(s) (resource-use valuation)?	For each technology report mean values of estimated costs and, where possible, information concerning distributions surrounding these estimates. Cost estimates from different viewpoints can be reported here (e.g., patient, hospital, societal). In addition, reporting disease-stage-specific cost estimates and costs estimated using varied discount rates. Providing the results in tabular form is recommended. Report the approach(es) and data source(s) used to estimate the costs associated with the technologies.	Critical	Partial	Yes	Market prices, companies, hospital accounting or reimbursement systems, as well as micro level costing studies/ABC-costing studies, or other information on unit cost s.	E0001, E0002	E0001, E0002	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al. {57}; Husereau et al. {51}.
E0005	Measurement and estimation of outcomes	What is(are) the measured and/or estimated health-related outcome(s) of the assessed technology and its comparator(s)?	For each technology report mean values of estimated effects and, where possible, information concerning distributions surrounding these estimates. It is suggested that estimates are expressed in natural units first, whenever possible, before using them in alternative forms such as QALYs. Report the approach(es) and data source(s) used to estimate the outcomes associated with the technologies.	Critical	Partial	Yes	Estimation of the incremental or other effects can be based on information provided in the Clinical effectiveness domain (e.g., mortality data). Additional information collection may be needed (e.g. on health-related quality of life indices). The incremental effectiveness may result from an economic model, where inputs from the effectiveness domain are used.	A0004, A0005, A0006, A0009 C0001, C0002, C0004, C0006, C0008 D0001, D0002, D0003, D0005, D0006, D0007, D0011, D0012, D0013,D0029 F0003,	A0004 C0008 D0001, D0005, D0006, D0007, D0012, D0029	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al. {57}; Husereau et al. {51}. Williams {60}; Johannesson et al. {61}.

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
								F0010, F0011 H0100		
E0006	Examination of costs and outcomes	What are the estimated differences in costs and outcomes between the technology and its comparator(s) ?	For each technology report mean values of estimated costs and effects together. There are numerous ways of highlighting or comparing the differences in the costs and effects of the technologies under assessment, typically, one or more of the following outcomes or approaches are used when reporting the results of health-economic evaluations: - listing the cost and outcomes of each technology in tabular form - an incremental cost-effectiveness ratio (ICER) - an incremental cost effectiveness plane or efficiency frontier - the net monetary benefit (NMB) and/or net health benefit (NHB) Report the approach(es) and data source(s) used to estimate the of costs, outcomes, or economic evaluation(s) associated with the technologies.	Critical	None	Yes	Relevant sources of data and evidence are specified in the relevant issues under the domains Safety , Clinical effectiveness and Costs and economic evaluation (bringing together the information collected in assessment elements E0009 and E0005). For example, ICER estimates from a de novo economic model could be reported, synthesising inputs from the Safety , Clinical effectiveness and Costs and economic evaluation domains.	E0001, E0002, E0005, E0009	E0001, E0002, E0005, E0009	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al. {57}; Husereau et al. {51}. Briggs et al. {26}.; Glick et al. {29}; Johannesson et al. {61}.
E0010	Characterising uncertainty	What are the uncertainties surrounding the costs and economic evaluation(s) of the technology and its	The effects of uncertainty should be reported separately for parameter, structural and methodological uncertainty, whenever possible. For example: - deterministic sensitivity analysis in tabular form or using a Tornado diagram	Important	Partial	Yes	Relevant sources of evidence are specified under relevant issues under domains Safety and Clinical effectiveness , as well as from within the Costs and economic evaluation domain.	E0006	E0006	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al. {57}; Husereau et

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		comparator(s)?	- probabilistic sensitivity analysis, e.g., in the form of a CEAC - value-of-information analysis The methods used in the sensitivity analysis should be reported in detail here.							al. {51}. Bojke et al. {74}; NICE {69}; Briggs et al. {26}.
E0011	Characterising heterogeneity	To what extent can differences in costs, outcomes, or 'cost effectiveness' be explained by variations between any subgroups using the technology and its comparator(s)?	If applicable, describe differences in costs, outcomes, or cost effectiveness that can be explained, e.g., by variations between (pre-defined) subgroups of patients with different baseline characteristics or other observed variability in effects. Providing the results in tabular form is recommended, but graphical representation using, e.g., 'Forest' plots may also be useful. The methods used in any sub-group analysis should be reported in detail here.	Important	Partial	Yes	Relevant sources of evidence are specified under relevant issues under domains Safety and Clinical effectiveness , as well as from within the Costs and economic evaluation domain.	C0005, E0006 H0012	E0006	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al. {57}; Husereau et al. {51}. Sculpher et al. {56}; Cleemput et al. {57}
E0012	Validity of the model(s)	To what extent can the estimates of costs, outcomes, or economic evaluation(s) be considered as providing valid descriptions of the technology and its comparator(s)	It would be valuable to report any of the numerous ways of assessing to what extent the estimates for the technologies can be considered valid, For example: - How well the model predicts health effects - Whether model includes all aspects of resource use and costs considered important - Estimates of the potential direction and/or potential magnitude of bias	Important	Partial	Yes	Relevant sources of evidence are specified under relevant issues under domains Safety and Clinical effectiveness , as well as from within the Costs and economic evaluation domain.	E0001, E0002, E0005, E0009, E0010, E0011	E0001, E0002, E0005, E0009, E0010, E0011	Gold et al. {59}; Drummond et al. {1}; CADTH {18}; Kristensen and Sigmund {3}; Cleemput et al. {57}; Husereau et al. {51}. Eddy {38}

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		?	induced - An attempt to identify key factors that could compromise the validity of the model The process of validation and the types of validation addressed in the model should be reported here.							

