Assessment element tables for HTA Core Model Application for Diagnostic Technologies (3.0)

Contents

1 Health Problem and Current Use of the Technology

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
A0007	Target Population	What is the target population in this assessment?	Relevant for all assessments: Both safety and effectiveness depend largely on the subpopulation towards which the intervention is targeted. The technology may be used on all patients with the condition, or only on those in the early stages, or at a specific level of severity, or on those at moderate risk of having the condition. Personalised medicine divides the target population into even smaller units when targeting the intervention onto specific subgroups, based on e.g. genetic profile.	Critical	None	Yes	Use the target population defined in the scope of the project for assessment, and consider adding further details and description of who defined the selected subgroups, and why. Point out, e.g., whether certain populations should be excluded from the analysis Sources: HTAs, guidelines, reviews, developers/manufacturers. Method: A descriptive summary.		
A0023	Target Population	How many people belong to the target population?	This information can be used to provide an idea of the resource requirements 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.		
A0002	Target Condition	What is the disease or	Indicate the target condition used in the	Critical	Complete	Yes	Use the target		

		health condition in the scope of this assessment?	project scope and consider providing a more comprehensive description of it.				condition and ICD codes defined in the scope of the project, and consider possibly adding details such as the 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 condition are defined in separate assessment elements and should not be repeated here: risk factors (A0003), natural course (A0004), symptoms (A0005), and burden of disease for the society (A0006). Sources: text books, HTAs, guidelines, epidemiological reviews or studies, WHO documents, disease registers. Method: A descriptive summary.		

A0003	Target Condition	What are the known risk factors for the disease or health condition?	Describing risk factors is especially important when the factors 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 being assessed. The risk factors for acquiring the condition, and the risk factors for relapses or a worsening of the condition should be reported here separately. The prevalence of various risk factors might differ depending on various geographic areas and 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.		
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 left untreated. This information is relevant for appraising the overall value of the technology. A technology targeted at curing a life-threatening condition – for example, a bypass surgery for severe coronary artery disease – has a different significance than a technology intended to alleviate the symptoms of a self-limiting condition, such as medications to alleviate the symptoms of common cold. Understanding the natural course of a disease may also guide the assessment of the predicted value or effectiveness of the technology, as technologies may work differently at a disease's different stages or grades of	Critical	Complete	Yes	Sources: text books, HTAs, guidelines, epidemiological reviews or studies. Method: A descriptive summary.		

			severity; there may also be a relationship between earlier intervention and a better prognosis. This element should also provide information on the time delay between the onset of disease and the symptoms or other findings which eventually trigger the need for diagnostics and care.						
A0005	Target Condition	What are the symptoms and the burden of disease or health condition for the patient?	Describe the patient's relevant symptoms before intervention with the technology, their severity, their urgency and whether they are persistent, intermittent, or undulating, taking into account different stages of the disease. Patients' perceptions of the burden of the disease are not always in line with the clinical seriousness of the disease or its societal burden. For example, back pain is rarely caused by a life-threatening disease, but it can still very negatively affect patients' quality of life and ability to work. 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. Knowing the severity and/or urgency 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	Critical	Complete	Yes	Sources: text books, HTAs, quality of life studies, qualitative patient perception studies. Method: A descriptive summary.		

			making decisions about whether or not to implement a technology.						
A0006	Target Condition	What are the consequences of the disease or health condition for the society?	Describe consequences and burden of the disease or health condition, by providing information on prevalence or incidence of the disease being prevented/treated with the technology.	Critical	Partial	Yes	Methods to use may include disease-specific mortality and disability, life years lost and/or disability-adjusted life years (DALYs), quality of life (QALYs). 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		
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) unaffected. The application of the diagnostic technology may target only one aspect of the burden of disease, e.g. disability, but not mortality. Or, on the other hand, it can target mortality but not symptoms.	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	

A0018	Current Management of the Condition	What are the other typical or common alternatives to the current technology?	Provide an overview of alternatives to using the technology under assessment. The focus should primarily be on those alternatives used within professional health care delivery. Consider also including technologies that people may commonly seek or use, even if these would not commonly be 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; A0025	
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 among differently diagnosed populations. A sensitive test tends to have low specificity, resulting in some people, who do not have the condition, to be 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.		
A0025	Current Manageme	How is the disease or	It is important to describe whether the	Critical	Partial	Yes	Provide an overview of	A0018;	

	nt of the Condition	health condition currently managed according to published guidelines and in practice?	technology is an add-on or a replacement for the existing management options, and what the other evidence-based alternatives are. When considering alternatives, note that element A0018 focuses on the alternatives and you can refer to it here. Are there differences in the treatment of diseases at their various stages? Identify practice variations resulting from differences in the forms, stages or severity of the disease. This may be useful in understanding the proper place of technology in the health care delivery process. Different stages of the disease may call for different therapeutic procedures (for example, aortic insufficiency is first treated with medication, but at a certain point of cardiac structural changes an operation is preferred). Identification of practice variations may imply differences in the quality of health care. Deviation from evidence-based guidelines may suggest over/under-use of the technology.				treatment alternatives, including also the technology/ies in this assessment. Likewise, diagnostic or monitoring methods used for various diseases may vary depending on the stage of disease. Clinical guidelines, recommendations 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 management pathways.	G0008, G0001	

A0001	Utilisation	For which health conditions and populations, and for what purposes is the technology used?	Include all relevant conditions and populations for which the technology has been proposed. This question is especially relevant when there are (1) multiple potential target conditions and populations for which the technology is used, or (2) multiple intended uses, both those (officially) indicated as well as others. There may also be differing views about the appropriate use of the technology that are essential to highlight. Describe the following: 1. Differences in the use of the technology for 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 are also used for first-line treatment. 2. Specific group(s) of patients on which the technology is used within the present assessment should be provided. 3. Aims of the technology (in terms of benefits to the target population).	Critical	Complete	Yes	Method: A descriptive summary. Sources: HTAs, guidelines, reviews, clinician consultation, developers/manufacturers.		

A0011	Utilisation	How much are the technologies utilised?	Provide national estimates for current and future utilisation rates, in the indication under assessment, for both the technology under assessment and its comparators. Variations in utilisation reflect market access, sales figures, actual usage on the hospital level, and adherence to the use of the technology by both professionals and patients. Data on current and previous utilisation reflects the phase that the technology is in (experimental, emerging, established or obsolete). This also has implications for the availability of evidence and the level of uncertainties.	Critical	None	Yes	National statistics, surveys, technology and procedure registers, disease management studies, utilisation studies, manufacturer sales data	G0009, G0010	
A0012	Utilisation	What kind of variations in use are there across countries/regions/settings?	This information can be useful for decision-makers in understanding regional variations in their own country, as well as understanding the situation in comparison to 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, discharge databases, reimbursement claims database).	G0009, G0010, G0007, G0008	
G0009	Utilisation	Who decides which people are eligible	Provide information on the key actors who decide on the use of the	Critical	Partial	Yes	Literature search, guidelines, documents	A0011, A0012;	

		for the technology and on what basis?	technology. Do most important decisions take place on the national level (e.g. population screening) or are they, for example, made 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 on the decision level and decision criteria has ethical implications. This issue may be especially important in the context of rare diseases. This issue is related to the issue of work processes (G0001).				of hospitals, own research: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory).	B0004, B0016; D0021; I0012; H0012, F0012; G0001	
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 in 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.		
A0020	Regulatory Status	For which indications has the	There are both international and national market authorisation systems.	Critical	Complete	Yes	CE-Approval, EMA, FDA, national	I0015;	

		technology received marketing authorisation or CE marking?	There are established systems for pharmaceuticals, but less so for devices and procedures. An overview of the authorisation systems status with regard to key processes, e.g. CE marking or EMA/FDA approval, is recommended. Information on national data and an analysis of possible discrepancies can also be highly useful. Imaging devices may require approval. Substances needed for obtaining images (e.g. radiotracers) may also require additional approval. In some cases, the approval for primary screening is different to that for clinical use (FDA recently licensed tests explicitly for screening), but approval is in most cases obtained for diagnostic use and the test is proposed for screening without any other formal approval.				authorities. Manufacturers should be contacted in order to identify which steps have they taken/ are they planning to take concerning market approval.	B0002	
A0021	Regulatory Status	What is the reimbursement status of the technology?	List information on national reimbursement status from different countries for the technology as well as the comparators, including key dates and anticipated licensing timeframe. Notice that reimbursement status may differ for different purposes, e.g., treatment vs. prevention. Information on full coverage, co-payments, coverage under special circumstances/conditional coverage is useful.	Important	Complete	Yes	Appendix 1 of REA model: List of websites of national agencies with information on reimbursement EVIDENT database.	I0012; B0002	

