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EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

Subgroup on Pharma Templates (SDAT-PHARMA)

Appendix 1
Survey to evaluate the pharma Assessment Report template: Results

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Executive Summary

A survey was conducted among potential producers and users of EUnetHTA Joint Action 3 (JA3) assessments of pharmaceutical technologies (PT) to collect feedback on the current Assessment Report template. The survey was carried out in June/July 2020, and provided a detailed feedback by 13 EUnetHTA partners with experience as members of assessment teams and/or users of Relative Effectiveness Assessments (REAs).

The sample of respondents is considered representative, even if small. Responders are considered to have adequate level of expertise both as members of authoring teams and as users of the final output (REAs).

A critical analysis of responses was conducted, giving attention to issue recurrence (i.e. the same problem or area of improvement is reported in different survey sections) and frequency of reporting (i.e. more than one respondent suggests the same issue).

The current template, even if perceived as a benchmark, is not yet considered optimal [see Chapter 3. Questions on overall feedback. Table 4].

The main limitations are due to:

- Low uniformity among assessments due to a lack of indications on specific methodological aspects (i.e. indirect comparisons, the use and role of PICO, identification and reporting of bias and uncertainties). Those aspects must be better addressed in the form of Guidance for authors.
- Lack of transparency. Transparency is requested for some PICO related aspects, such as reporting of deviations from planned PICO and selection of (and agreement on) comparators.
- Lack of alignment to Submission Dossier. Transparency is requested also on how discrepancies among REAs (and authoring team decisions) vs. Submission Dossier are managed.
- Difficulties in finding the information. Therefore, a revision of some headings/subheadings is suggested.
- Ongoing presence of redundancies.
- Lack of provision of relevant evidence for national adoption. Some misalignment of the Assessment Report template to the national reports is expected and considered acceptable, and in certain cases REAs are used as a basis for national assessments. But, at the same time, other responders identified some missing sections (i.e. Statistical section/analyses).
- High workload. Workload associated with the current report template is perceived as high and, in some cases, excessive compared to the usability of the final output at the national level.

Suggested solutions by responders are:

- Guidance for authors. Improved support to authors both from a methodological point of view and for a more uniform interpretation of template requirements is considered essential. In some cases, lack of guidance is also perceived by responders as a lack of agreement on methodological aspects among EUnetHTA partners.
- Improve synthesis and conclusiveness of the Discussions and Conclusion Section.

Sections in major need of revision are Methods and Results, followed by Discussions, and Executive Summary [see 4. Section specific questions: Summary – Table 16].

The survey results showed that the following issues, specific to the different template sections, should be given priority in the revision of the template structure [see 5. Section specific questions: Details]:

- Executive Summary. It is necessary to work on its length (i.e. to avoid too long summaries without losing completeness) and clarity of scope.
- Background Section. To better connect this section to the following one (Objective and Scope). The role of the section should be more evident.

- Objective and Scope section. Deviations from submission file and the level of agreement on the final PICO should be better reported.
- Methods section. Uniformity among methods sections reported in REAs should be reached. Clarity and completeness in the information reported for data extraction could be improved.
- Results section. Avoiding duplication of data on information retrieval and the improvement of reporting of study results are both suggested by responders. In addition, a more granular template for results would help to find data of interest.
- Discussions section. The aim should be to make it more conclusive and specific for each selected comparator. Areas of uncertainty should be identified.
- Conclusion section. More clear conclusions are requested by some survey responders. In some cases, it was perceived as not being conclusive enough on the results of the assessment.
- Appendix. As a result of collected suggestions for improvement, Appendix could help to simplify the content and length of REAs. At the same time, relevance of some elements (i.e. description of national guidelines) and associated workload (i.e. evidence gaps) were criticalities raised by responders.

In addition, there is still space for improvement for tables and graphs/figures, to investigate both the possibility to use tables to reduce length of REAs and to move the more complex ones to the Appendix. Some responders suggested to update specific tables (e.g. the risk of bias tables to reflect the new Cochrane Risk of Bias tool 2.0).

For all responders, the publication of the Core Submission Dossier [see 7. Questions to help formulate recommendations for a future template], in addition to REAs, is useful. While no agreement was reached among responders on the way in which evidence should be reported in the template (PICO vs. study level) [see 7. Questions to help formulate recommendations for a future template].

Then, the proposal to report results separately for each data source [see 7. Questions to help formulate recommendations for a future template] was accepted with a preference for reporting data separately for indirect comparisons and meta-analysis, as well as for pivotal studies.

Conclusions

Future revision of the template should be conducted at different levels:

- **Structure**. The way in which methods and results are reported impact the template structure. Alternative approaches investigated by the survey were: PICO vs. study level, comparator or data source-specific reporting.
- Specific **headings/subheadings**. Clearer headings are requested and more detailed subheadings could help to improve some sections.
- **Format** to report data/evidence. Tables and graphs/figures could be still improved. Level of details, where to report them, and how to use graphs to improve analysis are issues to address.
- **Guidance for authors** to facilitate a more uniform interpretation of template requirements, i.e. what information should be included and where.
- **Appendix** could help to improve readability and length of the final REAs.
- **Additional documentation.** The publication of the Core Submission Dossier should be continued, can help reduce length of REAs, and can improve their readability.

1.Introduction

The aim of the survey was to collect feedback on the current EUnetHTA Assessment Report template for Pharmaceutical technologies (PT). The final aim is to improve the quality and usability of EUnetHTA assessments and increase their adoption at the national/local level.

This survey was aimed at all the potential producers and users of EUnetHTA Joint Action 3 (JA3) PT assessments: members of assessment teams during JA3, EUnetHTA partners, and users of European HTA assessments.

The survey was launched June 17th 2020 and kept open till June 30th 2020, with an extension till July 13th 2020.

The survey responders were first asked to provide some overall feedback on the template, and thereafter feedback related to the specific template sections. At the end of the survey, some additional questions on template structure and content, and responders preferences, were included. In this report, detailed survey responses are reported following the structure of the survey. When cited, responses are reported without any kind of editing.

2.Responders

13 agencies (EUnetHTA partners) responded to the survey. Despite the focus on the five JAs which used the current template version (Table 3), the survey was not limited to members of those assessment teams.

Six responders were also users of Relative Effectiveness Assessments (REAs), while the remaining seven qualified themselves only as EUnetHTA partners.

All responders had participated as author, co-author, dedicated reviewer or observer in at least one PT assessment.
Four responders had experience in only one role, while six of them in two roles. The remaining three had experienced more than two roles.
The majority of responders had acted as dedicated reviewers at least one (n=12, 46.2%, Table 1). Five responders were authors at least once. Only one responder acted as project manager in an assessment. Five observers responded to the survey. Four of them were also dedicated reviewers.

Table 1. Role in assessments for pharmaceutical products during JA3

Role	N	%
Author	5	19.2%
Co-author	3	11.5%
Dedicated Reviewer	12	46.2%
Observer	5	19.2%
Project Manager	1	3.8%
Total	26	100.0%

One responder had participated only in one assessment (Table 2), whereas the majority (n=8, 61.6%) had contributed to three or more assessments.

Table 2. Number of assessments for pharmaceutical products during JA3 in which agency/organisation participated

N. of assessments	N	%
1	1	7.7%
2	4	30.8%
3	5	38.5%
More than 3	3	23.1%
Total	**13**	**100.0%**

Only three responders had not participated in any of the assessments of interest (PTJA04-06-07-08-09), i.e. assessments published during JA3 that had used the current Assessment Report template. The others had at least a role as a dedicated reviewer or an observer (Table 3). Five responders had been part of an authoring team.

Table 3. Did your agency/organisation participate in one of the following assessments?

Project ID	Title	Authoring team	Dedicated Reviewer / Observer
PTJA04	Sotagliflozin for adult patients with Type 1 Diabetes Mellitus who have inadequate blood glucose control using insulin or insulin analogues	2	1
PTJA06	Polatuzumab vedotin in combination with bendamustine and rituximab for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL)	1	3
PTJA07	Ustekinumab for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic, or have medical contraindications to such therapies	0	3
PTJA08	Siponimod for the treatment of adult patients with secondary progressive multiple sclerosis (SPMS) with active disease evidenced by relapses or imaging features of inflammatory activity	1	3
PTJA09	Brolucizumab for the treatment of adults with neovascular (wet) age-related macular degeneration (AMD)	1	3

3.Questions on overall feedback

According to responders, the current template is not yet optimal given difficulties in finding the information needed, presence of redundancies, and provision of relevant evidence for national adoption (Table 4). Level of detail and synthesis could be still improved.

Table 4. Ability of the current Assessment Report template to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information/is complete	3	69.2%	30.8%	1	1	2	5	4
Simple to use/to find the information needed	3	53.8%	7.7%	1	2	3	6	1
Able to provide relevant evidence for national adoption	3	76.9%	7.7%	1	1	1	9	1
Able to provide a useful level of evidence synthesis	3	76.9%	23.1%	0	1	2	7	3
Has an adequate level of detail	3	76.9%	15.4%	1	1	1	8	2
Is without redundancies	3	53.8%	7.7%	0	2	4	6	1
Uses clear wording	3	69.2%	15.4%	0	1	3	7	2

In addition, responders reported issues with consistency among assessments, methodology (i.e. on how to report meta-analysis) and level of details (data granularity) and, at the same time, ability to give relevance to most critical aspects) (Table 5).

Table 5. Collected responses on limitation of the current assessment template.