6 Ethical analysis

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
F0100	Beneficence /nonmaleficence	What is the severity level of the condition that the technology is directed to?	Knowing the severity level of the condition the technology is directed to is relevant in the ethical analysis of the technology. Information about the severity level is also important to decision-makers when making decisions about whether or not to implement a technology.	Important	Complete	Yes	Literature search. Expert opinion		A0002 A0007 A0005 A0024 A0025	48
F0010	Beneficence /nonmaleficence	What are the known and estimated benefits and harms for patients when implementing or not implementing the technology?	Decisions concerning implementation of new technologies generally require careful consideration of the balance between benefits and harms. Examples of questions that can be asked are: Who is the right candidate for the technology? What is the balance between benefits and harms? For instance, is the technology estimated to improve health, health-related quality of life, quality of life and/or survival compared to alternative technologies? Can the technology harm individual patients, or any other stakeholder, in any way? How many	Critical	Partial	Yes	Information from other domains (links). Literature search. Expert opinion. Stakeholder hearing		D0001, D0002, D0029, H0001, H0004, H0005, H0006, C0001, C0005, A0010 D0017 D0027, D0028 D0031, D0024, D0030,	47

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			patients might face harm in order for the technology to have a benefit for one patient? What is the extent of these benefits and harms? What are the perceived benefits and harms of the technology in the eyes of the patients/users themselves? It might be useful to note that the patient is often the best judge of benefits and harms for themselves.						D1019	
F0011	Beneficence /nonmaleficence	What are the benefits and harms of the technology for other stakeholders (relatives, other patients, organisations, commercial entities, society, etc.)?	Can the technology have positive effects for other stakeholders? Can the technology harm any other stakeholders? Some technologies have the potential to unfold unwanted or harmful effects not only on the patients that the technology is directly applied to but also indirectly on other stakeholders. For example results of genetic tests may negatively interfere with the family planning and social life of not only the individual being tested but also of his or her relatives. Another example is how the caregivers' burden and well-being will be affected by the technology. Benefits and harms to individuals must be balanced with benefits and harms that can have impact on society as a whole (social utility, maximizing public health). These harmful effects may manifest in the physical, social, financial or even other domains of life. Changes in the availability of new, more effective technologies may significantly alter the requirements placed on the	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		D0029, H0001, H0002, C0020, C0040, A0006, E0006, D0017 I0008	1, 47

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			health care system. Is the symbolic value of the technology of any moral relevance? Another relevant question is how the assessed technology relates to more general challenges of modern medicine (over-diagnosis, medicalization)? Table 1 (link) in the process description can be used to describe benefits and harms.							
F0003	Beneficence /nonmaleficence	Are there any other hidden or unintended consequences of the technology and its applications for different stakeholders (patients/users, relatives, other patients, organisations, commercial entities, society etc.)?	The technology may be used for other indications (extended use) or other purposes, e.g., in combination with other technologies (unintended use). It may have side-effects in addition to those following from the intended use. Ethical analysis of the technology should consider not only the consequences of the formal intended use of the technology, but also the ethical consequences of unintended and extended use. If unintended consequences are not well-known, they should be speculated and elaborated upon. The intended purpose and uses of the technology should be evaluated against the likely uses and consequences of the technology in reality. The mode of delivery, the need of laboratory tests or clinical follow-up to ensure safe and effective dose, and way of delivery (at home, outpatient or in-patient) may have large impact on the health care processes, systems and on individuals. They may also change the	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		D0030, D0022, D0023, I0008, C0006	49, 50

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			concepts of disease and normality (e.g. change an untreatable cancer into a chronic disorder or changing the border values when the concept of normality also changes). New technologies tend to lead to new areas of inventions and give rise to new ethical questions (e.g. IVF and development of genetic testing has led to questions of preimplantation genetic diagnostics (PGD)). As pre-symptomatic screening tests have become available, the health care system has to be prepared to handle moral issues raised by true positive and false negative findings. The mode of delivery, the need of laboratory tests or clinical follow-up to ensure safe and effective dose, and way of delivery (at home, outpatient or in-patient) may have large impact on the health care processes, systems and on individuals. They may also change the concepts of disease and normality (e.g. change an untreatable cancer into a chronic disorder or changing the border values when the concept of normality also changes). Another relevant question is whether or not there will be a moral obligation related to the implementation, withdrawal, or use of the technology (e.g. check-ups or alternative procedures). Diagnostic technologies may also have effects on relatives. Not only genetic tests, but all							

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			diagnoses of hereditary disorders, also provide knowledge of relatives. Diagnostic information may also affect social relations (e.g. STD)".							
F0005	Autonomy	Is the technology used for patients/people that are especially vulnerable?	The right and justification to use the technology for persons who are vulnerable has to be clarified. Persons that are vulnerable could for example be pregnant women as to protect their unborn child, critically ill patients or individuals that have reduced decision making capacity (children, persons with cognitive disabilities or patients that due to their illness/state have limited decision making capacity). Who has the right to balance the benefit against possible harm in these situations? On what grounds can these decisions be made? Is the technology so valuable, as to justify its use on people who cannot give informed consent?	Critical	Complete	Yes	Literature search. Expert opinion. Stakeholder hearing		C0005	52
F0004	Autonomy	Does the implementation or use of the technology affect the patient´s capability and possibility to exercise autonomy?	Many technologies can alter a person´s self-determination. The technology may interfere with patients' right to autonomy directly or indirectly by influencing/subtracting the decisional capacity. However, patients have in most cases a right to autonomy, i.e. right to be self-governing agents. This means both the right to decide (not to) use/participate, and the right to receive relevant information. Drugs for sedation and surgical treatment of severely ill patients are examples where patient autonomy may be reduced. Technology may require users/patients to behave in a certain way (e.g. dietary restrictions for fecal blood test). In order	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		H0013	49, 52

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			to be able to decide autonomously, the user/receiver of the technology should understand all alternative treatments or different therapeutic paths following test results. They should be able to make informed consent at every step. The practical challenge with treatment technologies is that in order to be fully autonomous, the patient should understand not just direct risks of the treatment, but also all alternatives if side effects take place and how these can affect the living quality or choices (eg car driving, nutrition).							
F0006	Autonomy	Is there a need for any specific interventions or supportive actions concerning information in order to respect patient autonomy when the technology is used?	Is the common professional practice of discussing the technology with patients enough, or is special information needed to decide on this technology? Can the technology entail special challenges/risks that the patient/person needs to be informed of? Should the patient be explicitly informed, for example, that false positive results of a test may lead to unnecessary further investigations and treatments, sometimes with serious harms. An example is screening programmes for early identification of life-threatening situations that may have life-threatening side effects such as invasive surgery with risk of death. Technology used for off-label use may have unexpected severe side-effects (e.g. patients with comorbidities or children). The information should enable the user/receiver of the technology to understand the technology and its	Critical	Complete	Yes	. Expert opinion. Stakeholder hearing		H0013, H0007, H0008, C0008, B0014, I0002, I0036, C0005 C0001	51