2 Description and technical characteristics of technology

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
B0001	Features of the technology	What is this technology and the comparator(s)?	This is relevant for all assessments. Use the descriptions of the technology and comparator(s) defined in that scope and elaborate them in more detail. The technology may include a single device, a questionnaire, imaging or a sequence of technologies. The HTA may address one or several similar technologies. Separately describe the technology and the comparator. The description should include the type of device, technique, procedure or therapy; its biological rationale and mechanism of action; there should also be a description of how the technology differs from its predecessors, and of 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	
B0002	Features of the technology	What is the claimed benefit of the technology in relation to the comparators?	This issue is especially relevant for new technologies with uncertain expectations and claims of benefit. Describe the following aspects: • How is it expected to be an improvement over previous/existing	Important	Complete	Yes	Manufacturers´ sites, HTAs, effectiveness studies, clinical experts, published literature including reviews, introduction sections of research articles, grey literature,	A0001, A0009; C0008	

			technologies used for the same health problem? What are the claimed objectives? (e.g. increased safety, health benefit, accuracy or patient compliance) • Is the technology intended to replace or to supplement existing technologies. • Is the technology licensed as a mono-intervention, or in addition to current 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.				hand-searches and conference proceedings, consulting clinical professionals, lay journals and websites.		
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 of technologies that are at an earlier stage in their development, as during that time the evidence base may change rapidly. It is also important to establish whether new versions of the technology, which	Critical	Partial	Yes	Manufacturers´ sites and effectiveness studies, HTAs, guidelines, published literature including reviews, textbooks, introduction sections of research articles, grey literature, hand-	A0020, A0021, A0011, A0019, A0020; F0001	

			include substantial improvements, are expected in the near future. It is useful for end users 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 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				searches and conference proceedings.		

			or produces incidental findings that can have consequences relevant to EFF, SAF, ORG, SOC and ETH?						
B0004	Features of the technology	Who administers the technology and the comparators and in what context and level of care are they provided?	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 caregivers, 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? Describe the level of care in which the technology is used: self-care, primary care, secondary and/or tertiary care; furthermore, If used in secondary or tertiary care, describe whether it is intended to be used in the outpatient or inpatient setting. The technology's role in the management pathway can be a replacement, an add-on, or for triage	Critical	Partial	Yes	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; G0001, G0005	
B0018	Features of the	Are reference values or cut-	Are conflicting/varying definitions of an	Important	Partial	Yes	Manufacturers´ sites,		

	technology	off points clearly established?	abnormal finding likely to affect the interpretation of the results? (If so, please describe them.)				published literature including reviews, textbooks, handbooks, introduction sections of research articles, interviews with specialists, as well as grey literature, hand-searches and conference proceedings.		
A0020	Regulatory Status	For which indications has the technology received marketing authorisation or CE marking?	There are both international and national market authorisation systems. There are established systems for pharmaceuticals, but less so for devices and procedures. An overview of the authorisation systems status with regard to key processes, e.g. CE marking or EMA/FDA approval, is recommended. Information on national data and an analysis of possible discrepancies can also be highly useful. Imaging devices may require approval. Substances needed for obtaining images (e.g. radiotracers) may also require additional approval. In some cases, the approval for primary screening is different to that for clinical use (FDA recently licensed tests explicitly for screening), but approval is in most cases obtained for diagnostic use and the test is proposed for screening without any other formal	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	

			approval.						
A0021	Regulatory Status	What is the reimbursement status of the technology?	List information on national reimbursement status from different countries for the technology as well as the comparators, including key dates and anticipated licensing timeframe. Notice that reimbursement status may differ for different purposes, e.g., treatment vs. prevention. Information on full coverage, co-payments, coverage under special circumstances/conditional coverage is useful.	Important	Complete	Yes	Appendix 1 of REA model: List of websites of national agencies with information on reimbursement EVIDENT database.	I0012; B0002	
B0007	Investments and tools required to use the technology	What material investments are needed to use the technology?	These can include devices, machinery, computer programs, etc. – those parts of the technology that need to be purchased (and often installed) by an organisation in order for the technology to be used. Includes the need for back-up investment to cover malfunctions in use.	Important	Partial	Yes	Manufacturers´ sites, published literature including reviews, textbooks, handbooks, 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.	E0001, E0002; G0006, G0003	
B0008	Investments and tools required to use the	What kind of special premises are needed to	Many technologies require purpose-built premises, such as radiation-secured areas, Faraday cages,	Important	Partial	Yes	User information from manufacturer and market approval		

	technology	use the technology and the comparator(s)?	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. Clearly describe the necessary facilities, rather than just using general statements (e.g. to be used in hospitals only).				authority. HTAs, applicability studies, interviews with clinical experts and hospital managers. National or local judgement can be also used.		
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 for identifying patients eligible for treatment.	Important	Partial	Yes	Information from manufacturer, HTAs, applicability studies, interviews with clinical professionals and hospital manager, user information. National or local judgement can be also used.	E0001, E0002; G0006	
B0010	Investments and tools required to use the technology	What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?	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 outpatient use, test results, review period, and health outcomes. In case of new technologies, consult	Important	Partial	Yes	Sources: Local authorities and legislation, administrative staff, clinical professionals, HTAs, National or local judgement.	G0008, G0003	

			EVIDENT database. Describe the general importance of having a registry for monitoring the use of this particular technology and the comparator is also needed. 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? National examples should be provided.						
B0012	Training and information needed to use the technology	What kind of requirements in terms 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 making clinical decisions and (3) taking care of service and maintenance. Describe the type of training materials (writing and/or translation, other adaptation) needed, and the characteristics of the personal training (individual and/or group sessions, number and length of sessions, number and qualifications of trainers)? Are regular or frequent standardisation or quality checks required (e.g. CME points)? Provide an estimate of the extent to which 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 judgment can be used.	G0003; C0020, C0062, C0063; E0001, E0002; G0006	
B0013	Training and	What kinds of skills and	Describe the type of training materials	Important	Partial	Yes	Manufacturer,	G0003;	

	information needed to use the technology	training characteristics and information are needed for the personnel/caregivers using this technology?	(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). If the technology requires a specific skill that is developed while using the technology over a period of time (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 of the extent to which the training and quality assurance measures may affect the efficacy and safety of the technology.				effectiveness studies, observational studies, applicability studies, clinical experts, user information, HTA-reports. National or local judgement.	C0020, C0062, C0063; I0008; F0006	
B0014	Training and information needed to use the technology	What kind of training resources and information should be provided to the patient who uses the technology, or for his family?	Describe the type of training materials that should be provided (writing and/or translation, other adaptation), by whom they should be provided, and the characteristics of the personal training (individual and/or group sessions, number and length of sessions, number and qualifications of trainers) and if an informed consent regarding this type of training 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	C0008, C0003, C0005, C0007, C0062; F0004, F0006; G0004; H0003, H0007, H0008; I0002	
B0015	Training and	What information	Describe what type of information	Important	Partial	Yes	Manufacturer data,	F0005,	

	information needed to use the technology	about the technology should be provided to patients outside the target group and to the general public?	materials that should be provided (writing and/or translation, other adaptation), and whether informed consent for this type of training participation is required.				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	F0011; G0004; H0002, H0007, H0008; I0002, I0008	
A0022	Other	Who manufactures the technology?	Please provide information on national, European and international level about the manufacturer of this technology.	Important	Partial	Yes	Manufacturers´ information, clinical guidelines, legislation, HTAs, approving authority National or local judgement.		I0037