Issue	Responses
Usability	*The template is not easy to use (as an author), since no proper formatting has been performed. In general, the online tool is very difficult to work with (navigation/comments).*
Consistency	*I think that once there is greater consistency between the reports then it will be simple to use, but there are elements of each that I find easier to follow.*
Coherence	*Report template does not enable coherent reporting.*
Misalignment between Submission Dossier and Assessment Report	*It is not clear why the Submission Dossier does not match the assessment template. All tables included in the assessment template should also be included in the MAH file. Ideally, these two are identical, which would allow the authors to directly work in the submission file without having to copy paste and fill in additional tables e.g. information on the course of therapy.*
Reporting	*The examples for figures are scarce, and very open compared to tables. Perhaps the experts on meta-analysis could contribute with some instructions for future doers of assessments.*

Methodology	• *GRADE not included in each report.* • *In the Scope, no mentioning of Study designs or Time is included (PICOTS).* • *The examples for figures are scarce, and very open compared to tables. Perhaps the experts on meta-analysis could contribute with some instructions for future doers of assessments.*
Granularity of data	*The templates require a higher level of granularity, specifically in the section on results for effectiveness and safety, to ensure that all required content is provided.*
Find information	• *It is not clear from the headings where to find the relevant comparators. It would be beneficial to have a separate heading for the comparator and a description that it was agreed on a European basis with the other HTA agencies for transparency.* • *Descriptions are lacking to some extent on what is expected from authors, e.g. how to display indirect comparisons.* • *It is not clear where the supplementary search strategies should go.*
Transparency	*It is not clear from the headings where to find the relevant comparators. It would be beneficial to have a separate heading for the comparator and a description that it was agreed on a European basis with the other HTA agencies for transparency.*
Identify critical/relevant issues	*The template does not focus on critical and the most relevant issues. In lengthy and such detailed reporting, all important details are lost.*
Meet information needs	• *There is always likely to be some misalignment between our information needs and there will be more information redundancy than for those partners who have more of a REA focus in decision-making.* • *Costs and cost-effectiveness analyses may facilitate the adoption of the Assessment Report at the national level. It is clear, however, that it is not realistic to provide this type of information for all involved countries.*
Length	*The executive summary, if the instructions are followed to the letter, could be too long. In our opinion, tables should keep to a minimum in the executive summary.*

Despite there still being room for improvement (i.e. level of granularity, agreement on some methodological aspects) and its implications (i.e. required resources), the overall perception of the assessment template is positive (Table 6).

Table 6. Collected responses on current perception.

Issue	Responses
Positive perception	• *Good benchmark to follow.* • *The document is divided into sections, which enables good navigation throughout the document. Differences in national clinical practice are addressed by the PICO survey at the beginning of the assessment. The amount of evidence included is adequate and evaluated in an appropriate manner.* • *In general, the template is well structured.* • *Clear and well structured.* • *Useful, full of instructions, constrained as any template.* • *Includes all needed information.*
Provide a general overview	• *Gives a complete overview of evidence.*

Address relevant aspects	• *The current Assessment Report addresses the relevant aspects.*
Level of detail and length	• *From our point of view the templates requires a higher level of granularity, specifically in the section on results for effectiveness and safety, to ensure that all required content is provided. This would support authoring teams in providing the required content and readers to find what they are looking for. The Table of Contents should reflect the granularity to guide readers to the sections they are looking for.* • *It's too complicated, it takes too many resources.* • *The reports are long and the text remains quite dense in places (though an improvement on JA2).*
Methodology	• *The template suffers from the fact that a number of methodological questions are not solved within EUnetHTA.*
Alignment with national templates	*Subheadings do not reflect the format that we are used to applying in national assessments.*

Investigating the major limitations, responders identified: the need for a clearer guidance for authors in order to also improve uniformity among assessments, length, and the need for more clear conclusions. National adoption and different national requirements are among the main responder worries. (Table 7)

Table 7. Collected responses on major limitation(s) of current assessment template.

Issue	Responses
Guidance for authors	• *Due to lack of clarity, different agencies and assessors fill in the reporting template differently.* • *The template does not clarify the required content for the Assessment Report to a sufficient level of detail. This results in highly variable Assessment Reports (depending on the authoring team's interpretation of the requirements). It is difficult to prepare for use of Assessment Reports when the content to be expected is unclear.*
Consistency	*That two groups can interpret the template so differently. I would have expected that using a template would produce a more consistent output.*
Uniformity	*GRADE not always included.*
Adaptation	*Will need to adapt to local requirements to use the information.*
Need of more clear conclusions	*Unclear conclusions can be presented and without recommendations for use.*
Section specific aspects	*The methods section is too extensive.*
Missing data	*Missing cost and cost-effectiveness information.*
Duplication	*Duplications between summary and the body of the assessment.*
Length	*The report is too long to read. It should help a decision-maker, and it should be possible to read it (but of course keep the quality).*
Acceptable limitations	*No major limitations.*

Therefore, the aspects in which the current assessment template could improve are data analysis, adopted methods, and identification of strengths and limitations of evidence (Table 8-9).

Table 8. Ability of the current Assessment Report template to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Research question and scope (including inclusion/exclusion criteria)	4	92.3%	61.5%	0	0	1	4	8
Methods (i.e. information retrieval and study pool)	3	76.9%	46.2%	0	2	1	4	6
Data analysis and synthesis of study results	3	69.2%	38.5%	0	2	2	4	5
Results of individual studies	4	76.9%	61.5%	0	0	3	2	8
Identification of strengths and limitations of the evidence	4	84.6%	53.8%	0	1	1	4	7

Table 9. Open-ended answers on the ability of the current assessment template to cover specific aspects.

Issue	Responses
Specific areas of improvement (examples)	• *When GRADE is used, risk differences are presented in the summary of findings table. No mention of this kind of information in the assessment.* • *Scope does not include restrictions concerning study designs and/or timing, tables do not match the MAHs submission file.*
For further elaborations	*If some calculations had to be done to check results, I wouldn't know how to proceed to report them.*
Compare to other/national template	*The assessment combined with the company submission provides the information needed for the clinical effectiveness section of our work. The data analysis and synthesis of study results, and strengths and limitations, are marked down because of our specific information needs.*

On the aspects/sections which are well addressed by the current template, issues emerge again in terms of uniformity/consistency among different assessments. Some sections (i.e. scope and background) seem to be already well covered/addressed (Table 10).

Table 10. Collected responses on aspects/sections well addressed by the current template.

Issue	Responses
Scope and background	• *Scope and background.* • *The definition of the PICO and the characterisation of included studies are well addressed.* • *Research question and scope, identification of strengths and limitations of the evidence.*
Methods	*Methods*
Results	*Results*

Discussions	*Evidence description and limitations.*
On specific REAs	*I find that difficult to comment on as the assessments appear so different.*
Areas of improvement	*Indirect comparison should be addressed.*
Improvement compared to previous template	*Nice, concise tables, and redundant information has been removed in comparison to previous versions.*
Overall good perception	*Overall, we find the template appropriate.*

Different methodological aspects (i.e. indirect comparison, assessment of outcome data and evidence gap), involved by the current template, are perceived as being in need of urgent improvement. In general, guidance for authors is suggested in order to align method application.

Table 11. Collected responses on aspects/sections in need of urgent improvement.

Issue	Responses
Assessment of outcome data	*The presentation and assessment of outcome data need improvement.*
Evidence gap	*Reporting evidence gaps requires clarity.*
Indirect comparisons	*Reporting indirect comparisons needs clarity.*
Statistical aspects	*There is no separate statistics chapter - this should be added.*
Synthesis	*Everything needs to be simplified in order to find agencies to write the reports.*
Identify relevant aspects	*We should only present the most relevant results.*
Guidance for authors	• *Guidance for authors for what to include in the template to support better consistency seems far more important than making changes to the report structure.* • *Better instructions for Risk of Bias assessment*

The current assessment template is perceived as too long and detailed by the relative majority of responders (46.2%, Table 12). At the same time, for two responders (15.4%) it is too short and lack relevant evidence. Length is associated with difficulties in finding relevant data, and with data not being relevant for national decision-makers (Table 13). Differences between national templates are another potential barrier to adoption.

Table 12. Collected responses on impact of length of template on national/local adaptation.

Length of the Assessment Report template	N	%
Too long and detailed	6	46.2%
Of appropriate length and with an adequate level of detail	5	38.5%
Too short and lack relevant evidence and/or references	2	15.4%
Total	13	100.0%

Table 13. Open-ended responses on length of template.

Issue	Responses
Find relevant data	*Important details are difficult to find from the report.*
Limitation for national adaptation	• *Too detailed for national use* • *The length does not have to have an impact on decisions about adaptation by an HTA agency.*
Differences between the national templates	*We don't use GRADE, we don't have an Executive Summary AND Summary.*

4.Section-specific questions: Summary

When requested to rate ability to address specific aspects for each template section (Table 14), responses show how the Results, Discussion and Methods section are the most critical ones. These responses are aligned to those on the sections in need of revision. Methods and Results are the sections with major need of revision, followed by the Discussions and Executive Summary sections (Table 16).

Some common issues missing or not adequately addressed by more than one template section (Table 15) are: level of details, length of the document, and methodological issues as indirect comparison.

Guidance for authors emerged as a priority to address. Improvement of the clarity on goals of the sections and on comparators could guide revision of the template (Table 17).

Table 14. Ability of each section to address/cover specific aspects. . (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Executive Summary Section								
Includes all needed information – The section is complete	3	76.9%	46.2%	0	0	3	4	6
Easy to read and interpret	3	53.8%	38.5%	0	1	5	2	5
Able to summarise the most relevant evidence for national adoption	3	61.5%	30.8%	0	1	4	4	4
Background Section								
Includes all needed information- The section is complete	4	76.9%	53.8%	0	1	2	3	7
Able to provide relevant evidence for national adoption	3	76.9%	46.2%	0	1	2	4	6
Easy to read and interpret	4	84.6%	53.8%	0	1	1	4	7
Without redundancies	4	76.9%	53.8%	0	1	2	3	7
Objective and Scope Section								
Includes all needed information - The section is complete	3	76.9%	46.2%	0	0	3	4	6
Able to provide relevant evidence for national adoption	4	92.3%	53.8%	0	0	1	5	7
Easy to read and interpret	4	76.9%	61.5%	0	1	2	2	8
Without redundancies	4	84.6%	61.5%	0	1	1	3	8
Methods section								
Includes all needed information - The section is complete	3	69.2%	38.5%	0	1	3	4	5
Easy to read and interpret	3	61.5%	30.8%	0	2	3	4	4
Clear and transparent	3	61.5%	46.2%	0	2	3	2	6
Able to provide relevant evidence for national adoption	3	61.5%	38.5%	0	2	3	3	5
Relevant for the national context	3	69.2%	38.5%	0	2	2	4	5
Results section								
Includes all needed information - The section is complete	4	84.6%	53.8%	0	1	1	4	7
Easy to read and interpret	3	76.9%	38.5%	0	3	0	5	5
Able to provide relevant evidence for national adoption	3	76.9%	38.5%	0	2	1	5	5
Able to provide an useful level of evidence synthesis	3	76.9%	46.2%	0	2	1	4	6