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			associated risks/challenges. It should be in accordance to their personal values and intellectual capacity, thereby enabling users to decide accordingly. The patient should be explicitly informed, for example, that the treatment may have serious side effects, may have an effect on personality or lead to increased need of sleep or overweight. They should also be informed of that the mode of delivery or action may affect their daily life (eg. no car driving allowed, restricted travelling).							
F0007	Autonomy	Does the implementation or withdrawal of the technology challenge or change professional values, ethics or traditional roles?	Technologies may change the relationship between physician and patient, challenge professional autonomy or otherwise interfere with professional ethics and values. The patient-physician relationship is traditionally based on mutual trust, confidentiality and professional autonomy so that individual treatment decisions can be made in the best interest of the patient. Technologies that interfere with core values and principles of medical and professional ethics challenge the professional integrity of the physicians or other health care professionals (eg. screening for drug abuse when use is denied). Technologies that align with professional ethics are more likely to be implemented successfully. For example, people may ask for the technology for many reasons, while the professionals may see them as unnecessary and even potentially harmful (e.g. antibiotics, sleep medicine, antidepressants, whole body MRI scans).	Critical	Partial	Yes	Expert opinion		G0010	49, 53
F0008	Respect for persons	Does the implementation or use of the	Especially technologies that are applied for persons with reduced autonomy (children, mentally impaired, severely ill),	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing			49, 54

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		technology affect human dignity?	may violate a person's dignity i.e. challenge the idea that all human beings have intrinsic value, and should thus not be seen as means to others ends. Labelling people as result of use of the technology may also threaten their dignity. Some technologies may cause labelling healthy people as sick (eg PSA for prostate cancer) or otherwise less worthy, abnormal, less clean, etc. For instance labelling people as needing psychiatric medication for their behavioural difficulties may threaten their dignity. People with physical disabilities may be labelled by prenatal screening programmes, which imply that their handicap is an indication for abortion.							
F0009	Respect for persons	Does the implementation or use of the technology affect the user´s moral, religious or cultural integrity?	The technology can challenge integrity by preventing (or tempting to prevent) patients to live according to their moral convictions, values, preferences or commitments. It may also interfere with the coherent image or identity of the users´ selves. This is especially important to analyse for vulnerable patient groups. The technology may challenge religious, cultural or moral convictions or beliefs of some groups (e.g. pharmaceuticals produced from human blood given to cultural groups that will not tolerate blood transfusion, pharmaceuticals used for abortion in cultural groups that will not tolerate abortion and assisted reproductive technologies that have separated the concept of genetic,	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		H0011, H0013	49, 50

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			biological and social motherhood). The technology may change generally or locally accepted social arrangements by challenging traditional conceptions or social roles. For instance ADHD medication might challenge the integrity of people who value personality, and cochlear implants may be problematic for those who do not see deafness as a disability. Identifying the conceptions behind the beliefs and values may help put them in perspective, when considering the ethical consequences of use and the overall acceptability of the technology. When possible, considering other acceptable alternatives for the affected groups of users is important. Use of the technology can also be detrimental to integrity if it is associated with discouraging honesty or ethical conduct, e.g., systems that encourages users to lie about their health state in order to get better service/treatment.							
F0101	Respect for persons	Does the technology invade the sphere of privacy of the patient/user?	The sphere of privacy can be invaded both virtually and physically. Does the technology affect the population's possibility to have control over personal information? Is dissemination or gathering of information regarding the individual patient or the population justified? Is cooperation and sharing of information with professional groups outside the health services needed? Is the handling of personal information reasonable given the purpose of using	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		B0010, B0011, D0011, I0007, I0009, I0010, I0033	51

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			the technology? Is the technology more or less invasive than the alternatives, regarding the physical body and/or the spatial sphere? Is a violation of the privacy of the patient or population necessary and reasonable to achieve desired outcomes?							
F0012	Justice and Equity	How does implementation or withdrawal of the technology affect the distribution of health care resources?	Many technologies imply substantial costs, sometimes covered with resources from other areas. A new technology may require reallocation of human resources, funding and training. A large reallocation of resources may seriously jeopardize other patient groups (e.g. new technology that requires human resources in acute care or new diagnostic technology that uncovers a large pool of unmet needs for treatment). How this reallocation affects the existing health care system has to be studied. Who will gain and who will lose? Is the prioritization explicit or implicit? Diagnostic technologies sometimes acquire significant symbolic value (e.g. fetal ultrasound, PSA) that may create demands for tests that are not justified on health grounds.	Critical	Partial	Yes	Expert opinion.		G0007, E0001,E0002, E0009	49, 55, 56
F0013	Justice and Equity	How are technologies with similar ethical issues treated in the health care system?	Clearly presenting how technologies with similar ethical issues are treated in a health care system may help to adopt coherent and just health policies, either by applying past precedents to current cases, or showing that past cases need reconsideration. Similarity is to be defined individually for each technology. The idea is to concentrate only on the similarities relevant for solving the ethical problems found important for the current HTA project. The similar ethical problems can be related to similarities in the	Important	Partial	Yes	Literature search. Expert opinion			49

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			technology's medical, technological, economic, social, organisational or legal nature.							
H0012	Justice and Equity	Are there factors that could prevent a group or persons to participate?	Can the technology be applied in a way that gives equal access to those in equal need? How can this be guaranteed? Could potential discrimination or other inequalities (geographic, gender, ethnic, religious, and employment, insurance) prevent access? Potential inequalities and discrimination should be justified. Issues of access to a technology as well as labelling and potential discrimination of persons receiving and not receiving treatment should be considered. Are special groups discriminated?. Ethical and social issues have often been considered in academic articles and discussions in the HTA field, but they have rarely been translated into practice.	Critical	None	Yes	Implement the best available evidence about social restrictions, social pressure, social attitudes	SHARED with SOC domain H0012 Legal domain	G0009, G0101 A0012 I0011	See social domain
F0014	Legislation	Does the implementation or use of the technology affect the realisation of basic human rights?	The basic human rights are most notably declared in the United Nations Declaration of Human Rights. They are universal and consider the most important goods, protections and freedoms for mankind. For HTA, perhaps the most relevant are the rights to equality, non-discrimination, safety, adequate standard of living and health care.	Critical	Complete	Yes	Literature search. Law, rules and regulations. Expert opinion. Stakeholder hearing	SHARED with legal domain?	H0012	49, 57
F0016	Legislation	Can the use of the technology pose ethical challenges that have not been considered in	Is legislation and regulation to use the technology fair and adequate? Use of the technology may lead to ethical issues that make current regulations inadequate. Screening and diagnostic technologies are commonly differently regulated than treatments, especially medications. Ethical reflection is essential in order to	Important	None	No	Law, rules and regulations. Stakeholder hearing. Expert opinion	SHARED with legal domain?	B0010, B0011, I0011, I0009, I0036,, I0026, I0028 I0008, I0035	49, 58

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		the existing legislations and regulations?	assess what kind of legislation, regulation or amendments is needed (see also legal domain).							
F0017	Ethical consequences of the HTA	What are the ethical consequences of the choice of end-points, cut-off values and comparators/controls in the assessment?	Is there a risk that the chosen end points, cut-off values or comparators/controls may give a biased description of the results of the technology? Clinical effectiveness should ideally be directly related to the disease under treatment. This is not always fully possible so other endpoints may have to be used (e.g. surrogate markers for preventing a life-threatening disease). In addition, the technology may have several aims (e.g. those related to treating the disease and preventing secondary morbidity). The choice of cut-off values for sensitivity and specificity should be done considering the moral value of different results – for example, high specificity is required if false positives have serious consequences.	Critical	Partial	Yes	Other domains:, safety, effectiveness. Expert opinion, Stakeholder hearing		See methodological description in EFF and SAF B0018 D1004 D1005 D1006	49
F0102	Ethical consequences of the HTA	Does the economic evaluation of the technology contain any ethical problems?	It is important to consider whether there are any ethical problems related to the data or assumptions that have been used in the economic valuation. An example is whether or not indirect costs have been valued in a fair and adequate way.	Important	Partial	Yes	Literature search, Expert opinion		See methodological description in ECO	9, 51
F0103	Ethical consequences of the HTA	What are the ethical consequences of the	At what time of the lifetime of the technology is it assessed? Who will (not) get access to the new technology, as a result of the conclusions of the HTA?	Important	Partial	Yes	Expert opinion, Stakeholder hearing			49

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		assessment of the technology?	What are the consequences of assessing the technology with respect to prioritisation?							

7 Organisational aspects

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
G0001	Health delivery process	How does the technology affect the current work processes?	Current tasks and work processes should be described. This help to make a picture of the whole process as well as the continuity of care across professional and organisational boundaries. Who is doing what in the process? There are many actors at different levels (intra-organisational, inter-organisational and health care system level) in the process. Continuity should be ensured so that there will be no gaps between the steps of the process. It should be explained what kind of changes a new technology could have: it might replace or reduce some activities. This issue is about patient path way by the point of view of patient/participant. Patient path should be described step by step. This includes also the waiting times for diagnosis and/or treatment and waiting time for analysis of the technology. Preparations that patients/participants need to do before and after (e.g. diet before bariatric surgery) must be taken	Critical	Partial	Yes	Literature search, guidelines, annual reports and statistics, reports and own study (e.g. questionnaires and interviews of different actors) Literature search, guidelines, annual reports and statistics, reports and own study (e.g. questionnaires and interviews of different actors)	: A0013, A0014,A0024, B0004, B0005,C0063, D0020, D0021, D0023, F0001, F0007, I0002, I0010	A0007, A0023, A0011 Order of doing; to be answered prior to: E0001	{1, 14} {1, 14}

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			into account, as well as need for self/home monitoring. The implementation of a new diagnostic test can substantially increase (or decrease) number of patients needed to be treated, thus changing relations between different organizations and influencing the health care system as a whole.							
G0100	Health delivery process	What kind of patient/participant flow is associated with the new technology?	This issue is about patient path way by the point of view of patient/participant. Patient path should be described step by step. This includes also the waiting times for diagnosis and/or treatment and waiting time for analysis of the technology. Preparations that patients/participants need to do before and after (e.g. diet before bariatric surgery) must be taken into account, as well as need for self/home monitoring.	Critical	Partial	Yes	Literature search, guidelines, annual reports and statistics, reports and own study (e.g. questionnaires and interviews of different actors)		A0010, H0003 Order of doing; to be answered prior to: E0001	{1, 14}
G0002	Health delivery process	What kind of involvement has to be mobilized for patients/participants and important others?	This issue is about the role of patients/participants. A new technology may require distribution of tasks among the people involved in the treatment and care. Patients/participants and their important others may be more actively involved in own care and treatment – or tasks they used to carry out may be taken over by health professionals. Some diagnostic tests are used by patients at home and patients should be taught how to use them.	Important	None	No	Literature search, annual reports and statistics reports, hospital documents and own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants).	B0014, H0003, H0010, H0006, H0007, H0008, H0009, H0013	A0007 Order of doing; to be answered prior to: H0002	{14}
G0003	Health delivery process	What is the process ensuring proper education and training of the	New technology may require new kind of professionals or new tasks for existing personnel. This issue is about how the organisation can manage to ensure proper education. It had to take into account how training affects the	Critical	Partial	Yes	Literature search, guidelines, reports and documents of the hospital or hospital districts and own study: interview or questionnaires of different actors of the process.	A0013, A0014, B0012, C0063, D0023, E0001,	B0013 Order of doing; to be answered prior to: E0003	{1, 14, 26}