3 Safety

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
C0008	Patient safety	How safe is the technology in relation to the comparator(s)?	Identify and describe the direct harms of the use and the administration of the technology and the comparator(s). 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 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. User-dependent harms are described in C0007. Harms are identified in placebo-controlled trials, observational studies, and in registries. It is important to refer to the source and report identified harms separately. Report harms per indication or target population. Categorise the identified harms 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 each harm's occurrence s usually presented in comparison with placebo or no treatment, as percentages or risk ratios. Finally, the harms should be	Critical	Partial	Yes	Placebo controlled trials, observational research, FDA database, safety monitoring databases, observational research, registers, statistics registers, statistics, research articles, manufacturers' product data sheets. Other HTA reports or systematic reviews of main comparators. Method: Systematic review. Results should be presented by risk level (i.e. the product of severity and frequency of harm).	B0001, A0018; D0009, D0003; A0001, A0007	B0001; A0018, A0001, A0007

			grouped by their severity and frequency, and ordered in such a way that the severe and/or frequent harms are presented first. If there are many different harms reported in the literature, focus on reporting the most serious and the most frequent ones.						
C0002	Patient safety	Are the harms related to dosage or frequency of applying the technology?	Include information on whether safe use of the technology is sensitive to even small changes in dosage, 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.	A0025; B0001	A0025; B0001
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 evidence of safety, and in technologies with steep learning curves. Describe how the safety profile of the technology varies between different generations, approved versions or products, and whether there is 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.	D0001, D0008, D0009; B0004, B0001	B0004, B0001
C0005	Patient safety	What are the susceptible patient groups that are more	Typically, these are people with comorbidities and co-medication, pregnancy, intolerances, or specific genetic profiles, elderly people,	Important	Complete	Yes	HTAs, guidelines, market access authorities, manufacturers' product	D0008, D0009; B0016,	B0016, B0001

		likely to be harmed through the use of the technology?	children and immunosuppressed patients. Report any relevant contra-indications or interactions with other technologies.				information, label warnings, safety monitoring databases. Method: Descriptive summary.	B0001	
C0006	Patient safety	What are the consequences of false positive, false negative and incidental findings generated by using the technology from the viewpoint of patient safety?	Describe the consequences of false positive, false negative and incidental findings generated by using the technology. False negative test results (Type II error) incorrectly identify sick people as healthy with the possible consequence of incorrectly rejected or delayed treatment. The volume of false negative test results can be estimated to be 1- sensitivity of the test. False positive test results (Type I error) incorrectly identify healthy people as sick with the possible consequence of overtreatment. The 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.	Critical	Partial	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases	D0028, D0027, D0009; B0001; E0001; F0001; G0001, G0100	B0001
C0007	Patient safety	Are the technology and comparator(s) associated with user-dependent harms?	Describe the current knowledge on 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 device malfunctioning due to deficient user training or personal attitude; or a risk of errors related to reconstitution, dosage,	Important	Partial	Yes	Sources: Studies on effectiveness, safety and health services research; manufacturers' product data sheets, safety monitoring databases, label warnings.	B0006, B0001	B0006, B0001

			administration, or storage of medicines, that may have serious consequences? Is there a risk of addiction? Describe what is known about the learning curve, intra- or inter-observer variation in the interpretation of outcomes, errors or other user-dependent concerns in the quality of care. For further information see Endpoint used in REA of pharmaceuticals – Safety.				Method: Systematic review		
C0020	Occupational safety	What kind of occupational harms can occur when using the technology?	Consider whether there are possible harms to professionals applying the technology: working positions, radiation or infection risks, etc.	Important	Complete	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases	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 related to endocrine modulators and disruptors and nanoparticles. The statistical risk of radiation at the public level should also be described here.	Optional	Partial	No	Method: Systematic review. Research articles, manufacturers' product data sheets, safety monitoring databases		
C0062	Safety risk management	How can one reduce safety risks for patients (includingtechnology-, user-, and patient-	Describe whether there is 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	Critical	Complete	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases	F0006; B0012, B0014, B0015	

		dependent aspects)?	communication is needed for patients, citizens and decision-makers can be included.						
C0063	Safety risk management	How can one reduce safety risks for professionals (including technology-,user-, and patient-dependent aspects)?	Report possible requirements for specific training, use of a protocol, or available guidelines 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 can be included.	Important	Partial	Yes	Research in occupational health and safety research literature		
C0064	Safety risk management	How can one reduce safety risks for environment (including technology-,user-,and patient-dependent aspects)	Report possible requirements for specific training, use of a protocol, or available guidelines 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 can be included.	Important	Partial	Yes	Research articles, manufacturers' product data sheets.		
B0010	Safety risk management	What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?	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 outpatient use, test results, review period, and health outcomes. In case of new technologies, consult	Important	Partial	Yes	Sources: Local authorities and legislation, administrative staff, clinical professionals, HTAs, National or local judgement.	G0008, G0003	

			EVIDENT database. Describe the general importance of having a registry for monitoring the use of this particular technology and the comparator is also needed. 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? National examples should be provided.						

4 Clinical Effectiveness

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
D0001	Mortality	What is the expected beneficial effect of the technology on mortality?	Mortality is the preferred, objective endpoint for assessments of life-threatening conditions. A distinction is made between overall mortality and disease-specific mortality. Overall mortality refers to all-cause mortality. It is expressed either as mortality rates (incidence in given population, at a given time point and usually risk-standardised), or survival (number of people alive for a given period after an intervention). Disease-specific mortality is a proportion of the all-cause mortality. Note 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 screening trials, where it is considered to be subject to bias. Supplement with relevant data if differences can be expected for specific subgroups. In diagnostic and screening technologies, this issue refers to the expected beneficial effect of the test-	Critical	Partial	Yes	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. Absolute mortality (compared to placebo or waiting list) and mortality relative to the comparator should be considered separately. See also Methodological guideline for REA of pharmaceuticals:	E0005, F0001	

			treatment-chain,				Clinical endpoints available at http://www.eunethta.eu/eunethta-guidelines Systematic reviews of trials, trials, both placebo-controlled and with active control. In the absence of head-to-head trials, studies with indirect comparisons (see Methodological guideline for REA of pharmaceuticals: Direct and indirect comparison, avaliable at http://www.eunethta.eu/eunethta-guidelines. If these are not available, non-controlled studies and respective systematic reviews. Health care register data. Modelling studies.		
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. For example, treatment may work differently in screening-identified cases than in cases that are diagnosed at regular physician's	Important	Partial	Yes	Trials, observational studies, accuracy studies		

			appointment						
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, with it,improved outcomes.	Critical	Partial	Yes	Accuracy and other observational studies, trials, qualitative research	H0005	
D0011	Function	What is the effect of the technology on patients' body functions?	International classification of function proposes the following categories for body functions: mental; sensory and pain; voice and speech; cardiac; respiratory and immune functions; genitourinary and reproductive functions; movement-related functions; and skin functions. Report the results both in absolute terms and relative to the comparator. Supplement with relevant data if differences can be expected for specific subgroups.	Critical	Partial	Yes	Trials and observational studies with functioning as an outcome. The instruments for outcome reporting should be validated	H0005; E0005; F0101	
D0014	Function	What is the effect of the technology on work ability?	Describe the intervention's effects 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	

D0015	Function	What is the effect of the technology on return to previous living conditions?	Discharge of the patient to the living conditions in which they lived before admission is one of the most important treatment goals, particularly for elderly patients. Implications for family members and caregivers should be considered too.	Critical	Partial	Yes	Trials and observational studies using one of the several evaluation tools, such as the Katz ADL scale, the Lawton 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-centred models, such as the Programme of All-Inclusive Care for the Elderly (PACE).	H0005	
D0016	Function	How does the 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, and comprising those activities or tasks that people undertake routinely in their everyday lives. 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 Methodological guideline for REA of	Critical	Partial	Yes	Trials and observational studies reporting ADL outcomes	H0005	

			pharmaceuticals: 1) Health-related quality of life and 2) Clinical endpoints, both available at http://www.eunethta.eu/eunethta-guidelines Supplement with relevant data if differences can be expected for specific subgroups.						
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 which measure either 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). There are two available basic approaches to quality-of-life measurement: (1) generic instruments that provide a summary of HRQL, and (2) 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 available at http://www.eunethta.eu/eunethta-guidelines	Critical	Partial	Yes	Trials, observational and qualitative studies	H0005; E0005	

