

Number of comment	Page	Line	Comment	Character of comment <ul style="list-style-type: none"> • “major”¹ • “minor”² • “linguistic”³
1	General	NA	COCIR appreciates the development of these guidelines. However, we would like to share some general comments: <ul style="list-style-type: none"> - Availability of RCT data at this stage of technology development is almost extremely limited (only short term). Other evidence will then be required. - We support the need for alternative methodologies (ref The Netherlands methods ref Beschikbaar als pdf) - Database to track long term effects are becoming increasingly valuable and thus should be more used and referred to, but still there is a need to avoid bias of some of those databases 	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic
2	6	21	To amend the text as follows: “From the perspective of the HTA assessor both problems can be partially addressed by a more detailed analysis of the available evidence considering these factors” For example, in radiotherapy, detailed RCT will not address the challenges from incremental medical device changes resulting from the fact that many new radiation techniques are clinically introduced to reduce the risk on side effects. Such changes are introduced without being documented through RCTs. These are introduced based on a risk reduction principle named ALARA and are reducing the dose given outside the tumour to Organs at Risk (OAR) which automatically will reduce the risk on side effects. Long term effects and side effects of the treatments are not detected with RCT as long latency times are necessary to detect tumour recurrence, secondary cancers, side effects such as Cardiac complication. Long term trials are one way, but more & more we expect to have those long term effects analyzed through patient registries or clinical databases.	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic
3	7	1	In table in Fifth recommendation, it mentions that RCT should be preferred but evidence is frequently lacking for medical device interventions. Same comment as comment#2 and: As it is known, HTA methods differences between Medical Technologies and Medicines needed to facilitate rapid technology adoption. In large scale randomised controlled trials (RCTs), results often come after technology has	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic

¹ “major” indicates that a comment points to a highly relevant aspect and that the author / the draft group is expected to give a thorough answer

² “minor” means that a given comment does not necessarily have to be answered in a detailed manner

³ “linguistic” labels problems with grammar, wording or comprehensibility

			<p>been superseded. As it is performed in Radiotherapy in Germany and the Netherlands, why not keeping the text open for novel approaches based on evidence from retrospective interrogation of linked clinical data sources rather than randomized clinical trials. See: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3981478/</p> <p>This is more and more common and the HTA guideline should allow for the analysis of massive amounts of multi-modal and multi-sourced data as hidden patterns can be retrospectively detected and knowledge created, complementing traditional ways of doing clinical research (prospective clinical trials). This predictive analytics (predict the future by looking back) and prescriptive analytics (decision support) shows the promise of considerable support of the anamnesis and the diagnostic process.</p> <p>➔ Sequential prospective cohort studies with standard follow up programs (usually named “Model based SELECTION and VALIDATION method”) are more common in comparing new treatment modalities to already applied ones (=relative effectiveness assessment (REA)) in radiotherapy</p>	
4	12	3	<p>“Health technology assessment (HTA) is aiming to inform decisions on adoption to benefit catalogues, reimbursement, best practice, and on disinvestment of health technologies”</p> <p>If payers & providers were to say they will not pay for any device until it’s undergone an HTA, then due to the current randomised Clinical trial (*) methodology requirements of HTA any non-drug technologies, would already be obsolete by the time it is fully approved for full release and distribution. The current benefits afforded patients by the use of technologies early in their lifecycle by the current CE marking process, EC/93/42 Directive, would be markedly affected, and the resultant anticipated affect in slowing of innovation and development of technologies within the European setting might also be expected to be impacted.</p> <p>(*): to avoid such delays, Medical Devices should need to apply new predictive analytics (predict the future by looking back) and prescriptive analytics (decision support) to support HTA studies in collaboration with “EUnetha JA3 WP7 - Methodology development and evidence generation”. In Medical Devices, Relative Effectiveness Assessment (REA) implementing sequential prospective cohort studies with standard follow up programs (usually named “Model based SELECTION and VALIDATION method”) are common for comparing new treatment modalities to already applied ones</p>	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic
5	12	14-15	Same comment as comment#3	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic
6	22	12	If this is referring to big data analytics, and in this case the reference material from internal publication should be mentioned such as:	<input type="checkbox"/> major

JA2- WP7- SG 3 – **Public** consultation on the methodological guideline “Therapeutic medical devices”
 2nd draft version of guideline

REVIEW by

COCIR



			“HOW SHOULD HEALTH DATA BE USED? Privacy, Secondary Use, and Big Data Sales”, Bonnie Kaplan, PhD, FACMI - Yale Interdisciplinary Bioethics Center, Yale Information Society Project, Yale University, ISPS14-025 ; 7 OCTOBER 2014	<input checked="" type="checkbox"/> minor <input type="checkbox"/> linguistic
7	26	18	Radiotherapy makes also comparative studies available and examples can be found in: In [...] rapid-learning [...] data routinely generated through patient care and clinical research feed into an ever-growing [...] set of coordinated databases. <i>Abernethy, J Clin Oncol 2010;28:4268</i>	<input type="checkbox"/> major <input checked="" type="checkbox"/> minor <input type="checkbox"/> linguistic
7	30	30	Reference to the ISPOR method is coming from Pharmacoeconomics. For medical devices such as in radiotherapy, other modelling studies validation is used such as the model for prospective cohort studies on multivariable normal tissue complication probability (NTCP). This could be mentioned as to vary from the Pharmaceutical industry used methods	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic