

JA2- WP7- SG 2 – **Public** consultation on the Position Paper “How to decide on the appropriate study design”

Second draft of the position paper (29 March 2015)

Number of comment	Page	Line	Comment	Character of comment	Response
<b>EFPIA 1</b>	General	General	This is a very crucial guideline that would potentially help both developers and HC stakeholders to optimize research resources , however there are too many editorial coments and opinions that are not acceptable in a guideline document . Guidelines from EunetHTA are expected to be evidence based, opinion and prejudices free and with appropriate quotations.	<ul style="list-style-type: none"> <li>• “major”<sup>1</sup></li> <li>• “minor”<sup>2</sup></li> <li>• “linguistic”<sup>3</sup></li> </ul>	<p>This document is not a guideline but a position paper that presents a view of EUnetHTA members as to the best approaches to specifying primary research methods to follow from systematic review type HTA reports.</p> <p>It was built on a mix of highly objective evidence, and opinion where the evidence wasn't there. What opinion is there has been guided and refined by the reviewers listed in the document.</p>
<b>EFPIA 2</b>	7	9	In The Executive Summary: I would delete „systematic “between International and review organizations. This is not a systematic review, (it not includes meta-analytic techniques)	<input type="checkbox"/> major <input type="checkbox"/> minor <input checked="" type="checkbox"/> linguistic	<p>(i) The statement is not claiming that this document is a systematic review. The claim is we looked at current practice in organisations carrying out systematic reviews</p> <p>(ii) A systematic review does not necessarily have to include meta-analysis.</p>
<b>EFPIA 3</b>	7	22	Still in the executive summary: I would delete the example here “because there is a party with vested interest. This type of sentence are not acceptable in a guideline document and promotes adversarial	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic	The statement is not adversarial – it’s not pointing at particular groups and accusing them of partisanship. It has been redrafted in order to avoid misunderstanding.

<sup>1</sup> “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

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

<sup>3</sup> “linguistic” labels problems with grammar, wording or comprehensibility

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			positioning		
<b>EFPIA 4</b>	15	1	It would be useful to present a PRISMA flow diagram to show number of articles excluded (with reasons) and retained, from 93 identified.	<input type="checkbox"/> major <input checked="" type="checkbox"/> minor <input type="checkbox"/> linguistic	Thank you, it has been added to the document.
<b>EFPIA 5</b>	15	2	Please specify which international governmental and HTA agencies websites were searched.	<input type="checkbox"/> major <input checked="" type="checkbox"/> minor <input type="checkbox"/> linguistic	Those of EUnetHTA partners experienced with Additional Evidence Generation, as well as CMS, AHRQ, MSAC etc.
<b>EFPIA 6</b>	28	11	After section 5.1.8 (Switzerland); I would also report what is happening in Belgium, with KCE providing input concerning future research.	<input type="checkbox"/> major <input checked="" type="checkbox"/> minor <input type="checkbox"/> linguistic	Thank you, it has been added.
<b>EFPIA 7</b>	32	12	It is write „It is often the <i>advantage</i> of a manufacturer“. It should say, to accomplish with regulatory authorities’s evidentiary requirements, industry tend to comapare with placebo. Also, lack of consensus about treatment standar of care among countries or changes in clinical practices over time could prevent to choose the right comparator for direct head to head comparison	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic	Thank you, the paragraph has been redrafted.
<b>EFPIA 8</b>	32	20	Social and Ethical Reasons: The entire sentence show prejudices in terms of presuming dishonesty or ignorance of Industry developers. Comments and opinions are not acceptable in a methodological guideline	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic	This paragraph is nothing to do with industry. There are many clinicians, patient groups, and representatives of the public who will try to stop research they don’t like with arguments like these.
<b>BIOGEN</b>	34	Section 7.1.	Mixed treatment comparisons (MTCs) or adjusted indirect comparisons should be recognized in the document as a form of evidence for estimating relative clinical effectiveness as a first step before	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic	This is true, but this document does not address the methods of evidence synthesis. We assume that appropriate evidence synthesis work (e.g. systematic review, meta-

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			embarking on de-novo evidence generation, particularly for the purposes of Health Technology Assessment. Fully leveraging the value of evidence based medicine (by synthesizing published randomized trials in this way and estimating relative treatment effects prior to embarking on a head-to-head trial) should be a pre-requisite before embarking on costly and time-consuming primary research.		analysis, models of mixed / indirect treatment comparisons) have been undertaken before recommending further primary research. A paragraph has been added in order to further clarify this in the text.
<b>EFPIA 9</b>	34	18	In table describing class of gaps, starting design and why I would add <i>challenges to overcome</i> and add under this column agreement <i>on appropriate comparator</i>	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic	The information asked for seems to already be in the table.
<b>EFPIA 10</b>	36	19	New technologies- are viewed as having great potential for impact for theoretical reasons... it should say potential impact due to several reasons that not always are confirmed, such as rational knowledge of disease physiopathology and biological plausibility among others.	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic	Thank you, it has been reformulated.
<b>EFPIA 11</b>	41	22	To ensure the most appropriate comparator. Appropriate to whom or to which context? Country? Region Global? Comparator for Europe? Please clarify or explicitly comment the challenges for both developers and HTAs	<input checked="" type="checkbox"/> major <input type="checkbox"/> minor <input type="checkbox"/> linguistic	The appropriate comparator is the one most useful to the decision make which can actually be compared – e.g. it’s pragmatic.
<b>EFPIA 12</b>	43	21	First item: I would suggest the systematic reviewer should also prioritise the clinical uncertainties.	<input type="checkbox"/> major <input checked="" type="checkbox"/> minor <input type="checkbox"/> linguistic	Thank you, it has been added.
<b>EFPIA 13</b>	44	2	The example “because there is a party with vested interest “must be deleted. This type of value	<input checked="" type="checkbox"/> major	It’s not a value judgement. It’s a statement of fact – vested interests have attempted to sink

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			judgment are not acceptable in a guideline document	<input type="checkbox"/> minor <input type="checkbox"/> linguistic	more than one trial that they didn't like. The statement has been redrafted in order to avoid misunderstanding.
<b>EFPIA 14</b>	47	17 18 19	Opinions and value judgment are not appropriate in a methodological guideline: All models are wrong, but some are useful. Please delete the sentence, as it seems a personal judgment or approach this issue giving scientific arguments: “So the main question for us is to what extent are models of health care useful?”	<input type="checkbox"/> major <input checked="" type="checkbox"/> minor <input type="checkbox"/> linguistic	This is a well-known quotation which describes the problem concisely and in an accurate way. The statement is discussed further in both Box's book, and an in paper he published in the Journal of the American Statistical Society. As a scientific paper published in a reputable journal, it stands to be quoted.