			Supplement with relevant data if differences can be expected for specific subgroups.						
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 which measure either 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). There are two available basic approaches to quality-of-life measurement: (1) generic instruments that provide a summary of HRQL, and (2) 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 available at http://www.eunethta.eu/eunethta-guidelines Supplement with relevant data if differences can be expected for specific subgroups.	Critical	Partial	Yes	Trials, observational and qualitative studies	H0005; E0005	
D0030	Quality of life	Does the knowledge of the test result	The test result may alleviate, trigger, or worsen symptoms, as well as improve	Important	Partial	Yes	Qualitative research, observational studies,	H0005, H0006,	H0006

		affect the patient's non-health-related quality of life?	or worsen the quality of life, although there is no effectiveness on the primary outcome.				trials	F0001, F0003	
D0017	Patient satisfaction	Were patients satisfied with the technology?	Describe patients' overall perception of the value of the intervention and their satisfaction with the treatment. ('Was the use of the technology worthwhile?') Differences in acceptability may predict the overall uptake of the technology and would impact on the overall effectiveness.If a technology can be used repeatedly it can also be asked whether the patient would be willing to use this technology again. See also Methodological guideline for REA of pharmaceuticals: Clinical endpoints available at http://www.eunethta.eu/eunethta-guidelines	Critical	Partial	Yes	Surveys, qualitative research, observational studies, trials	H0006; F0001, F0011	H0006
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 the existence of an effective treatment for the target condition, and its availability to the patients.	Critical	Partial	Yes	Trials, observational studies	F0001	
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 the technology compares 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?	In addition, consider the situations where there is no proper reference standard.	Important	Partial	Yes	Accuracy studies		
D1004	Test accuracy	What are the requirements for accuracy in the context the technology will be used?	Discussion of what could be an estimate for an 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. An 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 order to avoid further testing which may be more harmful to the patient, and more expensive.	Critical	Partial	Yes	Accuracy studies, modelling studies	C0008, F0017	
D1007	Test accuracy	How does test accuracy vary in different settings?	Describe how 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, on optimal age range for a screening programme and on adjustments in different populations.	Important	Partial	Yes	Accuracy studies in different settings, descriptive literature, expert advice	B0004	B0004
D1008	Test accuracy	What is known about theintra- 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 specific or safer than the old one?	If there is effective treatment for a condition, then a new diagnostic technology with similar sensitivity, but greater safety or specificity, may be seen as improved effectiveness.	Important	Partial	Yes	Accuracy studies, trials, observational studies	C0008, F0001	C0008

C0006	Patient safety	What are the consequences of false positive, false negative and incidental findings generated by using the technology from the viewpoint of patient safety?	Describe the consequences of false positive, false negative and incidental findings generated by using the technology. False negative test results (Type II error) incorrectly identify sick people as healthy with the possible consequence of incorrectly rejected or delayed treatment. The volume of false negative test results can be estimated to be 1- sensitivity of the test. False positive test results (Type I error) incorrectly identify healthy people as sick with the possible consequence of overtreatment. The 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.	Critical	Partial	Yes	Research articles, manufacturers' product data sheets, safety monitoring databases	D0028, D0027, D0009; B0001; E0001; F0001; G0001, G0100	B0001
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 sufficiently change the pre-test probability that 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, the ability of users to make a correct diagnosis may depend on their knowledge and their ability to interpret the results.	Important	Partial	Yes	Trials, accuracy studies, before-after studies, interrupted time series, change-in-management studies	G0001	

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 of, ability for, and attitude toward decision-making. Management decisions subsume both testing and treatment decisions.	Important	Partial	Yes	Change-in-management studies, qualitative research	G0001, G0008, G0009	
D0022	Change-in management	Does the test detect other potential health conditions that can impact the subsequent management decisions?	Management decisions subsume both testing and treatment decisions. Notice issue C0006 which deals also with incidental findings.	Important	Partial	Yes	Trials, accuracy studies	F0003	
D0010	Change-in management	How does the technology modify the need for hospitalisation?	In addition, consider changes at different levels of care e.g. ward instead of intensive care.	Important	Partial	Yes	Trials, observational studies	E0001; G0001	
D0029	Benefit-harm balance	What are the overall benefits and harms of the technology in health outcomes?	This question integrates all benefits and 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 a balanced and meaningful presentation is difficult to reach even qualitatively.	Critical	Partial	Yes	Trials, observational studies, modelling studies	A0007, A0011; C0008, C0003, C0004, C0005, C0006, C0007, C0061; E0005; F0001,	A0007, A0011, C0008, C0003, C0004, C0005, C0006, C0007, C0061

			The integration of information across domains into the benefit-harm-balance is essential. This issue provides input for ETH (F0010) and ECO (E0005) in order 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 should the benefits and harms of subsequent diagnostic testing and treatments in patients with a true positive test result in a prior diagnostic or screening test.					F0011	

5 Costs and economic evaluation

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
E0001	Resource utilisation	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	Healthcare registers and databases, RCTs with resource utilisation 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, A0024, A0025; B0007, B0008, B0009; D0010, D0014, D0023; F0012; G0001, G0003, G0004, G0005, G0006, G0007; H0003, H0010	A0024, A0025; B0007, B0008, B0009; D0010, D0023; G0001
E0002	Resource utilisation	What amounts of resources are used when delivering the assessed technology and its comparators (resource-use measurement)?	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 tabular form is recommended. Report the approach(es) and data source(s) used to measure resource use associated with the technologies.	Critical	Partial	Yes	Healthcare registers and databases, RCTs with resource utilisation data, reimbursement databases, micro-level costing studies/ABC-costing studies	E0001	E0001

E0009	Resource utilisation	What were the measured and/or estimated costs of the assessed technology and its comparator(s) (resource-use valuation)?	For each technology report, provide 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. It is recommended to provide the results in tabular form. 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 costs.	E0001, E0002	E0001, E0002
D0023	Resource utilisation	How does the technology modify the need for other technologies and use of resources?	New (less invasive) interventions may reduce the need for surgical interventions. Some treatments require ongoing monitoring and healthcare visits, including hospitalisation.	Critical	Partial	Yes	Trials and pharmaco-economic studies, guidelines on utilisation of resources. Observational studies, statistics	B0013, E0001, E0002, E0009, F0003, G0001, G0003, G0004, G0007	G0001, G0003, G0007
G0007	Resource utilisation	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. It is possible to undertake a budget impact analysis which attempts to examine the likely impact of introducing a technology on finances or budgets from e.g. the perspective of	Critical	None	Yes	Literature searches, reports questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital	A0011; B0007, B0009, B0012; D0023; F0012	

			different payers. Different payers include: government-level institutions; 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 organisation? 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.				districts, laboratories), as well as information from manufacturers.		
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) (outcome identification, measurement and	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 expressing outcomes in alternative forms such as QALYs. Report the approach(es) and data source(s) used to estimate the health-related outcomes associated with the	Critical	Partial	Yes	An estimation of the incremental or other effects can be based on information provided in the EFF domain (e.g., mortality data) or on information from the SAF domain (e.g., morbidity data related to adverse events). Additional information collection may be needed (e.g.	A0004, A0005, A0006, A0009; C0008, C0002, C0004, C0006; D0001, D0003, D0005, D0006, D0007,	

		valuation)?	technologies, in a way which makes the identification of relevant health-related outcomes transparent. The measurement or estimation of health-related outcomes should reflect the information available from the SAF domain and the EFF domain, or should be otherwise justified. The valuation of health-related outcomes should also be reported in a transparent manner.				on health-related quality of life indices). The incremental effectiveness may result from an economic model, where inputs from the EFF domain are used.	D0011, D0012, D0013, D0029; F0003, 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.	Critical	None	Yes	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	E0001, E0002, E0005, E0009	E0001, E0002, E0005, E0009

							approach(es) and data source(s) used to estimate the of costs, outcomes, or economic evaluation(s) associated with the technologies. Relevant sources of data and evidence are specified in the relevant issues under the SAF, EFF and ECO domains (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 SAF, EFF and ECO.		
E0010	Characterising uncertainty	What are the uncertainties surrounding the costs and economic evaluation(s) of the technology and its comparator(s)?	Report the effects of uncertainty should be separately for structural, methodological and parameter uncertainty, whenever possible. The methods used in the sensitivity analysis should be reported in detail here.	Important	Partial	Yes	For example: • Deterministic sensitivity analysis in tabular form or using a Tornado diagram • Probabilistic sensitivity analysis, e.g., in the form of a CEAC	E0006	E0006

							• Value-of-information analysis Relevant sources of evidence are specified under relevant issues under SAF and EFF domains, as well as from within the ECO domain.		
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 in SAF and EFF domains, as well as from within the ECO domain.	C0005, E0006, H0012	E0006
E0013	Validity of the model(s)	What methodological assumptions were made in relation to the technology and its comparator(s	Report the following aspects of the research, with appropriate justification: • Perspective(s) of the analysis or analyses • Time horizon(s) • Discount rate(s) used	Critical	Partial	Yes	Relevant sources of evidence are specified under relevant issues in SAF and EFF domains, as well as from within the ECO domain	E0001, E0002, E0005, E0009, E0010, E0011	E0001, E0002, E0005, E0009, E0010, E0011