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		staff?	management and effectiveness. Implementing a technology can change the job and thus have influence on job satisfaction.					E0002, F0007, legal?		
G0004	Health delivery process	What kind of co-operation and communication of activities have to be mobilised?	Co-operation and communication is crucial for fluent patient pathway. Implementing a technology can demand new co-operation and communication in- and outside the organization, e.g. other hospitals, pharmacies and manufactures. Therefore structure of co-ordination is important. Also, interaction and communication with patients/participants and their important others could change. Adaptation of self/home monitoring needs close co-operation and fluent communication.	Important	Partial	Yes	Literature search, guidelines, reports and documents of hospital and hospital districts, guidelines, own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants).	B0014, B0015, C0063, D0023,H0010, H0007, H0008, H0009, H0013, I0002		{1, 14} {27}
G0012	Health delivery process	How is the quality assurance and monitoring system of the new technology organised?	A new technology usually have an effect on current quality assurance not only inside the organization but also outside in different health care levels. To assure the quality, a monitoring system with standards and indicators are needed. There could be variations how quality assurance and monitoring system has been implemented. It had to be taken into account who is responsible for quality assurance and for monitoring system and how follow up has been arranged. It had to take into account how quality assurance and monitoring system affects the management and effectiveness. There could be international, national, regional and/or (cross) organisational demands for quality assurance (e.g.	Important	Partial	Yes	Literature search, annual reports and statistics reports of hospitals and own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratories). Information from manufacturers. .	B0010, B0011, B0012, B0020, C0007, B0012, B0010, B0011, E0001, E0002,	B0020 Order of doing: to be answered prior to E0003	{14}

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			quality standards and monitoring) and for registration.							
G0005	Structure of health care system	How does de-centralisation or centralization requirements influence the implementation of the technology?	The setting (primary - secondary - tertiary care) can vary between different countries depending on the health care system. (De)centralisation could have some economical and qualitative benefits. Centralisation could make the technology more difficult to access. Usually, expensive technologies are centralised to tertiary care units with special educated staff.	Critical	Partial	Yes	Literature search, guidelines, reports and documents of hospital and hospital districts, health information databases (DRG etc.), own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants). Literature search, guidelines, reports and documents of hospital and hospital districts, health information databases (DRG etc.), own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants).		B0004, B0005, F0012	{1, 14, 26, 27}
G0101	Structure of health care system	What are the processes ensuring access to care of the new technology for patients/participants?	Access to care is often measured in terms of utilisation. There are different viewpoints: individual, population-specific and health system factors. Access to care is related to e.g. social, cultural, economic, organisational, relational or geographical factors. Access to care by wide definition includes availability, accessibility, accommodation, affordability and acceptability. This issue is related to the issue of acceptability of new technology (G0010)	Critical	Partial	Yes	Literature search, guidelines, reports and documents of hospital and hospital districts, health information databases (DRG etc.), own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants).		A0001, H0012	
G0006	Process-	What are the	Implementing the required changes in	Critical	Partial	Yes	Literature search, guidelines,		B0007,	{14}

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
	related costs	processes related to purchasing and setting up the new technology?	e.g. premises may be costly for organisations. High costs can influence the decision to introduce the new technology. There may be division of costs such that some organisation(s) is(are) responsible for the acquisition costs and others for the running costs. Investments by, at all stages of the process, should be taken into consideration.				reports and documents of hospitals and hospital districts and manufacturers (e.g. producer handbook), own study: questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital districts, laboratory		B0008, B0009, Order of doing: to be answered prior to E0001	
G0007	Process-related costs	What are the likely budget impacts of implementing the technologies being compared?	Whenever a technology is introduced, there will be an impact on health care budgets. Budget impact analysis attemps to examine the likely impact of introducing a technology on financial outlays from, e.g., the perspective of different payers. Different payers include: government-level insittutions; regions; municipalities; employers; insurance companies and patients/participants. The relevant perspective from which to estimate budget impact may change during different phases of the management process and incentives are connected to this issue. For example: What kind of incentives does the budget impact impose on different actors? How might this potentially impact on each organization? What is the estimated net financial (e.g. annual) cost of introducing the technology? Budget impact analysis provides data to inform an assessment of the affordability of a technology. It also provides a service planning tool to inform decisions about taking the technology into use.	Critical	None	Yes	Literature search, reports questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital districts, laboratory), information from manufacturers.	A0011, A0020, B0007, B0009,D0023,	Order of doing; to be answered prior to:E0001	{14, 28}
G0008	Management	What management problems and	The issue concerns the administrative / managerial questions of technology: management of resources (e.g.	Important	Partial	Yes	Literature search, guidelines, reports and documents of hospitals, own study:	A0011, A0012, A0015,		{28} {29}{14}

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		opportunities are attached to the technology?	investments), co-ordination (in relation to different levels and different steps of the process), establishment of objectives, monitoring and control (how quality assurance affects management or effectiveness), evaluation and sanctioning. Data/information management systems connected to each of these points have to take account. This issue includes also risk management and safety issues (e.g. safety of personnel).				questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory).	A0016, A0017, A0025, B0020, C0063, D0021, H0009, I0009		
G0009	Management	Who decides which people are eligible for the technology and on what basis?	Provide information on who are the key actors in deciding on the use of the technology. Do most important decisions take place on the national level (e.g. population screening) or for example by individual professionals (e.g. surgical method for a specific disease)? How is the decision made; are there some documented criteria? Information about the possible variations in the decision level and criteria has ethical implications. This issue is related to the issue of work processes (G0001)	Critical	Partial	Yes	Literature search, guidelines, documents of hospitals, own study: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory).	A0011 A0012 :B0016, D0021, F0012, I0012, H0012		Kristensen 2007 {24} {14}
G0010	Culture	How is the technology accepted?	Acceptance should be looked at by different perspectives: by organisation, by personnel and by patients/participants. Organisational view can be separated out intra-organisational (primary care), inter-organisational (secondary care) and health care system level. In all these actors/views acceptance could vary. Alternative ways to introduce a new	Important	Partial	Yes	Literature search, own study: questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital districts, screening units, laboratory, staff, participants).	F0001, F0003, F0007, H0006, H0007, H0011,H0012		{14}