With an adequate level of detail	3	69.2%	46.2%	0	2	2	3	6
Without redundancies	3	61.5%	30.8%	0	2	3	4	4
Covers the aspects needed in evidence based decision making	3	61.5%	30.8%	0	2	3	4	4
Discussions section								
Includes all needed information - The section is complete	4	76.9%	53.8%	0	1	2	3	7
Able to provide relevant evidence for national adoption	3	69.2%	38.5%	0	2	2	4	5
Easy to read and interpret	3	69.2%	38.5%	0	1	3	4	5
Clear and transparent	3	61.5%	38.5%	0	1	4	3	5
Without redundancies	3	69.2%	38.5%	0	2	2	4	5
Conclusions section								
Includes all needed information - The section is complete	4	69.2%	53.8%	0	2	2	2	7
Able to provide relevant evidence for national adoption	3	69.2%	38.5%	0	3	1	4	5
Easy to read and interpret	3	84.6%	46.2%	0	1	1	5	6
Clear and transparent	3	76.9%	46.2%	0	1	2	4	6
Without redundancies	3	76.9%	46.2%	0	1	2	4	6
Appendix section								
Includes all needed information - The section is complete	4	76.9%	53.8%	0	2	1	3	7
Able to provide relevant evidence for national adoption	3	69.2%	38.5%	0	1	3	4	5
Easy to read and interpret	3	69.2%	46.2%	0	2	2	3	6
Clear and transparent	3	69.2%	46.2%	0	1	3	3	6
Provides useful additional information to the Assessment Report	3	69.2%	46.2%	0	2	2	3	6
Without redundancies	3	61.5%	46.2%	0	1	4	2	6

Table 15. Collected responses on missing aspects or those inadequately addressed by each template section.

Executive Summary	Background	Objective and Scope	Methods	Results	Discussions	Conclusions
Too detailed	Comparator selection criteria	Comments on submission file/company position	Description of additional work done	Outcomes	Scope/Goal	Improve conclusions
Clarity in scope	Patient subgroups	Deviation from planned PICO	Data extraction	Description of studies	Uncertainty	Final recommendation
Discussions	Standard of care		Indirect comparison	Indirect comparison	Place in therapy	Separate Conclusions and Discussions

Conclusions	Differences in national approaches		Relevance for national adoption	Add section on report differences	Strengths and limitations	Indirect comparison
Guidance for authors			Lacking elements	Uniformity	Indirect comparison	
Relevance for national adoption			Proposal for elimination	Specific elements	To support adoption	
			On specific REAs	Guidance for authors	Length	
					Guidance for authors	

According to responders, Methods and Results are the sections with a major need of revision, followed by Discussions and Executive Summary sections.

Table 16. Responses on the need of revision of each section.

	Need revision	%
Executive Summary	5	38.46%
Background	3	23.08%
Objective and Scope	4	30.77%
Methods	8	61.54%
Results	8	61.54%
Discussions	7	53.85%
Conclusions	4	30.77%

Table 17. Collected responses on reasons for revision of each template section.

Executive Summary	Background	Objective and Scope	Methods	Results	Discussions	Conclusions
Scope	Discussion of clinical practice in European countries	Agreement on comparators	Information retrieval and data extraction	Selection of what to report in Results and Methods	Goal	Ongoing activities
Length	Justification for the comparators	Deviation from submission file	Indirect comparison	Indirect comparison	Discussion comparator-specific	Separate Conclusions and Discussions

Guidance for authors	Remove tables from Background Section		Level of uncertainty	Assessing tools	Strengths and limitations	Alignment to the template
User-friendly			Assessing tools	More detailed template	Indirect comparison	
			Guidance for authors	Appendix	Guidance for authors	
			Relevance for national adoption	Length		
			Consider for elimination	Guidance for authors		

5.Section-specific questions: Details

Executive Summary

The Executive Summary is not easy to read and interpret, according to responders. The need emerged to better summarise available evidence in order to support national adoption (Table 18 – Figure 1). To improve the Executive Summary, a guidance for authors could help (Table 19) to improve uniformity among REAs. Balance between a comprehensive and an overly detailed Executive Summary should be found (Tables 20-21). In just one case the Executive Summary was considered as not relevant for national adoption.

Table 18. Rating of the ability of the Executive Summary section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information - Executive Summary Section is complete	3	76.9%	46.2%	0	0	3	4	6
Easy to read and interpret	3	53.8%	**38.5%**	0	1	5	2	5
Able to summarise the most relevant evidence for national adoption	3	61.5%	30.8%	0	1	4	4	4

Figure 1. Rating of the ability of the Executive Summary section to address/cover specific aspects.

Table 19. Detailed responses on ability of the Executive Summary to address specific aspects.

Issue	Responses
Length	• *Executive summary is far too long.* • *The summary section is really good and usable. We could use the parts with the indirect comparisons and it saved us some time in our national report.*
On specific REAs	*I cannot really judge as the executive summaries are so very different.*

Table 20. Collected responses on the aspects the Executive Summary is well able to address.

Issue	Responses
Comprehensive	*Summary is comprehensive but far too detailed.*
Concise	*Concise overview on the overall assessment.*
Adequate given its goal	*The goal of the Executive Summary being an independently readable overview and the requirement of achieving this among other things by tabular presentation of results is addressed well.*
Able to report …	• *PICO, Methods, Results* • *Results* • *Scope of the assessment* • *The overall overview of efficacy and safety of the assessed product as well as limitations of the evidence.*
Not the primary aspect to improve	*I think the Executive Summary isn't something to worry about too much, but more guidance to authors on the level of detail to include would be good to improve consistency.*

Table 21. Collected responses on missing or inadequately addressed aspects the Executive Summary.

Issue	Responses
Too detailed	*Summary is comprehensive but far too detailed.*
Discussions	• *Strengths and limitations of studies, level of evidence.* • *No structure is suggested for the discussion and conclusion. At least for the discussion, bullet points suggesting what to address can be added. At the section conclusion, a reminder can be added in a grey box, indicating that appraisal is to be avoided.*
Conclusions	*Final conclusions*
Guidance for authors	• *The template of the Executive Summary might benefit from example text sections to help authors.* • *There are no instructions about length, number of words, number of tables, avoiding redundancies or duplicities, etc.*

Five out of 13 responders (38.46%) suggested to conduct a revision of the Executive Summary Section (Table 16).

Four out of 13 responders (30.77%) suggest to present the Executive Summary as a separate document. Answers were motivated as reported in Table 23. Executive Summary could be sufficient in some contexts, not in all.

Table 22. Suggestions to improve the Executive Summary.

Issue	Responses
Scope	*Tabulate the scope and include the scope in the Exec Summary. It is the item we all read first to judge relevance.*
Length	• *Summary needs to be much shorter and focus on the most relevant aspects and results of the assessment.* • *Instructions about the length.*
Guidance for authors	*The template of the Executive Summary might benefit from example text sections to help authors.*
User-friendly	*Needs to be more visual and reader-friendly.*

Table 23. Collected responses on the Executive Summary as a separate document.

Issue	Responses
WP7 Decision	*In one of the WP7 meetings it became clear that different agencies have different requirements concerning the length and level of detail of an Assessment Report. Having a full detailed Assessment Report plus an independently readable Executive Summary was identified as a solution to these diverging requirements.*
To meet user/decision maker needs	*For those to want to read a direct and short report/summary, it would be much easier to have a separate document instead of the longer version.*
Visual identity	*It is not needed but perhaps it could be designed to be visually different from the rest of the assessment. This could be helpful to identify the end of the summary.*
Not necessarily	• *Makes it more difficult, and if it can be used as a stand-alone summary of the whole assessment there is no need to have a separate document.* • *We suggest having it in the main report as well as in a separate document.*

Nine out of 13 responders (69.23%) are in favour of tables in the Executive Summary. In any case, the use of tables should be limited and they should be adequately designed to be informative (Table 24).

Table 24. Collected responses on tables in the Executive Summary.

Issue	Responses
Relevance of quantitative data	*For those agencies which mainly would work with the Executive Summary, the Executive Summary should provide the required numerical data. Presentation of numerical data is much clearer and more readable in a table format than in a text format.*

Table format useful for	• *For PICO, and in some cases, this might be needed to report results in tables.*
Limited use of tables	• *No tables should be in the summary.* • *If deemed necessary and if simplified, will probably help to better summarise the report and improve readability.* • *But only if their presence will considerably reduce the text length and redundancy between text and tables is low.*
Associated risks	*Links to tables in Results section should be enough. It is risky to have them in the executive summary: a lazy reader could look at these tables and do not pay attention to other relevant information in other tables or in the text. It makes the summary too long.*

Background

The Background section is not always able to provide relevant evidence for national adoption (Table 25 – Figure 2). Collected suggestions from improvements are different and not homogenous (Table 26). Criteria adopted to identify and choose comparators should be better explained (Table 28). At the moment, the Background section is already able to introduce the disease and interventions (Table 27). Only two out of 13 responders (23.08%) suggested to conduct a revision of the Background Section (Table 16). Revision should focus on comparators and introduction/discussion of clinical practice among EU partners (Table 29).

Table 25. Rating of the ability of the Background section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	%3-4	%4	N				
				0	1	2	3	4
Includes all needed information - Background Section is complete	4	76.9%	53.8%	0	1	2	3	7
Able to provide relevant evidence for national adoption	3	76.9%	46.2%	0	1	2	4	6
Easy to read and interpret	4	84.6%	53.8%	0	1	1	4	7
Without redundancies	4	76.9%	53.8%	0	1	2	3	7

Figure 2. Rating of the ability of the Background section to address/cover specific aspects.