		)?	• To what extent the model includes all aspects of resource use and costs which could be considered important • To what extent the model includes all aspects of effectiveness which could be considered important						
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 can be expected to predict health effects • How well the model can be expected to predict resource use and costs • Estimates of the potential direction and/or potential magnitude of bias induced • An attempt to identify key factors that could compromise the validity of the model Here, report the process of validation and the types of validation addressed in the model.	Important	Partial	Yes	Relevant sources of evidence are specified under relevant issues in SAF and EFF domains, as well as from within the ECO domain	E0001, E0002, E0005, E0009, E0010, E0011, E0013	E0001, E0002, E0005, E0009, E0010, E0011, E0013

6 Ethical analysis

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
A0005	Benefit-harm balance	What are the symptoms and the burden of disease or health condition for the patient?	Describe the patient's relevant symptoms before intervention with the technology, their severity, their urgency and whether they are persistent, intermittent, or undulating, taking into account different stages of the disease. Patients' perceptions of the burden of the disease are not always in line with the clinical seriousness of the disease or its societal burden. For example, back pain is rarely caused by a life-threatening disease, but it can still very negatively affect patients' quality of life and ability to work. 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. Knowing the severity and/or urgency 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.	Critical	Complete	Yes	Sources: text books, HTAs, quality of life studies, qualitative patient perception studies. Method: A descriptive summary.		
F0010	Benefit-harm	What are the known and	Decisions concerning the	Critical	Partial	Yes	Information from other		D0001,

	balance	estimated benefits and harms for patients when implementing or not implementing the technology?	implementation of new technologies generally require carefully considering the balance between benefits and harms. Examples of questions that can be answered 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 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.				domains (links). Literature search. Expert opinion. Stakeholder hearing		D0029; H0001, H0004, H0005, H0006; C0008, C0005; A0010; D0017 D0027, D0028 D0031, D0024, D0030, D1019
F0011	Benefit-harm balance	What are the benefits and harms of the technology for relatives, other patients, organisations, commercial entities,	Examine the following: Can the technology have positive effects for others apart from the patients in question? Can the technology harm relatives, other patient groups, organisations, commercial entities, society, etc.? Some technologies have the potential to unfold unwanted or harmful effects not only on the patients	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing	G0011	D0029, H0001, H0002, C0020, C0040, A0006, E0006, D0017

		society, etc.?	that the technology is directly applied to but also indirectly on others. 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 themselves 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 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 in the process description can be used to describe benefits and harms.						I0008
F0003	Benefit-harm	Are there any other hidden	The technology may be used for other	Critical	Partial	Yes	Literature search.		D0030,

	balance	or unintended consequences of the technology and its applications for patients, relatives, other patients, organisations, commercial entities, society etc.?	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. 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. Evaluate the intended purpose and uses of the technology against the likely uses and consequences of the technology in reality. The mode of delivery, the need for laboratory tests or clinical follow-up to ensure safe and effective dosage and the way of delivery (at home, outpatient or in-patient) may have a 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). New technologies tend to lead to new areas of inventions and give rise to new ethical questions (e.g., in vitro fertilisation (IVF) and development of genetic testing has led to questions of preimplantation genetic diagnostics				Expert opinion. Stakeholder hearing		D0022, D0023, I0008, C0006

			(PGD)). As pre-symptomatic screening tests have become available, the healthcare system has to be prepared to handle moral issues raised by true positive and false negative findings. 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 diagnoses of hereditary disorders, also provide knowledge about relatives. Diagnostic information may also affect social relations (e.g. STD)'.						
F0104	Benefit-harm balance	Are there any ethical obstacles for evidence generation regarding the benefits and harms of the intervention?	When assessing benefits and harms of an intervention there may be ethical obstacles to the conduct of further research in order to strengthen the scientific basis. This concerns issues like the following: • When clinical experience shows that the intervention has an effect on a group for whom there are no treatment alternatives and it would thus be ethically unacceptable to conduct a study in which the comparative group would be denied the procedure, • In the case of a vulnerable group of	Critical	Partial	Yes	Literature search. Expert opinion.		D0029, F0010

			subjects who are difficult to study, • Where specific integrity problems would arise if research were to be conducted.						
F0005	Autonomy	Is the technology used for individuals that are especially vulnerable?	Clarify the right and justification to use the technology on vulnerable persons. Persons who are vulnerable could, for example, be pregnant women (in which case their unborn child needs to be protected), 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
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 a patient's right to autonomy, directly or indirectly, by influencing/subtracting their decisional capacity. However, patients have, in most cases, a right to autonomy, i.e. a right to be self-governing agents. This means they possess both the right to decide (not) to use/participate, and the right to receive relevant information. Drugs for sedation and surgical	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		H0013, D0012, D0013, D0016

			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 faecal blood test). In order 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, whether side-effects take place, and how these can affect the living quality or choices (e.g. 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	Focus on the following: 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	Critical	Complete	Yes	Expert opinion, stakeholder hearing		H0013, H0007, H0008, C0008, B0014, I0002, C0005

		used?	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 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 serious weight gain. They should also be informed of when the mode of delivery or action may affect their daily life (e.g. no car driving allowed, restricted travelling).						
F0007	Autonomy	Does the implementation or withdrawal of the technology challenge or change professional values, ethics	Technologies may change the patient-physician relationship, 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	Critical	Partial	Yes	Expert opinion		G0010

		or traditional roles?	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 healthcare professionals (e.g. screening for drug abuse when use is denied). Technologies that are aligned 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).						
F0008	Respect for persons	Does the implementation or use of the technology affect human dignity?	Especially those technologies that are applied to persons with reduced autonomy (children, mentally impaired, severely ill) 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 using the technology may also threaten their dignity. Some technologies may cause healthy people to be labelled as sick (e.g. 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	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		

			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 patient's moral, religious or cultural integrity?	A technology may challenge integrity by preventing (or having the possibility 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 user's self. 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 do not accept blood transfusion, pharmaceuticals used for abortion in cultural groups that do not accept abortion, and assisted reproductive technologies that have separated the concept of genetic, 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	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		H0011, H0013

			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. Describe, e.g., these issues: 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 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	Critical	Partial	Yes	Literature search. Expert opinion. Stakeholder hearing		B0010, D0011, I0007, I0009, I0002

			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 re-allocation of human resources, funding and training. A large re-allocation of resources may seriously jeopardise 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 prioritisation explicit or implicit? Diagnostic technologies sometimes acquire significant symbolic value (e.g. foetal ultrasound, PSA) that may create demands for tests that are not justified on health grounds.	Critical	Partial	Yes	Expert opinion.		G0007, E0001, E0002, E0009
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 healthcare system may help in adopting coherent and just health policies, either by applying past precedents to current cases, or by showing that past cases need reconsideration. Similarity is to be defined individually for each technology. The idea is to focus only on the similarities relevant for solving	Important	Partial	Yes	Literature search. Expert opinion		

			the ethical problems considered important for the current HTA project. The similar ethical problems can be related to similarities in the technology's medical, technological, economic, social, organisational or legal nature.						
H0012	Justice and Equity	Are there factors that could prevent a group or person from gaining access to the technology?	This issue concerns inequality in health. Investing in the reduction of health inequalities is a target of the European Commission, as it contributes to social cohesion and breaks the vicious spiral of poor health being a contributor to, and a result of, poverty and exclusion. 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, employment, insurance) prevent access?	Critical	None	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups. See also:http://ec.europa.eu/health/strategy/docs/swd_investing_in_health.pdffor more information.		G0009, G0101, A0012, I0011
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 (http://www.un.org/en/documents/udhr/). 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 healthcare.	Critical	Complete	Yes	Literature search. Laws, rules and regulations. Expert opinion. Stakeholder hearing		H0012