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			technology into the organisation could influence problems e.g. resistance among staff and dysfunction of processes. Acceptability is related to access to care.							
G0011	Culture	How are the other interest groups taken into account in the planning / implementation of the technology?	It may be useful to know who are the possible stakeholders, as well as what kind of co-operation exists and what kind of interaction is needed. The stakeholders could be e.g. the pharmaceutical industry and companies offering technologies for screening, authorities (national / regional), registry, administrative parties, municipalities, policy makers / decision makers, staff groups, GPs/primary care physicians and patient organisation. One can also ask: Has the patient organisation taken part into the evaluation process? Has it been involved from the beginning (in the planning) or in the later stages for example as commentator?	Critical	None	Yes	Literature search, reports and documents of hospitals, own study: questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital districts, screening units, laboratory, manufacturers, registry, participants).	A0022, B0015, F0003, F0011,		{1, 14, 27}

8 Social aspects

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
H0100	Individual	What kind of changes do patients or citizens expect?	What do the patients expect to get out of the intervention before, during and after the intervention? Are there temporary changes that should be explained?	Critical	Partial	Yes		ETH		
H0001	Major life areas	Which social areas does the use of the technology influence?	Map the major life areas of the patient and the important others (family life, day care, school, work, leisure time, lifestyle, or other daily activities), where the technology is going to be used or where its use may have a direct or indirect	Critical	Partial	Yes	Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and			

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			influence. Map the major life areas of the patient and the important others (family life, day care, school, work, leisure time, lifestyle, or other daily activities), where the technology is going to be used or where its use may have a direct or indirect influence.				content experts can be consulted.			
H0002	Individual	Who are the important others that may be affected, in addition to the individual using the technology?	Describe who are the important other people that are involved in the use of technology in addition to the patients (parents, children, friends, people at work place etc) Describe who are the important other people that are involved in the use of technology in addition to the patients (parents, children, friends, people at work place etc)	Critical	Partial	Yes	Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and content experts can be consulted.	ETH and LEG		
H0003	Individual	What kind of support and resources are needed for the patient or citizen as the technology is introduced?	This issue is about any kind of support and resources (practical, physical, emotional, personal social, nurturing, financial etc.) that need to be mobilized, and organized - or might be released - in order for the patient to use the technology with satisfactory results. It covers all arrangements or adjustments that may be needed (e.g. alteration of special tasks, working time, adjustments in the physical environment, emotional support). This issue is about any kind of support and resources (practical, physical, emotional, personal social, nurturing, financial etc.) that need to be mobilized, and organized - or might be released - in order for the patient to use the technology with satisfactory results. It covers all arrangements or adjustments that may be needed in the major life areas (e.g. alteration of special tasks, working time, adjustments in the physical environment, emotional support).	Critical	Partial	Yes	Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and content experts can be consulted.	ORG Organisational		(35): environmental factors: support and relationships (chapter 3: e310-399); " activities and participation, chapter 6: d698, structural arrangements of patient's environment. (17, 15, 14) ICF(32) environmental factors: support and relationships (chapter 3: e310-399); activities and participation, chapter 6: d698, structural arrangements of patient's environment (10,

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
										12, 13)
H0004	Individual	What kind of changes may the use of the technology generate in the individual's role in the major life areas?	This issue is about the patient's social roles and ability to manage and maintain relations with other people in a socially appropriate manner in major life areas. This issue is about the patient's social roles and ability to manage and maintain relations with other people in a socially appropriate manner in major life areas.	Critical	Partial	Yes	Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and content experts can be consulted.	ETH and SAF Ethical. Effectiveness, safety		(35): activities and participation, interpersonal interactions and relationships (chapter 7, d710-779), community, social and civic life (chapter 9:d910-d999). (5, 7, 35, 36) ICF(32) activities and participation, interpersonal interactions and relationships (chapter 7, d710-779), community, social and civic life (chapter 9:d910-d999), (5, 7, 33, 34)
H0011	Major life areas	What kinds of reactions and consequences can the introduction of the technology cause at the overall societal level?	This issue is about the broader society. What social reactions can be expected for example from religious groups, specific patients and citizens organisations and associations and from any other stakeholder groups (social burden with accepted versus stigmatising diseases)? Are special (social) risk groups defined (ethnic, age etc.) and their possible reactions assessed?	Critical	Partial	Yes	Search for existing literature review, or collect primary studies and if possible conduct a litterateur review, or, if relevant data is not available, conduct a stakeholder analysis and a qualitative/quantitative primary study; if there's no time the systematic collection of opinion of some of the involved stakeholders and interest groups can be done. Patients, citizens and important others can be consulted.	Ethical, organizational and Legal domains		
H0006	Individual	How do patients, citizens and the important	This issue is about the patients and her important others' attitudes, perceptions, preferences, satisfaction and relations to the technology. This covers whether,	Critical	Partial	Yes	Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time	EFF Effectiveness		(35): body functions: mental functions (chapter 1:b110-b199),

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		others using the technology react and act upon the technology?	from a patient perspective, any positive or negative issues arise as a consequence of using the technology e.g. feelings of unity or empowerment and existential experiences (e.g. insecurity, worries, hope, anxiety, stigmatisation, social status, courage to face life, satisfaction, changes in self-conception). This issue is about the patients and her important others' attitudes, perceptions, preferences, satisfaction and relations to the technology. This covers whether, from a patient perspective, any positive or negative issues arise as a consequence of using the technology e.g. feelings of unity or empowerment and existential experiences (e.g. insecurity, worries, hope, anxiety, stigmatisation, person's value as a human being or social status, courage to face life, satisfaction, changes in self-conception).				for primary study, the opinion of health care professionals and content experts can be consulted.			environmental factors: attitudes (chapter 4:, e410-499), (3) ICF(32) body functions: mental functions (chapter 1:b110-b199) environmental factors: attitudes (chapter 4:, e410-499) , (3)
H0012	Individual	Are there factors that could prevent a group or persons to participate?	Can the technology be applied in a way that gives equal access to those in equal need? How can this be guaranteed? Could potential discrimination or other inequalities (geographic, gender, ethnic, religious, and employment, insurance) prevent access? Potential inequalities and discrimination should be justified. Issues of access to a technology as well as labelling and potential discrimination of persons receiving and not receiving treatment should be considered. Are special groups discriminated?. Ethical and social issues have often been considered in academic articles and discussions in the HTA field, but they have rarely been translated into practice.	Critical	None	Yes	Implement the best available evidence about social restrictions, social pressure, social attitudes	SHARED with SOC domain H0012 Legal domain	G0009, G0101 A0012 I0011	See social domain

