CRA Charles River Associates

Prepared For:

EFPIA

Leopold Plaza Building

Rue du Trône 108

B-1050 Brussels (Belgium)

EU REA – A discussion of barriers for adoption and possible actions to over-come them

Main findings

Prepared By: Tim Wilsdon, Michele Pistollato and Lilian Li

Charles River Associates

8 Finsbury Circus

London EC2M 7EA

Date: January 2017

CRA Project No. D22657-00

Introduction

EFPIA asked Charles River Associates (CRA) to analyse existing national barriers preventing the adoption of joint reports on European relative efficacy assessments at launch (EU REA) and discuss solutions to foster the acceptance of joint reports at the national level.

The project focused on nine EU countries[1] (referred to as "Wave 1 countries": England, France, Germany, Italy, the Netherlands, Norway, Poland, Spain, and Sweden) and CRA engaged with the national trade associations in these markets to understand the barriers to using EU REA and potential solutions to overcome these barriers. This was then discussed at a two-day workshop held on 17th and 18th November 2016 in Brussels, attended by 14 representatives from national trade associations, nine company representatives, mostly from EU market access and government affairs departments, and EFPIA staff (who hosted the workshop).[2] This report provides the main findings from these discussions and is complemented by a set of slides with additional details. Both documents should be therefore read concurrently.

An assessment of national barriers to using EU REA and potential solutions

Several barriers have been identified as potential hurdles to the national adoption of EU REAs. To enable a structured assessment across countries, a common template was used to collect information on each of the barriers, and the possible solutions, and this was subsequently discussed extensively in the workshop.

Barrier 1: Inconsistency between the EU REA and national HTA timelines and incorporation of joint reports in national processes

In this analysis, we assume the publication of EU REAs is concomitant with the publication of EPAR, as indicated by EUnetHTA in their idealised process: this has important implications for the adoption at national level when compared to national idealised processes[3]. In particular, it is possible to distinguish three different situations across Wave 1 countries.

1. In three countries (England, Italy, the Netherlands), the national process ends before the EU REA report is expected: Waiting for the publication of the final EU REA report would delay the national process for the majority of products, even though some specific product sub-categories follow different, compatible, timelines. However, the dossier submission occurs at the same time at EUnetHTA and national level (although in one case the national submission could occur even earlier), therefore both processes could be coordinated (which would require internal coordination between national HTA assessors and EUnetHTA

1 The nine countries were selected because of the interest shown by the national trade associations in participating in the EFPIA EU REA initiative.

2 One session of the workshop was also open to the European Commission, which provided its feedback and comments on the aggregated and anonymised findings from this study.

3 This analysis focuses on idealised processes, both for EUnetHTA and national processes. The same analysis based on average process is likely to bring different results.

assessors and between industry EU staff and affiliate staff). Moreover, in these countries EU REA adoption is still possible for a set of products which have a different timeline (in this case, the adoption process would be similar to that of countries in the second group).

2. In five countries (France, Germany, Sweden, Norway, Spain), the EU REA report is published before the completion of the national HTA process. In this case, incorporation of EU REAs in the national timeline is possible and differences in the national HTA process determine how the adoption of EU REAs could happen in practice.
   - For national HTA processes where only REA is undertaken, or REA and CEA are sequential, EU REAs can clearly substitute for the national REA process and any localisation can occur following EU REA (France, Germany, Spain)
   - For processes where REA and CEA are undertaken simultaneously, the timelines are more of a problem (as waiting for the EU REA could delay the CE analysis). In this case, it is possible for the data to be consistent with the EU REA (which brings benefits to the companies, as it would increase internal consistency and reduce internal duplication) but it is less clear how this substitutes for the assessment process. (Norway and Sweden). It is likely that EU REA would mainly be another source of information for the application and health economic assessment.
3. In one country (Poland), the HTA process starts considerably after the publication of EU REA (one year or later) according the schedule. In this case, it could be argued that, when adopted, EU REAs might not be up to date and new evidence might be available. However, according to feedback at the workshop, it is rare that there are significant changes in the evidence over a period of one year so this would be manageable. If there is a need to update the evidence, there could be several solutions: (1) new evidence can be anticipated in the EU REA or (2) new evidence could be included in a supplementary report by the national HTA. Another possibility is that the company submission to the national agency would occur earlier in the case of EU REA.

Finally, there are countries (not Wave 1 countries), typically Central and Eastern European countries (CEE), which do not have an established formal HTA process, in this case, EU REAs would be helpful to establish the national process and could directly be embedded into it.