F0016	Legislation	Can the use of the technology pose ethical challenges that have not been considered in the existing legislations and regulations?	Describe whether legislation and regulation to use the technology is fair and adequate. Use of the technology may lead to ethical issues that make current regulations inadequate. Screening and diagnostic technologies are commonly regulated differently than treatments, especially medications. Ethical reflection is essential in order to assess what kind of legislation, regulation or amendments are needed.	Important	None	No	Laws, rules and regulations. Stakeholder hearing. Expert opinion		B0010, I0011, I0009, I0002, I0026 I0037 I0008
F0017	Ethical consequences of the HTA	What are the ethical consequences of the choice of endpoints, cut-off values and comparators/ controls in the assessment?	Address any risks of the chosen end-points, cut-off values or comparators/controls giving 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 entirely possible, so other end-points may need 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	Critical	Partial	Yes	Other domains (SAF, EFF). Expert opinion, Stakeholder hearing		See methodological description in EFF and SAF B0018, D1004, D1005, D1006

			have serious consequences.						
F0102	Ethical consequences of the HTA	Are there any ethical problems related to the data or the assumptions in the economic evaluation?	Consider whether there are any ethical problems related to the data or assumptions that have been used in the economic evaluation. 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
F0103	Ethical consequences of the HTA	What are the ethical consequences of conducting the technology assessment at this point of time?	At what time of the technology's lifetime is the technology assessed? What are the consequences of assessing the technology with respect to prioritisation? Who would (not) get access to the new technology, as result of conducting HTA at this point of time? If there are methodological and ethical obstacles to fill a knowledge gap, what are the consequences for the patient group if the knowledge gap cannot be filled in the (near) future? Should the technology be made available to patients despite the inadequate scientific basis at the time of assessment?	Important	Partial	Yes	Expert opinion, Stakeholder hearing		D0029, F0104

7 Organisational aspects

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
G0001	Health delivery process	How does the technology affect the current work processes?	Describe current tasks and work processes. This helps illustrate 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. Explain what kind of changes a new technology could have: it might replace or reduce some activities. In addition, the new technology may have an impact on current pathways of care (e.g. shift towards community care or inpatient care). The implementation of a new diagnostic test can substantially increase (or decrease) the number of patients in need of treatment thus changing the relationships between different organizations and influencing the health care system as a whole.	Critical	Partial	Yes	Literature search, guidelines, annual reports and statistics, reports and own study (e.g. questionnaires and interviews of different actors)	A0007, A0011, A0023, A0024; B0004, C0063; D0010, D0020, D0021, D0023; F0001, F0007; I0002, I0009	E0001

G0100	Health delivery process	What kind of patient/participant flow is associated with the new technology?	This issue deals with the path of the patient/participant from their own point of view. Describe the patient's path step by step. This also includes waiting times for diagnosis and/or treatment and waiting times for the analysis of the technology. Take into account all preparations that patients/participants need to make before and after (e.g. diet before bariatric surgery), as well as the need for self/home monitoring. In addition, take into account the impact of the technology on current pathways of care. It may e.g. shift towards community care or inpatient care.	Critical	Partial	Yes	Literature search, guidelines, annual reports and statistics, reports and own study (e.g. questionnaires and interviews of different actors)	A0010, H0003	E0001
G0002	Health delivery process	What kind of involvement has to be mobilized for patients/participants and important others and/or caregivers?	This issue concerns the role of patients/participants. A new technology may require task distribution among the people involved in treatment and care. Patients/participants and their important others and/or caregivers may be more actively involved in their own care and treatment, or otherwise, 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).	A0007; B0014; H0003, H0010, H0006, H0007, H0008, H0009, H0013	H0002

G0003	Health delivery process	What kind of process ensures proper education and training of staff?	A new technology may require new kinds of professionals or new tasks for existing personnel. This issue deals with how the organisation can ensure proper education. Take into account the effect of training on the management and effectiveness Implementing a technology can change the nature of the work and thus have influence on job satisfaction.	Critical	Partial	Yes	Literature search, guidelines, reports and hospital/hospital district documents, as well as and own research: interview or questionnaires of different actors of the process.	B0013, B0012: C0063; D0023; E0001, E0002, F0007	E0003
G0004	Health delivery process	What kind of co-operation and communication of activities have to be mobilised?	Co-operation and communication is crucial in order to achieve a fluent patient pathway. Implementing a technology can demand new co-operation and communication in and outside the organization, e.g. with other hospitals, pharmacies and manufactures. Therefore structure of co-ordination is important. Also, interaction and communication with patients/participants and their important others and/or caregivers could change. Adaptation of self/home monitoring needs close co-operation and fluent communication.	Important	Partial	Yes	Literature search, guidelines, reports and documents of hospitals and hospital districts, guidelines, own research: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants).	B0014, B0015; C0063; D0023; E0001; H0010, H0007, H0008, H0009, H0013; I0002	
G0012	Health delivery process	In what way is the quality assurance and monitoring system of the new technology	A new technology usually affects current quality assurance not only inside the organization but also outside in different health care levels. To assure quality, a monitoring system with standards and indicators is needed; it is also possible for there to	Important	Partial	Yes	Literature search, annual reports and statistics reports of hospitals and own study: questionnaires and interviews of different actors of the		

		organised?	be variation in how the quality assurance and monitoring system is implemented. Take into account who the responsible person for quality assurance and for the monitoring system is, and how any follow up has been arranged. Additionally, consider how quality assurance and the monitoring system affect management and effectiveness. Other international, national, regional and/or (cross) organisational demands for quality assurance (e.g. quality standards and monitoring) and for registration could also be in place, and this is another thing to keep in mind.				process (monitoring authorities, hospitals, hospital districts, laboratories). Information from manufacturers.		
G0005	Structure of health care system	How do de-centralisation or centralisation 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 economic 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	B0004; E0001; F0012	

							of hospitals-and hospital districts, health information databases (DRG etc.), own research: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants).		
G0101	Structure of health care system	What are the processes ensuring access to 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 hospitals and hospital districts, health information databases (DRG etc.), own research: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory, participants).	H0012	
G0006	Process-related costs	What are the costs of processes related to acquisition and setting up the new technology?	Implementing the required changes in e.g. hospital premises may be costly for organisations. Starting costs or running costs of a new technology could be very high. High costs can influence the decision on whether to introduce the new technology. Costs	Critical	Partial	Yes	Literature search, guidelines, reports and documents of hospitals and hospital districts and manufacturers (e.g. producer handbook), own	B0007, B0008, B0009; E0001, E0002, E0009;	

			can be divided if some organisation(s) is(are) responsible for the acquisition costs and others for the running costs. Take into consideration any investments at all stages of the process.				research: questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital districts, laboratory	G0007	
D0023	Process-related costs	How does the technology modify the need for other technologies and use of resources?	New (less invasive) interventions may reduce the need for surgical interventions. Some treatments require ongoing monitoring and healthcare visits, including hospitalisation.	Critical	Partial	Yes	Trials and pharmaco-economic studies, guidelines on utilisation of resources. Observational studies, statistics	B0013, E0001, E0002, E0009, F0003, G0001, G0003, G0004, G0007	G0001, G0003, G0007
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. It is possible to undertake a budget impact analysis which attempts to examine the likely impact of introducing a technology on finances or budgets from e.g. the perspective of different payers. Different payers include: government-level institutions; 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	Critical	None	Yes	Literature searches, reports questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital districts, laboratories), as well as information from manufacturers.	A0011; B0007, B0009, B0012; D0023; F0012	

			to this issue. For example: What kind of incentives does the budget impact impose on different actors? How might this potentially impact on each organisation? 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.						
G0008	Management	What management problems and opportunities are attached to the technology?	The issue concerns the administrative/managerial questions of technology: management of resources (e.g. 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. Take into account the relevant data/information management systems connected to each of these points. This issue also includes risk management and safety issues (e.g. safety of personnel).	Important	Partial	Yes	Literature search, guidelines, reports and documents of hospitals, own research: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory).	A0011, A0012, A0015, A0016, A0025; B0010, B0020; C0063; D0021; H0009, I0009	
G0009	Management	Who decides which people are eligible for the	Provide information on the key actors who decide on the use of the technology. Do most important	Critical	Partial	Yes	Literature search, guidelines, documents of hospitals, own	A0011, A0012; B0004,	

		technology and on what basis?	decisions take place on the national level (e.g. population screening) or are they, for example, made 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 on the decision level and decision criteria has ethical implications. This issue may be especially important in the context of rare diseases. This issue is related to the issue of work processes (G0001).				research: questionnaires and interviews of different actors of the process (monitoring authorities, hospitals, hospital districts, laboratory).	B0016; D0021; I0012; H0012, F0012; G0001	
G0010	Culture	How is the technology accepted?	Look at acceptance from the perspectives of organisation, personnel, and patients/participants. The organisational view can be separated into the intra-organisational (primary care), inter-organisational (secondary care) and health care system level. Acceptance can vary on different levels and with different actors. Alternative ways to introduce a new technology into an organisation could cause problems such as resistance among staff and dysfunction of processes. Acceptability is related to access to care.	Important	Partial	Yes	Literature search, own research: questionnaires and interviews of different actors of the screening process (monitoring authorities, hospitals, hospital districts, screening units, laboratory, staff, participants).	A0011, A0012; F0007; H0006, H0007, H0011, H0012	