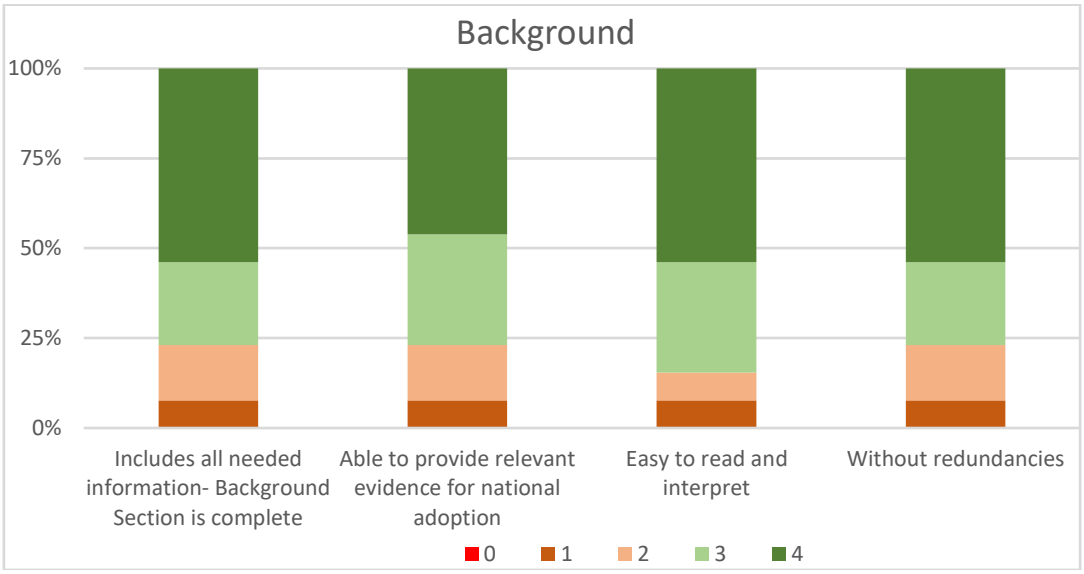

Table 26. Detailed responses on ability of Background to address specific aspects.

Issue	Responses
Length	*Too extensive.*
Level of detail vs. national adoption	*In most cases we will need to add local epidemiology and clinical information, and so in this case we only require basic background information about the technology and disease, and enough clinical and epidemiological information to understand how the authors got to the PICO in the assessment.*
Different national criteria	*We also take into account for our national assessments the actual use of comparators. Thus, the most commonly used in clinical practice is also of interest for our national procedures.*

Table 27. Collected responses on the aspects the Background section is able to address well.

Issue	Responses
Comprehensive	*Comprehensive and includes all relevant information.*
Help to understand the disease and intervention	• *Understanding of disease and current treatment.* • *Features of the intervention are addressed well.* • *The epidemiology, clinical practice and overview of the product.*
To work on the level of detail	*It is more a question of providing guidance about the level of detail required in the content.*

Table 28. Collected responses on missing or not adequately addressed aspects in the Background section

Issue	Responses
Comparator selection criteria	*From the background section it should be clear how the authors got to the comparators in the scope.*
Patient subgroups	*Missing: Information on relevant patient subgroups and respective prevalence and incidence should be provided.*
Standard of care	*Missing: Provide information on relevant maintenance dosage for the standard of care.*
Differences in national approaches	*If there are important differences across member states, this should be addressed.*

Table 29. Suggestion to improve the Background section.

Issue	Responses
Discussion of clinical practice in European countries	*We don't feel that an overview of clinical practice in European countries should be a requirement of a joint Assessment Report. Providing this overview is a high workload for the assessment team and it is unclear what this description adds for use in the national context.*
Justification for the comparators	*Ask authors to link between the clinical section and the scope.*

Objective and Scope

Despite being able to provide relevant evidence for national adoption, the content of the Objective and Scope section is not always uniform and its scope is not always clear to EUnetHTA partners/authors (Table 30 – Figure 3). Four out of 13 responders (30.77%) suggest to conduct a revision of Objective and Scope Sections (Table 16).
In particular, comparison with the submission file (and manufacturer perspective) and deviance from planned PICO would be considered relevant (Table 33). At the same time, how comparators are identified and how agreement on them was reached should be better reported (Table 34). In addition, a clearer guidance to author would help to avoid different approaches in different REAs (Table 31).

Table 30. Rating of the ability of the Objective and Scope section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information - Objective and Scope Section is complete	3	76.9%	46.2%	0	0	3	4	6
Able to provide relevant evidence for national adoption	4	92.3%	53.8%	0	0	1	5	7
Easy to read and interpret	4	76.9%	61.5%	0	1	2	2	8
Without redundancies	4	84.6%	61.5%	0	1	1	3	8

Figure 3. Rating of the ability of the Objective and Scope section to address/cover specific aspects.

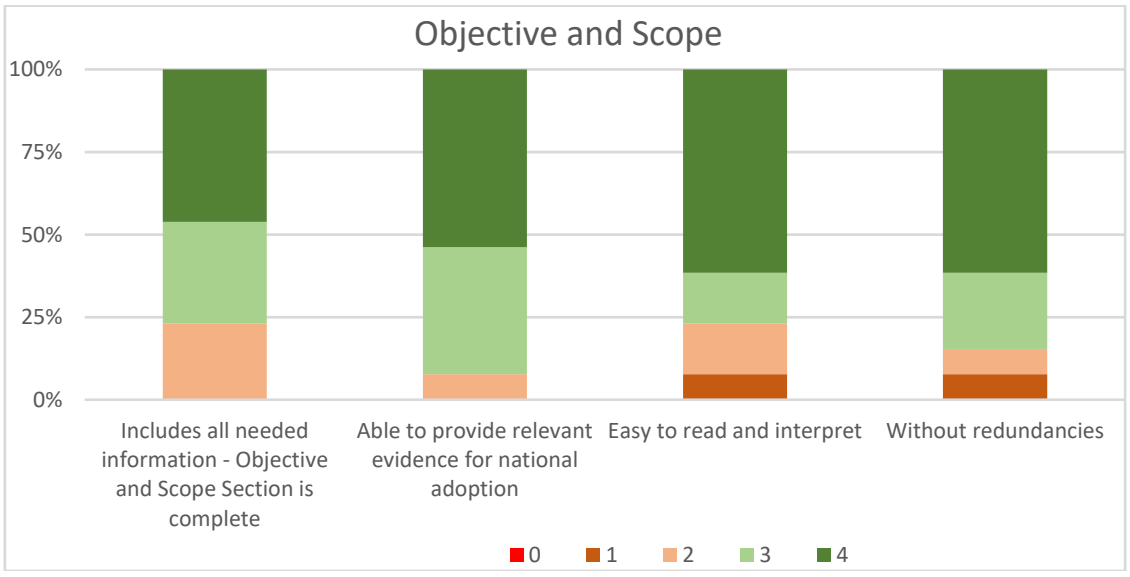

Table 31. Detailed responses on ability of Objective and Scope to address specific aspects.

Issue	Responses
Relevance of provided information	*If the scope is relevant then it gives us the information we need.*
Lacking aspects	• *We need a rationale for deviations from the company submission as well.* • *A better description of how to manage subgroup analyses is lacking.*
Guidance for authors	• *No proper guidance when to restrict to specific study designs or time points, and thus no common approach within EUnetHTA.*

Table 32. Collected responses on the aspects the Objective and Scope section is able to address well.

Issue	Responses
PICO	• *PICO format seems to work and scoping basically works* • *The clear relation of the Assessment Report PICO to the Project Plan PICO is addressed well*
Outcomes	*Outcomes*
Objective	*It is fine concise way of summarising the overall objective*

Table 33. Collected responses on missing or inadequately addressed aspects in the Objective and Scope section.

Issue	Responses
Comments on submission file/company position	• *Comparison on Company position and EUnetHTA position is currently lacking.* • *To understand the judgements the authors made we need to know deviations from the Project Plan and from the company submission so that users can understand why these deviations were made. This has become important to record in EUnetHTA assessments because the company submissions are published and so we need to know on what basis the authors made their decisions about comparators, outcomes, etc.*
Deviation from planned PICO	• *The deviation from the planned PICO could be better described after presentation of the planned PICO.* • *To understand the judgements the authors made, we need to know deviations from the ProjectPplan and from the company submission so that users can understand why these deviations were made.*

Table 34. Suggestion to improve the Objective and Scope section.

Issue	Responses
Agreement on comparators	*It needs to be clarified that the comparators are agreed on the EU level.*
Deviation from submission file	*Minor change to add deviations from company submission.*

Methods

The Methods section could be improved in terms of included data and its presentation, which are unclear to read (Table 35 – Figure 4). Critical appraisal of submission file and additional work performed by the authoring team should clearly emerge (Table 38). At the same time, guidance for authors would help to align methods among REAs and better interpret the section.

Eight out of 13 responders (61.54%) suggest to conduct a revision of the Methods Section (Table 16). Suggestions for revisions involve an information retrieval part, analysis/discussion on uncertainty of the evidence, and guidance for authors. Elimination of some sub-headings/sections has been proposed. The Methods section is redundant for only one responder.

Table 35. Rating of the ability of the Methods section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information - Methods section is complete	3	69.2%	38.5%	0	1	3	4	5
Easy to read and interpret	3	61.5%	30.8%	0	2	3	4	4
Clear and transparent	3	61.5%	46.2%	0	2	3	2	6
Able to provide relevant evidence for national adoption	3	61.5%	38.5%	0	2	3	3	5
Relevant for the national context	3	69.2%	38.5%	0	2	2	4	5

Figure 4. Rating of the ability of the Methods section to address/cover specific aspects.

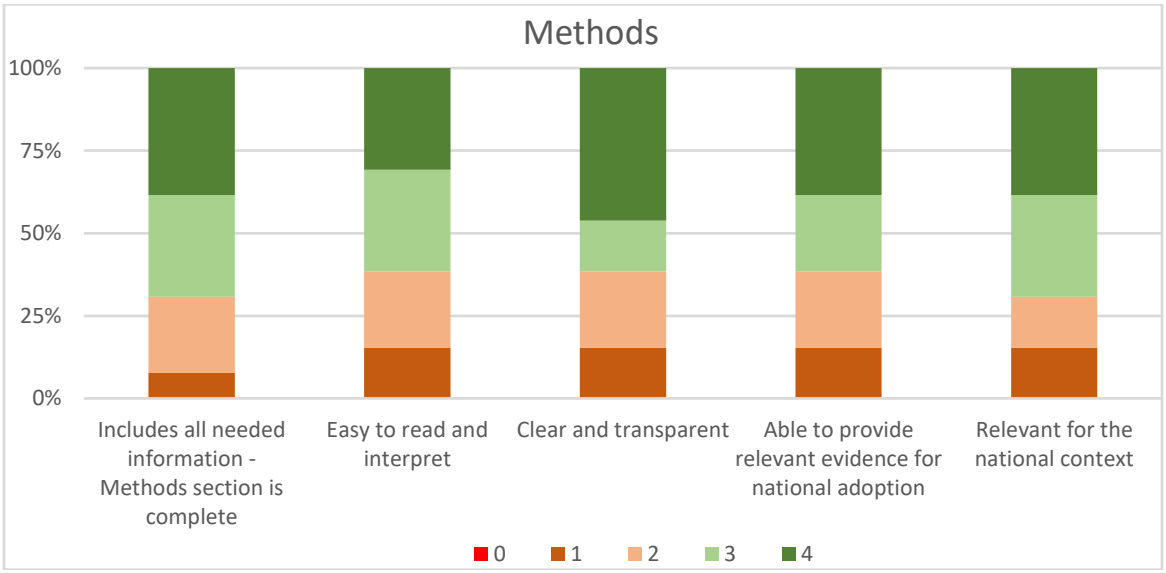

Table 36. Detailed responses on ability of Methods to address specific aspects.