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
H0007	Information exchange	What is the knowledge and understanding of the technology in patients and citizens?	This issue explores the patient's and important others' understanding of the technology in order to describe and decide what guidance and help (e.g. patient information leaflets, counselling processes, need of follow up consultation or help from other professionals) they need before, during and after the use of the technology. What kind of access do patients' and significant others' hav eto ask questions? How do they receive answers? How is information provided and received? This issue explores the patient's and important others' understanding of the technology in order to describe and decide what guidance and help (e.g. patient information leaflets, counselling processes, need of follow up consultation or help from other professionals) they need before, during and after the use of the technology.	Critical	Partial	Yes	Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and content experts can be consulted.	CUR and SAF Current use. Safety		
H0009	Major life areas	What influences patients' or citizens' decisions to use the technology?	What kind of societal influences lead patients to decide to participate? How do the provisional perceptions about the outcome influence the use of the technology This issue clarifies the possible implications from the patient's perspective to decision making e.g. limitations (dependent, passive user) and possibilities (empowered, active user) as a consequence of using the technology.	Critical	Partial	Yes	Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and content experts can be consulted.	ETH Organisatio nal. Ethical		
H0013	Information exchange	What are the social obstacles or prospects in the communicatio	E.g. limitations to decision making in participating or using the technology (dependent, passive user), and possibilities (empowered, active user)..	Critical	Partial	Yes	Search for existing literature review, or collect primary studies and if possible conduct a litterateur review,or, if relevant data is not available, conduct a primary study; if there's no time	Organisatio nal and Ethical Domains		

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		n about the technology?					for primary study, the opinion of health care professionals, patients, citizens, or important others can be consulted.			

9 Legal aspects

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
I0015	Authorisation and safety	Has the technology national/EU level authorisation (marketing authorisation, registration, certification of safety, monitoring, qualification control, quality control)?	Patient safety as expressed in product safety is one domain of health care technology assessment which clearly falls under the mandate of the European Union	Critical	Complete	Yes		Safety aspects		
I0019	Ownership and liability	Does the technology infringe some intellectual property right?	Issues in this topic are to be considered by the health care unit when considering the acquisition of a new technology. The wording of acquisition contract may affect liability sharing between the manufacturer and health care unit.	Important	Complete	Yes	Manufacturer, patent data bases, EPO Web site			European patent convention (EPC), Directive 98/44/EC, national legislation
I0002	Autonomy of the patient	Is the voluntary participation of patients guaranteed properly?	It is important to provide information on the (evermore complex) technologies in such a manner that the patient can truly understand it.	Critical	Partial	Yes	Explanatory report to Biomedicine convention			Biomedicince Convention Art 5
I0003	Autonomy of the patient	Are there relevant optional	The concept of informed consent includes also the possibility to consider other therapeutic options, if these are available.	Critical	Partial	Yes	Explanatory report to Biomedicine convention			Biomed conv Art 5

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		technologies that future patients should be allowed to consider?								
I0004	Autonomy of the patient	Is it possible to give future patients enough time to consider their decisions?	It is usually advised that the patient is given some time to think over the treatment decision, especially if the decision involves assimilating complex technical information or a tough weighing of risks and benefits of the procedure. It should be assessed beforehand if a given technology allows such time for consideration.	Important	Partial	Yes				
I0005	Autonomy of the patient	Is it possible to obtain an advance directive on the use of the technology?	If it is expected that the technology may be used in an emergency situation in the future it is advised that the patient is consulted beforehand and her opinion is recorded to the medical file as an advance directive on the use of a given technology.	Important	None	No				
I0007	Privacy of the patient	Does the use of the technology produce some additional (i.e. diagnostically or therapeutically irrelevant) information on the patient?	The protection of sensitive personal data is secured at the EU level. Privacy protection is a modern expression of the ancient ethical principle of confidentiality in doctor-patient relationship. The use of computerised patient record databases and modern genetic diagnostics means further challenges to this principle.	Critical	Complete	Yes	Z vs. Finland (ECHR February 25, 1997); M.S. vs. Sweden (ECHR August 28, 1997); national legislation; legal literature	Ethical aspects		Directive 95/46/EC, EU FR Charter Art 8, Biomedicine Convention Art 10, CM Recommendation R (97) 5
I0008	Privacy of the patient	Do laws/ binding rules require informing relatives about the	The results of a given diagnostic technology may indicate that the relatives of a patient may have a medical condition that would need to be addressed.The issue is on what conditions (if any) can the privacy of the original patient be	Important	Partial	Yes				

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		results?	broken in order to inform the relatives of their situation.							
I0009	Privacy of the patient	Do laws/ binding rules require appropriate measures for securing patient data?	At the era of computer-based patient records it is crucial that the health care unit has taken appropriate measures to secure the patient databases. Negligence may lead to liability.	Important	None	No		Organisational aspects		Directive 95/46/EC; Convention on Human Rights and Biomedicine Art 10,
I0010	Privacy of the patient	What levels of access to which kind of patient information exist in the chain of care?	During the therapeutic process many people may either need to get access or semi-accidentally get access to the personal medical data of patients. The delicacy of the information depends on the technology in question. Health care unit must be organised so that it minimises the number of people having access to patient data. Also other measures to minimise the risk of information leakage from health care unit must be taken.	Optional	None	No		Organisational aspects		
I0033	Privacy of the patient	Does the use of the technology produce such information on the patient that is not directly relevant to the current disease/condition?	Modern biomedicine may produce (genetic) information from the relatives of the patient as well as on patient herself. If this can be foreseen, appropriate procedures, according with the existing legislation, must be thought through beforehand: is the information to be revealed to or withheld from the relatives in question.	Critical	None	Yes				
I0011	Equality in health care	Do laws/ binding rules require appropriate processes or resources to	This topic operates both at national and international level. In general, equality in health care is spoken out in the EU Charter of Fundamental Rights and it is also one of the central principles of the Biomedicine Convention. In many	Critical	Partial	Yes		Social domain		EU FR Charter Art 35, Biomedicine Convention Article 3, CM RecommendationR (2006) 18