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 the possible stakeholders are, as well as what kind of co-operation exists and what kind of interaction is needed. The stakeholders could e.g.be the pharmaceutical industry and companies offering technologies for screening, authorities national or regional, registries, administrative parties, municipalities, policy makers/decision makers, staff groups, GPs/primary care physicians and patient organisations. One may 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 research: questionnaires and interviews of different actors involved in the screening process (monitoring authorities, hospitals, hospital districts, screening units, laboratory, manufacturers, registry, participants).	B0015, F0003, F0011	

8 Patients and Social aspects

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
H0200	Patients' perspectives	What are the experiences of living with the condition?	This issue concerns the patient's everyday life living with the disease, e.g. familiar, social and work related roles, ability to manage relationships with other people in a socially appropriate manner in major areas of life, ability to take care of one self etc. It includes: • Illness and treatment burden • Limitations to activities of daily living: work, family, social life, ability to care for oneself, leisure activities • Psychological issues: stigma, anxiety, fear, social acceptance • Financial implications, aids needed to support daily living	Critical	Partial	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups.	CUR, ETH	
H0100	Patients' perspectives	What expectations and wishes do patients have with regard to the technology and what do they expect to gain from the technology?	This issue concerns what patients and care-givers expect to gain from the technology; it includes e.g.: • Improved survival, delayed progression? • Improvement of specific symptoms (e.g. fatigue, incontinence, diarrhoea, mobility etc.)? • Improvements/changes related to implications of daily living, social	Critical	Partial	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups.	EFF, ETH, SAF	

			and psychological issues by using the current technology • What size of effect is important?						
H0006	Patients' perspectives	How do patients perceive the technology under assessment?	This issue is about the patients' attitudes, perceptions, preferences, satisfaction and expectations to the technology. This covers whether any positive or negative issues arise as a consequence of using the technology e.g. feelings of unity or empowerment, existential experiences (e.g. insecurity, worries, hope, anxiety, stigmatisation, social status, courage to face life, satisfaction, changes in self-conception). It includes: • What understanding do patients have of the technology? • What implications – positive and negative – does the technology have regarding activities of daily living, social life, psychological issues, financial implications, support and resources (practical, physical, emotional) and requirement in order for the patient to use the technology with satisfactory results? • Can the technology be used/taken easily? • What treatment benefits could be improved? • What side effects are most difficult to manage?	Critical	Partial	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups.	ETH, LEG, ORG	

H0002	Patients' perspectives	What is the burden on care-givers?	Describe who the important other people are that are involved in the use of the technology, in addition to the patients (parents, children, friends, people at work place etc.). What kind of support (practical, physical, emotional, financial, nurturing, personal) do care-givers mobilize? It includes e.g.: • What challenges do care-givers face when supporting patients to manage their condition and receive care? • How do care-givers perceive the new technology; what challenges and benefits might it offer? • What support and resources need to be mobilised in order for the patient ton use the technology satisfactorily?	Critical	Partial	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups.	ETH, LEG	
H0012	Social group aspects	Are there factors that could prevent a group or person from gaining access to the technology?	This issue concerns inequality in health. Investing in the reduction of health inequalities is a target of the European Commission, as it contributes to social cohesion and breaks the vicious spiral of poor health being a contributor to, and a result of, poverty and exclusion. 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, employment,	Critical	None	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups. See also:http://ec.europa.eu/health/strategy/docs/swd_investing_in_healt		G0009, G0101, A0012, I0011

			insurance) prevent access?				h.pdffor more information.		
H0202	Communication aspects	How are treatment choices explained to patients?	This issue is about patient participation, incl. what support or limit use of the technology in relation to communication aspects. It includes e.g.: • Do patients with the condition have good information sources to explain the condition and treatment options to them? • Are there good decision aids available to help shared decision making between patients and doctors and/or other health personnel? • Do patients feel themselves involved in a sufficient and appropriate way?	Critical	Partial	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups.	ETH	
H0203	Communication aspects	What specific issues may need to be communicated to patients to improve adherence?	This issue is about communication and how it influences the use of the technology, e.g.: • Preparation in advance of intervention, dosage instructions, side effects etc. • Is there information which patients would need that are not usually available?	Critical	Partial	Yes	Search for or conduct a literature review or, conduct a primary study for important questions that are not covered in the literature; gather evidence from patient groups.	EFF, ETH, SAF	

9 Legal aspects

ID	Topic	Issue	Clarification	Import.	Transf.	Is core	Methodology	Content relations	Sequential relations
I0002	Autonomy of the patient	What kind of legal requirements are there for providing appropriate information to the user or patient and how should this be addressed when implementing the technology?	Describe the rules and recommendations for what patients should know about the implications of using or not using the technology. The right of the patient not-to-know may also be important, as well as the patient's right to complain. These rules are likely to be helpful for the persons involved in implementing the technology to prepare proper information and counselling. This information may be particularly important with technologies carrying high risks of harm, technologies with the potential to provide information that is not directly relevant to the condition being tested, and in emergency situations in which the patient does not usually have sufficient time to consider the treatment decision.	Critical	Partial	Yes	Convention on Human Rights and Biomedicine CETS No: 164 (including the Explanatory report to Biomedicine convention). Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare, National laws specially on patients' rights. Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes, CETS No. 203.	B0014, B0015, C0002, C0005, C0007, C0008, F0004, F0006, F0010, F0016, G0004	B0014, B0015, C0002, C0005, C0007, C0008, F0004, F0010, G0004
I0034	Autonomy of the patient	Who is allowed to give consent for minors	According to law, a minor is a person under a certain age, usually the age of majority, which legally demarcates	Important	None	No	Convention on Human Rights and Biomedicine CETS	F0005, I0002	F0005, I0002

		and incompetent persons?	childhood from adulthood. The age of majority depends upon jurisdiction and application, but is generally 18. An incompetent person may be defined as one whose mind is unsound, deranged, or impaired in function, such as a slow I.Q., deterioration, illness or psychosis. What do laws/binding rules require when considering informed consent in these groups? See also I0002.				No.: 164 (including the Explanatory report to Biomedicine convention). National laws on patients' rights. Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes, CETS No.: 203. Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data, OJ 1995 L 281/31.		
I0007	Privacy of the patient	Is there a possibility that the use of the technology produces additional information	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	Critical	Partial	Yes	Case laws, medical case reports. Z vs. Finland (ECHR February 25, 1997); M.S. vs. Sweden (ECHR August 28, 1997); national	B0012, C0006, D0022, F0101	C0006, D0022, F0101

		that is not directly related to the current care of the patient and may violate their right to respect for privacy?	genetic diagnostics entail certain challenges to this principle. For example, in Z vs. Finland (ECHR February 25, 1997) there was a case of an HIV infected person whose HIV positive test was an incidental finding, not related to her healthcare intervention at the time.				legislation; legal literature.		
I0008	Privacy of the patient	What do laws/binding rules require with regard to informing relatives about the results?	A test result may indicate that the relatives of a patient may have a medical condition that would need to be addressed. If this can be foreseen, appropriate procedures, complying with the existing legislation, must be considered beforehand – is the information to be revealed to, or withheld from the relatives in question? Describe on what conditions (if any) the privacy of the original patient can be broken in order to inform the relatives of their situation. There may be situations, e.g. when treatment malpractice is suspected after the death of the patient, when (closest) relatives demand the results. Similar cases could occur in sudden, unexpected deaths and in some cases of highly infectious diseases.	Important	Partial	Yes	Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes, CETS No.: 203. Convention on Human Rights and Biomedicine CETS No.: 164 (including the Explanatory report to Biomedicine	B0014, F0011, G0004, H0002	B0014, F0011, H0002