Issue	Responses
Guidance for authors	*It seems as this section is hardly ever changed by authors. More detailed guidance on what is actually expected should be provided.*
Too short	*In general, the individual chapters are very brief.*
National templates	*In national assessments we don't have a comparable chapter.*

Table 37. Collected responses on the aspects the Methods section is able to address well.

Issue	Responses
Complete	*Methods section is complete.*
Not a problem with template but with its interpretation	*The template itself is okay, but there seems to be a problem with how the authors interpret it.*
Methods	*Literature search description, methods for risk of bias evaluation, description of evidence synthesis.*
Study selection	*Summary of information retrieval and study selection submitted by the MAH.*
Results	*Results and analyses of included studies.*

Table 38. Collected responses on missing or inadequately addressed aspects in the Methods section.

Issue	Responses
Description of additional work done	*The EUnetHTA report is a critical appraisal of a company submission that may include additional literature reviews and evidence synthesis. It should be more clear where:* *- The text is EUnetHTA critical appraisal.* *- Any additional work done by EUnetHTA.*
Data extraction	*Better information on data extraction.*
Indirect comparison	*Indirect comparison to be performer by EUnetHTA when relevant.*
Relevance for national adoption	*Too extensive. Not needed nationally.*
Lacking elements	• *We should discuss level of uncertainty in the results.* • *An evaluation of the limitation of the overall body of evidence derived from the included studies could be added.* • *Where is the section to report differences, if any, between meta-analysis by MAH and meta-analysis by reviewers.*
Proposal for elimination	*For us we can remove: Information retrieval - Data extraction - Risk of bias assessment.*

Table 39. Suggestions to improve the Methods section.

Issue	Responses
Information retrieval and data extraction	*Information retrieval and data extraction are poor subheadings and it is difficult to know what should be reported under these headings.*
Indirect comparison	*Indirect comparison to be performer by EUnetHTA when relevant.*
Level of uncertainty	*We should discuss level of uncertainty in the results.*
Assessing tools	• *The new RoB2 tool from Cochrane is available.*
Guidance for authors	• *There are a number of methodological questions which would need clarification within EUnetHTA. Currently, these are solved by authoring teams on an ad hoc basis.* • *Probably to improve guidance for authors.* • *The template refers to the Cochrane Risk of Bias from 2011, whereas the Risk of Bias - 2 tool is now available.* • *Instructions for coping with and reporting the differences between findings by reviewers and data included in the Submission Dossier.*
Relevance for national adoption	*Too extensive. Not needed nationally.*

Results

Redundancies and relevance of analysed aspects to support evidence-based decision-making are the most critical aspects for the Results section of the current assessment template (Table 40 – Figure 5). Eight out of 13 responders (61.54%) suggested to conduct a revision of Results Sections (Table 16). A specific guidance for authors able to clearly define what to report in Results and in Methods would help (Table 41). Table 43 reports most critical methodological aspects to agree on having for a more useful Results section (i.e. study description, indirect comparison).

Table 40. Rating of the ability of the Results section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information - Results section is complete	4	84.6%	53.8%	0	1	1	4	7
Easy to read and interpret	3	76.9%	38.5%	0	3	0	5	5
Able to provide relevant evidence for national adoption	3	76.9%	38.5%	0	2	1	5	5
Able to provide an useful level of evidence synthesis	3	76.9%	46.2%	0	2	1	4	6
With an adequate level of detail	3	69.2%	46.2%	0	2	2	3	6
Without redundancies	3	61.5%	**30.8%**	0	2	3	4	4
Covers the aspects needed in evidence-based decision-making	3	61.5%	**30.8%**	0	2	3	4	4

Figure 5. Rating of the ability of the Results section to address/cover specific aspects.

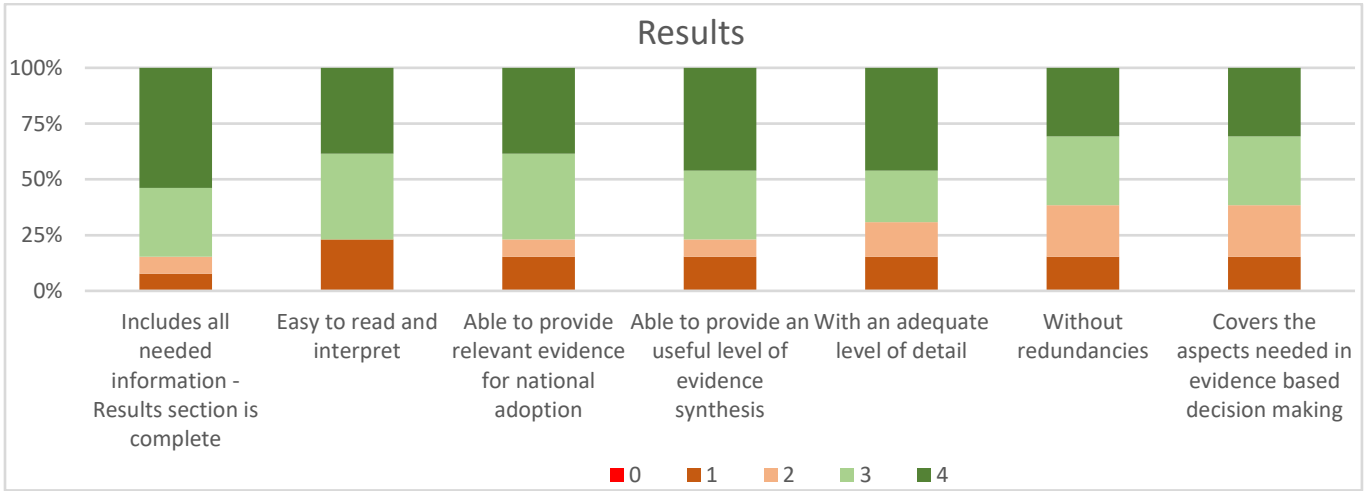

Table 41. Detailed responses on ability of Results to address specific aspects.

Issue	Responses
Selection of what to report in Results and Methods	*Results are too much focussed on information retrieval. These should be reported in the Methods section. The results should only cover the clinical results of the pharmaceutical under assessment.*
Outcome results	*The requirements for (outcome) results presentation are not sufficiently clear in the template. This might mainly be due to the fact that there still is no consolidated view within EUnetHTA on this question.*
Specific tables	*Tables 9 and 10 could be merged.*

Table 42. Collected responses on the aspects the Results section is able to address well.

Issue	Responses
Comprehensive/ Complete	• *Section is basically comprehensive.* • *Includes all needed information.* • *Generally well addressed.*
Concise	*Concise overview on the most important findings.*
Studies	• *Studies characteristics and efficacy/safety results* • *The studies included in the assessment and the characterisation of included studies are addressed well.* • *Characteristics of the studies included, risk of bias, results on clinical effectiveness when provided data is from controlled studies only.*
Tables/Graphs	• *The tables and graphs are helpful.* • *Tabulated evaluation of evidence and risk of bias.*
Guidance for authors	*Instructions for Tables*

Table 43. Collected responses on missing or not adequately addressed aspects in the Results section.

Issue	Responses
Outcomes	*Make it clearer which outcomes should actually be displayed here.*
Description of studies	• *Description of pivotal studies is not clear. A better description of the actual study design is lacking, including statistical considerations.*
Indirect comparison	*Indirect comparison*
Add section on…	*Where is the section to report differences, if any, between meta-analysis by MAH and meta-analysis by reviewers?*
Uniformity	*The required level of detail and the structure of results presentation are not clear from the template. This leads to highly variable data presentation which makes the planning of use of the Assessment Reports difficult (it is unclear what to expect from a report).*

Specific elements	• *Table 8 - patient population: no clear mention of exclusion criteria.* • *Table 8 - why is there indirect evidence mentioned and then in no other table? Decide on how/where indirect comparisons are displayed* • *Table 10 - treatment duration for each outcome separately.*
Guidance for authors	• *We need suggestions for authors how to present results regarding NMA and uncontrolled studies, as latter are provided by MAH.* • *Instructions for figures.* • *Patients section would benefit from more instructions, the link to a SOP, or some other guide.*

Table 44. Suggestion to improve the Results section.

Issue	Responses
Selection of what to report in Results and Methods	*Results are too much focussed on information retrieval.*
Indirect comparison	*Indirect comparison*
Assessing tools	*The table/text reflects the 2011 risk of bias taken, whereas it should now reflect the Cochrane RoB-2 tool of 2019.*
More detailed template	*From our point of view, we need more clarity on the structure of results.*
Appendix	*Perhaps I would put the table with excluded studies in the annex.*
Length	*Only the most relevant outcome measures should be there.*
Guidance for authors	*Guidance for authors.*

Discussions

Criticalities of the Discussions section deal more with data presentation than on the content itself (Table 45 – Figure 6). Seven out of 13 responders (53.85%) suggested to conduct a revision of the Discussions Section (Table 16).
For the Discussions section, the major suggestions provided by responders for improvement are to provide a clearer final message on available evidence – in general and comparator specific - for decision-making, and to clearly report areas of uncertainty (Table 48). A guidance for authors would help uniformity among REAs and give a clearer perception of the goal of the Discussions section.

Table 45. Rating of the ability of the Discussions section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information - Discussions section is complete	4	76.9%	53.8%	0	1	2	3	7
Able to provide relevant evidence for national adoption	3	69.2%	38.5%	0	2	2	4	5
Easy to read and interpret	3	69.2%	38.5%	0	1	3	4	5
Clear and transparent	3	61.5%	38.5%	0	1	4	3	5
Without redundancies	3	69.2%	38.5%	0	2	2	4	5

Figure 6. Rating of the ability of the Discussions section to address/cover specific aspects.