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
		guarantee equal access to the technology?	Constitutions equality of citizens covers also access to health care.							
I0012	Equality in health care	Is the technology subsidized by the society?	Governmental interventions or the lack of them may affect to the expected number of patients.	Important	None	No		Organisational and Costs Domains		Charter of Fundamental Rights of the European Union (2000/C 364/01). Art 35
I0013	Equality in health care	Is there a wide variation in the acceptability of the technology across Europe?	Varying legal regimes may lead to health-care tourism across the borders, especially if the technology in question is controversial.	Critical	Complete	Yes	Europe-wide legal comparison	Social domain		
I0014	Equality in health care	Is health-care tourism expected from/to other European countries?	Varying legal regimes may lead to health-care tourism across the borders.	Important	Complete	Yes	C-158/96 (ECJ), C-372/04 (ECJ), Europe-wide legal comparison	Social domain		
I0016	Authorisation & safety	Does the technology need to be listed in a national/EU register?	A European database of medical devices (EUDAMED) is under construction.	Important	Partial	Yes		Safety aspects		
I0017	Authorisation & safety	Does the technology fulfil product safety requirements?	The implication of findings in the safety domain should be discussed against the relevant European or national legal frameworks to ensure patient safety from using the technology:	Critical	Complete	Yes		Safety aspects		Directive 93/42/EEC, Directive 95/2001/EC
I0018	Authorisation & safety	Does the technology fulfil tissue safety requirements?	Many novel health technologies may utilise human cells or tissue (so called advanced therapy medicinal products). These products must fulfil the safety requirements issued by EC Directive	Critical	Complete	Yes	COM 567 (2005) final	Safety aspects		Directive 2004/23/EC

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
			2004/23/EC.							
I0020	Ownership & liability	Does the introduction of the technology presume some additional licensing fees to be paid?	As novel technologies build up on existing knowledge, the use of the technology may involve the payment of some additional fees to additional patent holders etc. In principle, the manufacturer should be able to clarify this to the health care unit/health care system in question.	Important	Partial	Yes	Manufacturer, patent data bases			
I0021	Ownership & liability	What are the width, depth and length of the manufacturers guarantee?	The terms of the manufacturers guarantee are of importance to the health care unit as well as to the society's health care sector when considering whether it is economically and/or liabilitywise advantageous to introduce the technology or not.	Critical	Complete	Yes	Manufacturer			
I0022	Ownership & liability	Is the user guide of the technology comprehensive enough?	The wording and clarity of the user guide of the technology can have legal effects on the liability issues in case the technology is not working as expected.	Critical	Complete	Yes	Manufacturer			
I0023	Regulation of the market	Is the technology subject to price control?	As health care technology is essential to everyone at some point in their lives, its pricing may be regulated.	Critical	Partial	Yes	C-317/05 (ECJ), C-283/03 (ECJ)			Directive 1989/105/EEC
I0024	Regulation of the market	Is the technology subject to acquisition regulation?	Expensive technology is subject to acquisition regulation.	Critical	Partial	Yes				Directive 2004/18/EC
I0025	Regulation of the market	Is the marketing of the technology to the patients restricted?	As health care technology is essential to everyone at some point in their lives, the way by which it can be marketed to consumers may be regulated.	Critical	Partial	Yes	T-179/00 (ECJ)			Directive 1989/105/EEC, directive 1992/27/EEC
I0026	Legal regulation of	Is the technology so	Modern biomedical sciences produce novel technologies which may not always	Critical	None	Yes				

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
	novel/experimental techniques	novel existing legislation was not designed to cover its regulation?	be unambiguously covered by existing provisions.							
I0027	Legal regulation of novel/experimental techniques	How the liability issues are solved according to existing legislation?	If the current law does not provide a straightforward answer to the liability issues it may be advisible to consult a legal expert on the interpretation of the existing provisions with regard to the technology in question. This way the health care unit can prepare itself for the possible future legal proceedings.	Critical	None	Yes				
I0028	Legal regulation of novel/experimental techniques	Are new legislative measures needed?	If the existing legislation is not satisfactory the introduction of a novel technology may require new legislative measures. At the level of a health care unit this may slow down the introduction, whereas at the level of the society it implies a need to use resources for preparing new laws.	Important	None	No				
I0029	Legal regulation of novel/experimental techniques	Is the voluntary participation of patients guaranteed properly?	Use of experimental technologies may not compromise patient safety. Patients must not be pressured into such treatments.	Critical	None	Yes				Biomedicine Convention Article 16
I0030	End-user	Who is the intended end-user of the technology?	Different requirements may apply depending on the answer. E.g. consumer Information, CE-marks, easiness of use, exactness of the results etc. are to be evaluated differently if the technology is intended to laymen's use.	Critical	Complete	Yes	In vitro diag. directive 98/79/EC; Council of Europe Gen testing protocol 2008			Directive 98/79/EC; Council of Europe Gen testing protocol 2008
I0031	End-user	Is the use of the technology limited in legislation?	Some countries may have restricted the use of some diagnostic technologies.	Critical	None	Yes		Ethical aspects		

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations	References
I0032	End-user	Is the health care personnel using the technology according the professional standards?	Health care personnel are obliged to follow professional standards and apply methods that are generally approved. When considering their professional liability towards patients it is very important that they know the limits and possibilities of diagnostical methods.	Critical	Partial	Yes		Ethical aspects		