							convention). National laws specially on patients' rights and data protection. Z vs. Finland (ECHR February 25, 1997); M.S. vs. Sweden (ECHR August 28, 1997).		
I0009	Privacy of the patient	What do laws/binding rules require with regard to appropriate measures for securing patient data and how should this be addressed when implementing the technology?	Provide an overview of the legal requirements regarding policies and procedures, as well as examples of: practical local solutions; securing the kind of patient data that will be generated when using of the technology. Who is allowed to save and store the patient-data, where is it saved, for how long, and who can have access to it? Does the use of the technology produce some additional (i.e. diagnostically or therapeutically irrelevant) information on the patient that could be relevant for, e.g., health insurance, marketing studies, or safety authorities and how should data protection be handled in these cases? Is it possible that legal data protection requirements have adverse consequences to the quality of care, e.g. by complicating the transfer of patient data in a screening process,	Important	Partial	Yes	Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. Convention on Human Rights and Biomedicine CETS No.: 164 (including the Explanatory report to Biomedicine convention). Recommendation R (97) 5 of the Committee of Ministers to Member States on the protection of	B0010, F0101, F0016	B0010, F0101, F0016

			and how should this be addressed?				medical data. National laws specially on patients' rights and data protection. Z vs. Finland (ECHR February 25, 1997); M.S. vs. Sweden (ECHR August 28, 1997).		
I0011	Equality in health care	What do laws/binding rules require with regard to appropriate processes or resources which would guarantee equal access to the technology?	In general, equality in health care is stipulated in the EU Charter of Fundamental Rights and it is also one of the central principles of the Biomedicine Convention. Moreover, in many national constitutions, equality of citizens also covers access to health care. However, there may be experiences on a national level of some specific difficulties in equal access to the technology, and there may probably also be proposed solutions, which could be helpful for decision-makers in other countries as well.	Critical	Partial	Yes	Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare. Recommendation R (2006) 18 of the Committee of Ministers to Member States on health services in a multicultural society. National laws. Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes, CETS No.:	F0012, F0014, F0016, G0009, G0101, H0012	F0012, F0014, F0016, G0009, G0101, H0012

							203. Case law: S.H. and others vs. Austria (ECtHR April 1, 2010). Gillberg vs. Sweden (ECtHR November 2, 2010). Commission vs. France (ECJ C-512/08) of October 5, 2010. R.R. vs. Poland (ECtHR May 26, 2011) Panaitescu vs. Romania (ECtHR Apri 10, 2012). Costa and Pavan vs. Italy (ECtHR August 28, 2012)		
I0012	Equality in health care	What are the consequences of various EU level and national regulations to the equal access to the technology?	The possible consequences of the EU Directive of cross border health care could be considered here. There may be nationally legally defined processes, including reimbursement and pricing, determining the implementation of and level of access to a technology. This information may give useful insight also beyond one's own country.	Important	Partial	Yes	Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare. National laws.	A0021, B0004, F0012, F0013, G0009, G0101, H0012, H0015	A0021, B0004, F0012, F0013, G0009, H0012, H0015

F0014	Ethical aspects	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 (http://www.un.org/en/documents/udhr/). 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 healthcare.	Critical	Complete	Yes	Literature search. Laws, rules and regulations. Expert opinion. Stakeholder hearing		H0012
F0016	Ethical aspects	Can the use of the technology pose ethical challenges that have not been considered in the existing legislations and regulations?	Describe whether legislation and regulation to use the technology is fair and adequate. Use of the technology may lead to ethical issues that make current regulations inadequate. Screening and diagnostic technologies are commonly regulated differently than treatments, especially medications. Ethical reflection is essential in order to assess what kind of legislation, regulation or amendments are needed.	Important	None	No	Laws, rules and regulations. Stakeholder hearing. Expert opinion		B0010, I0011, I0009, I0002, I0026 I0037 I0008
I0015	Authorisation and safety	What authorisations and register listings does the technology have?	Describe the register listings, both at EU level and national level, which might be relevant when implementing the technology and planning, e.g., local authorisation, monitoring or evaluation functions, as well as qualification and quality control. Examples include technology registers, registers for marketing authorisation, certification of safety and reimbursement. However,	Critical	Complete	Yes	Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage	A0020, B0010, C0002, C0007, C0060	A0020, B0010, C0002, C0007, C0060

			some of the registers, e.g. the one for medical devices (EUDAMED), are not open for HTA doers. Register listings information may be particularly relevant for the technologies which can be used off-label or as investigational intervention outside clinical trials (so-called expanded access or compassionate use).				and distribution of human tissues and cells. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. National laws.		
I0017	Authorisation and safety	What do laws/binding rules require with regard to the safety of the technology and how should this be addressed when implementing the technology?	List the legal requirements for safety of the technology and quality of care. Does the technology fulfil these requirements, and what should be done to ensure that the legal requirements maintain fulfilled when implementing the technology? Consider the findings of the SAF and ORG domains here, in the light of relevant European or national safety regulations. See also I0015.	Critical	Complete	Yes	Results from the Safety domain. Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. Directive 2001/95/EC of the European Parliament and of the Council of 3 December 2001 on general	B0002, B0003, B0008, C0002, C0020, C0040, C0062, C0063, C0064, G0012, I0015	B0002, B0003, B0008, C0002, C0020, C0040, C0062, C0063, C0064

							product safety. Council Directive 93/42/EEC of 14 June 1993 concerning medical devices. National laws.		
I0019	Ownership and liability	What should be known about the intellectual property rights and potential licensing fees?	This information is important because infringement of intellectual property rights can reduce the use of the technology and have implications for the wording of the acquisition contract of a new technology, and possibly also licencing fees.	Important	Complete	Yes	Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions. Directive 2004/18/EC of the European Parliament and of the Council of 31 March 2004 on the coordination of procedures for the award of public works contracts, public supply contracts and public service contracts. National laws. Patent data bases. Manufacturer's information.		

							C-317/05 (ECJ)		
I0021	Ownership and liability	What should be known about the legal or binding rules regarding the width, depth and length of the manufacturer s guarantee?	This issue may help the decision-maker to be aware of their legal rights when considering the manufacturer's guarantee. The user guide plays a part in determining the manufacturer's liability.	Critical	Complete	Yes	Manufacturer's information Sales/purchase contract		
I0023	Regulation of the market	What kind of legal price control mechanisms are there that are relevant to the technology?	Describe the adopted economic measures for controlling public health expenditures when adopting technologies. This information, although not transferable, gives insight to decision-makers in other countries too.	Critical	Partial	Yes	Directive 2004/18/EC of the European Parliament and of the Council of 31 March 2004 on the coordination of procedures for the award of public works contracts, public supply contracts and public service contracts. Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance	G0007	G0007

							systems. National laws. C-317/05 (ECJ), T-179/00 (ECJ)		
I0024	Regulation of the market	What kind of regulation exists for the acquisition and use of the technology?	Expensive technology and dangerous pharmaceuticals are typically subject to acquisition regulation.	Critical	Partial	Yes	Directive 2004/18/EC of the European Parliament and of the Council of 31 March 2004 on the coordination of procedures for the award of public works contracts, public supply contracts and public service contracts. National law. Case law: Commission vs. Poland (ECJ C-185/10) of March 29, 2012.	G0006, G0007	G0006, G0007
I0025	Regulation of the market	What legal restrictions are there for marketing the technology to the patients?	Describe general legal principles of the restrictions placed on the marketing of health technologies to lay people.	Critical	Partial	Yes	Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices.		

							Directive 93/42/EEC of 14 June 1993 concerning medical devices. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. National laws		
I0026	Regulation of the market	What should be known about the legal issues in cases of new technologies where the current legislation is not directly applicable?	Novel technologies may not always be unambiguously covered by existing legislation. Sometimes, an otherwise restricted technology can be used in clinical trials or as ‘compassionate use’, i.e. in extended use outside clinical trials. Important questions, such as 'How are the liability issues solved according to existing legislation?', or, 'Is the voluntary participation of patients guaranteed properly?' may be important to consider. If the current law does not provide a straightforward answer to the liability issues it may be advisable to consult a legal expert on the interpretation of the existing provisions with regard to the technology in question. Sometimes even new legislative measures are needed.	Critical	Partial	Yes	Consulting legal expert(s), possibility of analogical interpretation of law, court decisions, literature	B0002, B0003; F0003, F0016	B0002, B0003, F0003, F0016

I0037	Regulation of the market	Are there relevant concerns about conflicts of interest regarding the preparation of binding rules and their implementation?	Relevant concerns of partiality or conflicts of interest with regard to binding guidance may give useful insight to decision-makers about the importance of implementing a technology.	Critical	Partial	Yes	Literature		