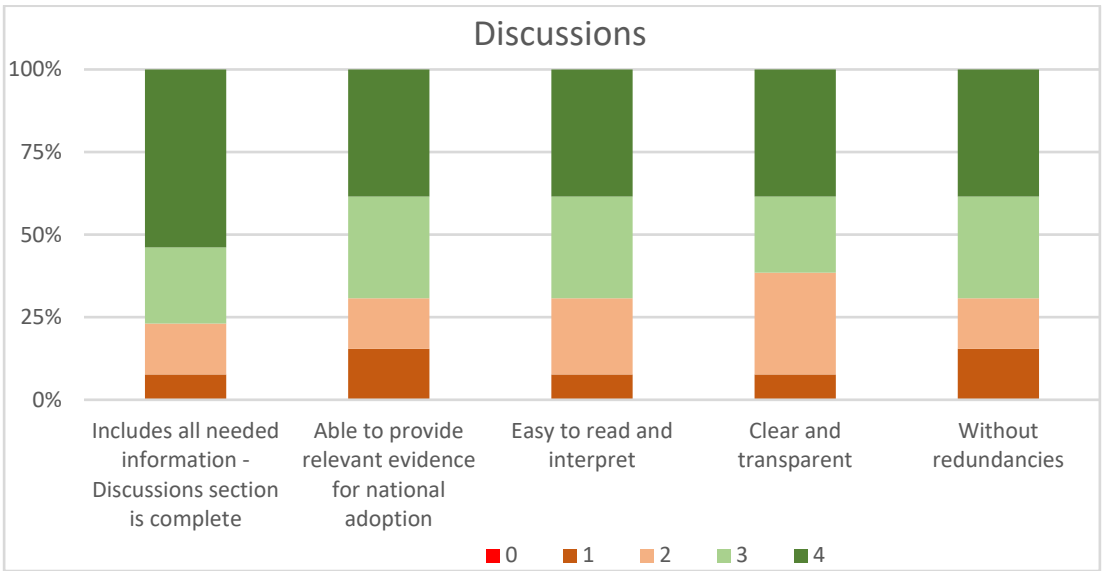

Table 46. Detailed responses on ability of Discussions to address specific aspects.

Issue	Responses
Specific for comparator	*It's important that the reader can see at a first glance what the conclusions are per comparator.*
Synthesis	*I liked the bulleted nature of the discussion and conclusions.*
Unclear goal	*The goal of the discussion section is unclear.*
Length	*Good with quite a clear structure, but too long.*

Table 47. Collected responses on the aspects the Discussions section is able to address well.

Issue	Responses
Limitations	*Highlighting the most important limitations.*
Clarity	*This section provides a clear summary of the evidence and shortcomings.*
Comprehensive	*All main aspects are covered.*
None	*None in particular.*

Table 48. Collected responses on missing or inadequately addressed aspects in the Discussions section.

Issue	Responses
Scope/Goal	*The goal and thus required content of this section is unclear.*
Uncertainty	*The Discussions section should outline all the concerns and uncertainties found during the assessment.*
Place in therapy	*This section is now too much focussed on replicating some results already reported in results section.*
Strengths and limitations	*Subheadings for strengths and limitations, short overview of overall results.*
Indirect comparison	*Indirect comparison.*
To support adoption	*More recommendation information for use the assesses technology in the report will be useful.*
Length	*An indication of expected length of the discussion might prove helpful.*
Guidance for authors	*I think again it is the guidance for authors about how far they can go.*

Table 49. Suggestion to improve the Discussions section.

Issue	Responses
Goal	*The goal and content of the discussion section should be clarified.*
Discussion comparator-specific	*Should be clearly structured to each relevant comparator.*
Strengths and limitations	*Subheadings strengths, limitations*

Indirect comparison	*Indirect comparison*
Guidance for authors	*Guidance for authors and a position from EUnetHTA.*

Conclusions

For the Conclusions section the main issue is the selection of contents (Table 50-51). Attention to both relevance of evidence for decision-making, clear recommendations, and transparency of conclusion is requested (Table 51-52-53-54).
Only four out of 13 responders (30.77%) suggest to conduct a revision of Conclusions sections (Table 16).

Table 50. Rating of the ability of the Conclusions section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information - Conclusions section is complete	4	69.2%	53.8%	0	2	2	2	7
Able to provide relevant evidence for national adoption	3	69.2%	38.5%	0	3	1	4	5
Easy to read and interpret	3	84.6%	46.2%	0	1	1	5	6
Clear and transparent	3	76.9%	46.2%	0	1	2	4	6
Without redundancies	3	76.9%	46.2%	0	1	2	4	6

Figure 7. Rating of the ability of the Conclusions section to address/cover specific aspects.

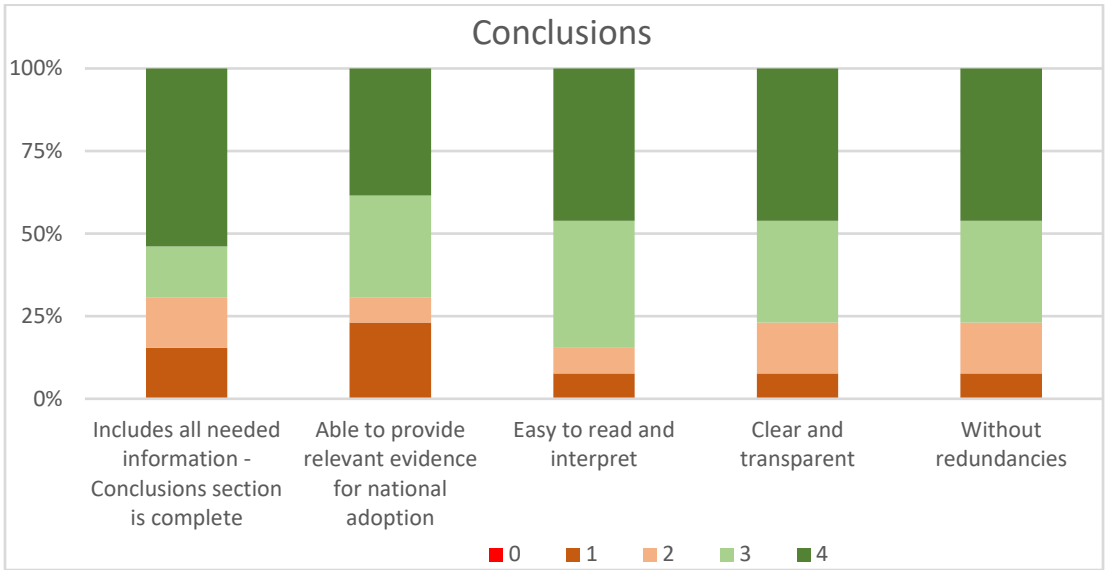

Table 51. Detailed responses on ability of Conclusions to address specific aspects.

Issue	Responses
Ongoing activities	*Need to define how it could best conclude in a joint assessment in the Common Phrases task group.*
Separate Conclusions and Discussions	*Conclusion and discussion should be separate in order to clarify to the reader, otherwise it's very unclear what is what.*
Positive feedback	*The conclusion section is clear.*

Table 52. Collected responses on the aspects the Conclusions section is able to address well.

Issue	Responses
Transparent	*Section is transparent and usually quite short, which is good.*
Short/Concise	• *Short conclusion of evidence included.* • *Concise overview on the overall assessment.*
Acceptable	• *These are reasonable.* • *Generally, well addressed.* • *Clear results of evidence.* • *This section provides a clear summary of the evidence and shortcomings.*

Table 53. Collected responses on missing or inadequately addressed aspects in the Conclusions section.

Issue	Responses
Improve conclusions	*Conclusion section should be conclusive.*
Finale recommendation	*Clear recommendation to use the technology.*
Separate Conclusions and Discussions	*Should have separate discussion and conclusion section.*
Indirect comparison	*Indirect comparison.*

Table 54. Suggestion to improve the Conclusions section.

Issue	Responses
Ongoing activities	*It still needs to be defined how we could best conclude in a joint assessment in the Common Phrases task group.*
Separate Conclusions and Discussions	*Should have separate discussion and conclusion section.*
Alignment to the template	*Authors need to abide by the template.*

Appendix

The Appendix section is not always able to provide relevant evidence for national adoption (Table 55 – Figure 8). In addition, time and workload requested by specific table is a debated issue (Table 56). In addition, the role and relevance of national guidelines should be better explained/clarified.

Table 55. Rating of the ability of the Appendix section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information - The Appendix section is complete	4	76.9%	53.8%	0	2	1	3	7
Able to provide relevant evidence for national adoption	3	69.2%	**38.5%**	0	1	3	4	5
Easy to read and interpret	3	69.2%	46.2%	0	2	2	3	6
Clear and transparent	3	69.2%	46.2%	0	1	3	3	6
Provides useful additional information to the Assessment Report	3	69.2%	46.2%	0	2	2	3	6
Without redundancies	3	61.5%	46.2%	0	1	4	2	6

Figure 8. Rating of the ability of the Appendix section to address/cover specific aspects.

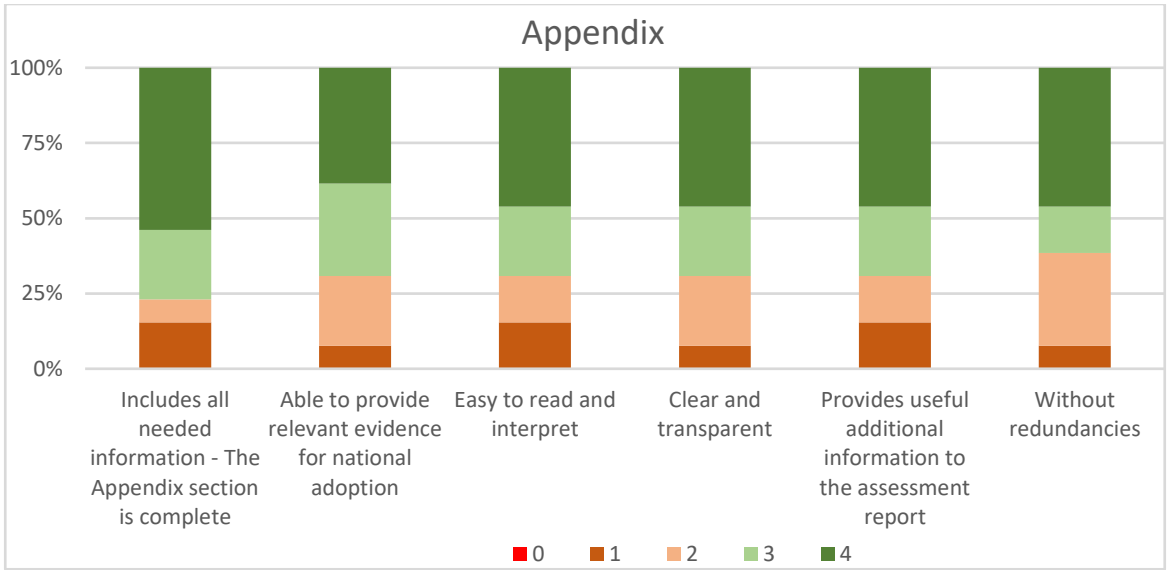

Table 56. Detailed responses on ability of Appendix to address specific aspects.

Issue	Responses
Evidence gaps	• *Appendix related to evidence gaps: This should be fully revised.* • *We feel the evidence gaps table is too extensive.* • *Appendix 3 (evidence gap) including recommendation for research is extremely interesting. However, we are not sure if this should be part of the Assessment Report as it is an additional time-consuming task.*
National guidelines	• *We are not sure that description of national guidelines adds to the report.* • *It can not be expected that all guidelines will be mentioned that may be relevant for national update (Appendix 1).*
Additional analysis	*I think the appendices are broadly fine. There seems to be some inconsistency with the amount of additional analysis that authors do.*
Flexibility	*Perhaps the appendix section should be a more open so [assessment] doers can add other appendixes not included in the template (as far as we see there is no instructions in the appendix section indicating that other appendixes can be added).*

6.Questions to authoring teams of PTJA04-09

Five agencies/organisations responded to Section 6. This survey section was only for authoring teams of PTJA04-09 (as specified in the survey).

In three out of five cases, challenges in using the Assessment Report template have been reported. Challenges are reported in Table 57. Again, a need for more detailed guidance for authors emerged.

Table 57. Main challenges encountered by authoring teams of PTJA04-09.

Issue	Responses
Differences compared to national templates	*The template does not follow the logic of national reports.*
Guidance for authors	• *It is sometimes difficult to know where (under which subheading, etc.) some of the information should be reported.* • *There was the need for discussion with co-authors because the requirements for data presentation were not clear.*
Length	*Too extensive.*

Only in one case (out of five) were difficulties in completing any of the requested tables mentioned. The issue was that table template does not fit for all purposes.

Three out of five responders consider the Submission Dossier template is not aligned with the Assessment Report template. Reasons of misalignment are reported in Table 58.

Table 58. Reasons why the Submission Dossier template was percevied as misagligned with the Assessment Report.

Issue	Responses
Project Plan	*The Submission Dossier did not consider the PICOs defined in the Project Plan.*
Headings	*Not the same headings.*

7.Questions to help formulate recommendations for a future template

This survey section was created to help us to better formulate some recommendations for the future revision of the Assessment Report template.

Submission Dossier

All 13 responders consider the publication of the Core Submission Dossier to be useful, in addition to the EUnetHTA Assessment Report. Table 59 reports motivation of the usefulness which range from transparency to support for national adoption.

Table 59. Reasons why the publication of the Core Submission Dossier is perceived useful.

Issue	Responses
Transparency	• *The publication of the Core Submission Dossier is required for transparency reasons. In addition, this helps avoiding lengthy duplication of dossier content (e.g. for explanation why the team deviated from the MAH's point of view) in the Assessment Report.* • *For us, we need it for transparency in case of a challenge to the decision.*
Support in national adoption	*It would be useful for transparency reasons and the external audit of our work as HTA agencies, but it shouldn't prevent us to synthesize and include in the assessment all the relevant data in the dossier.*
Useful information source	*Even though it is not really clear when a mere reference to the CSD is ok, the dossier is an important information source.*
Clarity in templates	*Having well structured and clear templates is always useful.*

11 out of 13 responders (84.62%) perceived the publication of the Core Submission Dossier for national adaption or re-use of REAs. Table 60 reports motivations.

Table 60. How the publication of the Core Submission Dossier would help national adoption.

Issue	Responses
Legal requirement	*Public availability of the Submission Dossier is a legal requirement at the national level.*
Potentially useful	*It might be used for national adaptation too.*
Useful with integrations	*For us, the assessments would be more useful if an (indirect) comparison was always made with the effectiveness of therapeutic alternatives and with the Standard of Care (SOC).*
Not necessary	*It is not a barrier but it is not needed either.*

Table 61 reports the rate results of alternative proposals to link the Assessment Report to the Core Submission Dossier (0=not useful, 4= fully useful). Reporting all relevant information in the Assessment Report emerged as the preferred solution, followed by the provision of a summary of the Core Submission Dossier.

Table 61. Proposal for linking Assessment Report to Core Submission Dossier. (0=not useful, 4=fully useful)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
In the Assessment Report, we should refer to the Core Submission Dossier as much as possible, and avoid repeating information that is already reported in the Core Submission Dossier	2	38.5%	15.4%	**3**	2	3	3	2
In the Assessment Report, we provide a summary of the Core Submission Dossier and reference to the Submission Dossier when necessary	3	61.5%	30.8%	1	1	3	**4**	**4**
We report all relevant information in the Assessment Report	3	61.5%	38.5%	**3**	1	1	3	**5**

Table 62. Open ended responses on proposal for linking Assessment Report to Core Submission Dossier.

Issue	Responses
Key role of Assessment Report	• *Refer as much as possible, but all necessary information to understand assessment should be in the Assessment Report.* • *The Assessment Report should be a stand-alone product, otherwise one has to check both documents due to the cross-referencing.*
Selection of what to report in the Assessment Report	• *We agree that using too much information of the Core Submission Dossier in the Assessment Report may reduce its readability. The reported information should be limited to the most relevant points and authors should refer to the Submission Dossier for more detailed descriptions.* • *There is no need to report all relevant information in the Assessment Report if links to the submission dosser are given.*
Case specific	*The information that needs to be duplicated from the Submission Dossier depends on the situation.*
Uniformity	*Moreover, is our mission to make homogenous reports that should include all the relevant data for the reader be able to find everything in one single document.*
Appraise data reported in the submission file	*If we refer to the Submission Dossier, we are endorsing the information included there instead of appraising them.*
Attention to invalid data	*However, any data that were assessed to be invalid would not have to be included but could just be referenced.*

Template structure

There is no agreement on how evidence should be reported in a EUnetHTA assessment (Table 63).

Table 63. Preferences on how should evidence be reported in REAs.

	N	%
At PICO level, providing available data explicitly for each PICO element as in Sections 4.6-4.7 of the Assessment Report in PTJA06.	7	53.85%
At study level, organising the assessment around available studies, as in the Assessment Report of PTJA09.	6	46.15%

Lack of agreement matches with difficulties in understanding the two proposed solutions (Table 64). National differences, multiple PICOs, and the need to adapt the approach to the specific assessment are the main (confounding) factors that emerged.

Table 64. Open-ended responses on how evidence should be reported.

Response	Issue	Responses
At PICO level		*Our answer may be influenced by the number of PICOs and the available studies.*
		If it is possible to build data for each PICO, this should be done. We have to try to synthesise data to be useful for the reader. If this is not possible, for example because pf heterogeneity, then the presentation of data study-by-study is an option.
At study level	National differences	*PICOs vary too much between countries.*
Not a unique approach if possible		*It is difficult to choose one of the suggested approaches.*
Other solutions	To be inclusive	*We wanted to tick both boxes here but that was not possible. We see that different countries have different requirements with regard to this question.*
Unclear		*I don't really understand this difference.*
		We don't really understand the difference between the two modes of presentations.

11 out 13 responders (84.62%) considered it useful to have a specific section dedicated to Comparators.
The section would cover selection of comparators, available data provided for each of them in the Submission Dossier, etc. That section would help at the national level.

Table 65. Open ended responses on a section dedicated to Comparators.

Issue	Responses
Available data	*We are not entirely sure what is meant here. However, a description what data is available versus what comparator would be helpful.*

Transparency and Agreement on choice of comparators	*It should be clear that the choice of the comparators has been agreed at the EU level.*
Need to clarify the proposal	*I don't think I understand the question. For direct comparisons we will have the relevant data for the comparator, for indirect comparisons you need the available data for the comparators to review the indirect comparison.*
Objective and Scope already address that	*This should be covered in Current clinical practice and Objective and Scope.*
Other	*Knowing that additional data may be available in the Submission Dossier may be of interest.*

To report results separately for each kind of conducted data source/analysis is perceived as useful (0=not useful, 4= fully useful). (Table 66).

Table 66. Preferences on report separately each kind of data source. (0=not useful, 4=fully useful)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Pivotal studies	3	84.6%	46.2%	0	0	2	5	6
Meta analysis	4	76.9%	53.8%	1	0	2	3	7
Indirect comparisons	4	84.6%	61.5%	0	0	2	3	8

Feedback on the question on results reported separately per each data source are visible in Table 67.

Table 67. Open-ended responses on reporting separately each type of data source.

Issue	Responses
Stratification of results	• *Results stratified according to data source/analysis may be helpful (for example it may be possible to identify sources/analyses more relevant for the country of interest).* • *They do not have to be reported separately but the type of study must be easily identified.*
Direct vs. Indirect Comparison	• *We would include direct comparisons and then meta-analysis and then in a separate section indirect comparisons. We would also have separate sections for randomised versus non-randomised data because the methods to critique these data are different.* • *Usually meta-analysis is not available for new products. However, a separate chapter on direct evidence and indirect evidence should be provided.*
Data source vs. PICO	*This is unclear to us. The results should be reported separately by research question (PICO). In practice, this often results in different data sources for different PICOs. It would be helpful if the Assessment Report template would provide a "module" for each type of data source/analysis.*

8.Final comments

Table 68 reports the final comments collected. Information from the Companion Guide could be incorporated in the assessment template. However, the Companion Guide is rather lengthy and then often not really clear. So, a shortened version with the most relevant information might be good.

Table 68. Final comments.

Issue	Responses
Simplify	*We need to simplify the template.*
Companion Guide	*Information from the companion guide could be incorporated in the assessment template. However, the companion guide is rather lengthy and then often not really clear.*

9.Sub-analyses on feedback provided by authoring agencies

We have conducted a dedicated analysis of responses provided by the five authors. All of them have significant experience in REAs as indicated in Tables A1 and A2.

Table A1. Number of assessments for pharmaceutical products during JA3

N. of assessments	N	%
1	0	0.00%
2	0	0.00%
3	3	60.00%
More than 3	2	40.00%
Total	**5**	**100.00%**

Table A2. Did your agency/organisation participate in one of the following assessments?

Project ID	Title	Authoring team	Dedicated Reviewer / Observer
PTJA04	Sotagliflozin for adult patients with Type 1 Diabetes Mellitus who have inadequate blood glucose control using insulin or insulin analogues	2	0
PTJA06	Polatuzumab vedotin in combination with bendamustine and rituximab for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL)	1	2
PTJA07	Ustekinumab for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic, or have medical contraindications to such therapies	0	1
PTJA08	Siponimod for the treatment of adult patients with secondary progressive multiple sclerosis (SPMS) with active disease evidenced by relapses or imaging features of inflammatory activity	0	2
PTJA09	Brolucizumab for the treatment of adults with neovascular (wet) age-related macular degeneration (AMD)	1	2

For these authors, the most common limitation of current Assessment Report template is the difficulty to use or find relevant information (Table A3), while redundancies are the lesser perceived criticality.

Table A3. Ability of the current Assessment Report template to address/cover specific aspects. . (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Includes all needed information/is complete	2	**40.0%**	20.0%	1	1	1	1	1
Simple to use/to find the information needed	1	20.0%	0.0%	1	2	1	1	0
Able to provide relevant evidence for national adoption	2	40.0%	20.0%	1	1	1	1	1
Able to provide a useful level of evidence synthesis	2	40.0%	0.0%	0	1	2	2	0
Has an adequate level of detail	2	40.0%	20.0%	1	1	1	1	1
Is without redundancies	3	**60.0%**	0.0%	0	2	0	3	0
Uses clear wording	2	40.0%	0.0%	0	1	2	2	0

Table A4. Collected responses on limitation of the current assessment template.

Issue	Responses
Usability	*The template is not easy to use (as an author), since no proper formatting has been performed. In general, the online tool is very difficult to work with (navigation/comments).*
Coherence	*Report template does not enable coherent reporting.*
Misalignment between Submission Dossier and Assessment Report	*It is not clear why the Submission Dossier does not match the assessment template.*
Reporting	*The examples for figures are scarce, and very open compared to tables. Perhaps the experts on meta-analysis could contribute with some instructions for future doers of assessments.*
Methodology	• *GRADE not included in each report.* • *In the Scope, no mentioning of Study designs or Time is included (PICOTS).*
Granularity of data (n=1)	*The templates require a higher level of granularity, specifically in the section on results for effectiveness and safety.*
Find information	• *It's not clear from the headings where to find the relevant comparators. It would be beneficial to have a separate heading for the comparator and a description that it was agreed on a European basis with the other HTA agencies for transparency.* • *Descriptions are lacking to some extent on what is expected from authors.*
Transparency	*It would be beneficial to have a separate heading for the comparator and a description that it was agreed on a European basis with the other HTA agencies for transparency.*

Length	*The report is too long.* *The conclusion is too long.*

Aspects in need of urgent improvements, reported by the authors, are presented in Table A5. Some of them are specific (reporting of evidence gaps, risk assessment, indirect comparisons) and some general (i.e. length). According to one responder, a statistical chapter could be a relevant improvement.

Table A5. Collected responses on aspects/sections in need of urgent improvement.

Issue	Responses
Evidence gaps	*Reporting evidence gaps requires clarity.*
Indirect comparisons	*Reporting indirect comparisons needs clarity.*
Risk assessment	*Better instructions for Risk of Bias assessment - which tool to use on which level taking (study/endpoint level) into account RoB2 tool of the Cochrane collaboration.*
Presentation of outcome data	*The presentation and assessment of outcome data needs improvement.*
Statistical chapter	*There is no separate statistics chapter - this should be added.*
Length	*Everything needs to be simplified in order to find agencies to write the reports.*

As reported in Table A6, methods and data analysis are the more critical aspects on which the rating of the ability of the template to capture them is more variable.

Table A6. Ability of the current Assessment Report template to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Research question and scope (including inclusion/exclusion criteria)	3	80.0%	20.0%	0	0	1	3	1
Methods (i.e. information retrieval and study pool)	2	**40.0%**	**40.0%**	0	2	1	0	2
Data analysis and synthesis of study results	2	**40.0%**	**20.0%**	0	2	1	1	1
Results of individual studies	2	40.0%	40.0%	0	0	3	0	2
Identification of strengths and limitations of the evidence	3	60.0%	20.0%	0	1	1	2	1

Authors identified the following limits in the current template (Table A7):

- Executive Summary: Inability to summarise the most relevant evidence for national adoption.
- Background Section: Limits providing relevant evidence for national adoption.
- Objective and Scope Section: Not all authors consider that the section is able to provide all needed information.
- Methods section: Ability to provide relevant evidence for national adoption is an issue.

- Results section: Readability could be improved.
- Discussion section: Readability and clarity are the major limitations of that section.
- Conclusion section: Completeness and provision of data relevant at national level must be improved.
- Appendix section: Readability, transparency, redundancies are still to be optimised.

Table A7. Ability of each section to address/cover specific aspects. (0=not addressed, 4=fully addressed)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Executive Summary Section								
Includes all needed information – The section is complete	3	60.0%	20.0%	0	0	2	2	1
Easy to read and interpret	2	40.0%	20.0%	0	1	2	1	1
Able to summarise the most relevant evidence for national adoption	**2**	40.0%	0.0%	0	1	2	2	0
Background Section								
Includes all needed information- The section is complete	4	80.0%	60.0%	0	1	0	1	3
Able to provide relevant evidence for national adoption	3	60.0%	20.0%	0	1	1	2	1
Easy to read and interpret	3	60.0%	40.0%	0	1	1	1	2
Without redundancies	3	60.0%	40.0%	0	1	1	1	2
Objective and Scope Section								
Includes all needed information - The section is complete	3	60.0%	20.0%	0	0	2	2	1
Able to provide relevant evidence for national adoption	3	80.0%	20.0%	0	0	1	3	1
Easy to read and interpret	3	60.0%	40.0%	0	1	1	1	2
Without redundancies	3	60.0%	40.0%	0	1	1	1	2
Methods section								
Includes all needed information - The section is complete	2	40.0%	20.0%	0	1	2	1	1
Easy to read and interpret	2	40.0%	20.0%	0	2	1	1	1
Clear and transparent	2	40.0%	20.0%	0	2	1	1	1
Able to provide relevant evidence for national adoption	2	20.0%	20.0%	0	2	2	0	1
Relevant for the national context	2	40.0%	20.0%	0	2	1	1	1

Results section								
Includes all needed information - The section is complete	3	60.0%	40.0%	0	1	1	1	2
Easy to read and interpret	**1**	40.0%	40.0%	0	3	0	0	2
Able to provide relevant evidence for national adoption	2	40.0%	40.0%	0	2	1	0	2
Able to provide an useful level of evidence synthesis	2	40.0%	40.0%	0	2	1	0	2
With an adequate level of detail	2	40.0%	40.0%	0	2	1	0	2
Without redundancies	3	60.0%	40.0%	0	2	0	1	2
Covers the aspects needed in evidence based decision-making	2	40.0%	40.0%	0	2	1	0	2
Discussions section								
Includes all needed information - The section is complete	3	60.0%	20.0%	0	1	1	2	1
Able to provide relevant evidence for national adoption	2	40.0%	20.0%	0	2	1	1	1
Easy to read and interpret	**2**	20.0%	20.0%	0	1	3	0	1
Clear and transparent	**2**	20.0%	20.0%	0	1	3	0	1
Without redundancies	2	40.0%	20.0%	0	2	1	1	1
Conclusions section								
Includes all needed information - The section is complete	**2**	40.0%	40.0%	0	2	1	0	2
Able to provide relevant evidence for national adoption	**1**	40.0%	40.0%	0	3	0	0	2
Easy to read and interpret	3	60.0%	40.0%	0	1	1	1	2
Clear and transparent	3	60.0%	40.0%	0	1	1	1	2
Without redundancies	3	60.0%	40.0%	0	1	1	1	2
Appendix section								
Includes all needed information - The section is complete	3	60.0%	40.0%	0	2	0	1	2
Able to provide relevant evidence for national adoption	3	60.0%	40.0%	0	1	1	1	2
Easy to read and interpret	2	40.0%	40.0%	0	2	1	0	2
Clear and transparent	2	40.0%	40.0%	0	1	2	0	2
Provides useful additional information to the Assessment Report	2	40.0%	40.0%	0	2	1	0	2
Without redundancies	2	40.0%	40.0%	0	1	2	0	2

When asked about the best way to integrate the Assessment Report and the Core Submission Dossier (Table A8), no agreement emerge among authors. The presence of all relevant information in the Assessment Report is considered useful by the majority.

Table A8. Proposal for linking Assessment Report to Core Submission Dossier. (0=not useful, 4=fully useful)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
In the Assessment Report, we should refer to the Core Submission Dossier as much as possible, and avoid repeating information that is already reported in the Core Submission Dossier	2	40.0%	0.0%	1	0	2	2	0
In the Assessment Report, we provide a summary of the Core Submission Dossier and reference to the Submission Dossier when necessary	3	60.0%	0.0%	0	1	1	3	0
We report all relevant information in the Assessment Report	3	60.0%	40.0%	1	0	1	1	2

At the author level, no agreement emerged on the best way to report evidence in REAs (Table A9).

Table A9. Preferences on how evidence should be reported in REAs.

	N	%
At PICO level, providing available data explicitly for each PICO element as in Sections 4.6-4.7 of the Assessment Report in PTJA06.	2	40%
At study level, organising the assessment around available studies as done in the Assessment Report of PTJA09.	3	60%

To report results separately for each kind of conducted data source/analysis is perceived as more useful (0=not useful, 4= fully useful) for pivotal studies and indirect comparisons. (Table A10).

Table A10. Preferences on reporting each kind of data source separately. (0=not useful, 4=fully useful)

	Median	% 3-4	% 4	N				
				0	1	2	3	4
Pivotal studies	4	80.0%	60.0%	0	0	1	1	3
Meta analysis	3	60.0%	40.0%	1	0	1	1	2
Indirect comparisons	4	80.0%	60.0%	0	0	1	1	3