The solutions to overcome the timeline barrier and the extent to which it is possible to replace parts of the national assessment with EU REA depends on which group a country belongs to. It is also important to note that this analysis is based on *idealised* timelines and there may be more compatibility in the *real* EUnetHTA and national assessment timelines.

Barrier 2: Changes required in national laws and regulations

The second barrier to using EU REA relates to the need for a change in the national legislation.

There are instances where unless EU REAs are mandatory it is likely that the national HTA agency would duplicate the assessment. This is clearly the case e.g. in Germany

where current rules require the national HTA agency to accept REA reports commissioned only from national agencies.

In some countries, changes in the legislation could also be required to ensure that EU REAs replace part of the national assessment (instead of being used as an additional input in the assessment, defeating the purpose of avoiding duplication) (e.g. Poland, Spain).

In other countries, a formal update to the appraisal process/methods guide would be required in order to consider adoption of EU REAs (e.g. England, France).

It is important to better explain the relationship between a European assessment (which is eventually carried out by appointed national HTA assessors) and the remaining national processes (appraisal, decision-making) to increase acceptance for European reports. Another way could be EU legislation requiring Member States to change their national legislation to make adoption of EU REAs possible.

Barrier 3: Differences between EU REA and national HTA methodology

The EU methodological framework for collaborative production and sharing of HTA information adopted by EUnetHTA was jointly developed by all national HTA agencies in Joint Action 1 and 2.[4] Nevertheless some divergences remain. When the methodology adopted by EUnetHTA to produce EU REAs is different from the methodology used by national HTA agencies, national adoption of EU REAs may be problematic if HTA agencies are not willing to accept the EUnetHTA methodology. This potential barrier can apply to all countries but was specifically highlighted in seven countries (England, France, Germany, the Netherlands, Poland, Spain and Sweden).[5]

A related issue reported in all the countries is HTA agencies questioning the rigour and the quality (e.g. inclusion of all the relevant evidence from the literature) of EU REAs when performed by less experienced HTA agencies.

However, it is important to note that EUnetHTA does not exist in isolation but that it is a network of national HTA agencies, which can therefore change and improve EUnetHTA methodology to fit requirements. At the product-specific level, EUnetHTA members can provide their comments to the draft assessment encouraging the EU REAs to include their perspectives. It is therefore important to ensure the right level of engagement by national agencies in the EUnetHTA process.

Barrier 4: Regionalisation of the HTA decisions

In some countries, the central (national) HTA agency is not the final recommendation body as regional or local agencies have the possibility to conduct a further HTA and are able to make autonomous decisions. This was highlighted as a specific issue in Spain. A solution to this barrier would be to have greater co-ordination between the regional HTA and the central agency. This also means that regional HTA agencies, provided they

4 EUnetHTA webpage [last access 30 November 2016]: http://eunethta.eu/sites/5026.fedimbo.belgium.be/files/HTACoreModel3.0.pdf

5 This barrier regards different aspects of the HTA methodology: choice of comparators and endpoints, comparison methods, subgroup identification and post hoc analysis.

represent the national integrated system, could be directly involved in EUnetHTA assessments.

Barrier 5: Position of relevant stakeholders

If relevant stakeholders do not perceive the value of EU REAs this could represent a barrier for adoption. One possible solution to the lack of engagement from politicians would be to emphasise that EU REA follows on from a joint regulatory-HTA scientific advice process to leverage common development of evidence in a resourceful manner to enable access for patients to appropriate innovative technologies in a timely manner.

In addition, HTA agencies may be reluctant to recognise a supranational recommendation.[6] To address this concern, it would be helpful to raise awareness of the EUnetHTA process. This would emphasise that national HTA agencies are fully empowered in EUnetHTA and that national HTA agencies perform the European assessment. In addition, at national level, HTA agencies appraise that evidence (i.e. make a national recommendation for a national decision *based on* the EU REA evidence assessment).

This also applies to industry. Industry supports European cooperation and sees the value of EU REA. However because of barriers highlighted above, questions remain in some countries as to the immediate value EU REA would bring to the national level. It is important to clarify across affiliates, together with authorities, how EU REA adoption and uptake would work at national level in order to reduce uncertainty and accelerate access.

Conclusions

All the countries identified barriers to the national adoption of EU REAs but also suggested it was possible to overcome these barriers.

The consistency of the EU REA timeline and the national timeline is seen as the main issue. In three countries, currently only products that do not follow the 'standard' process (typically orphan, more targeted therapies) would be theoretically compatible with the adoption of EU REAs. The EU REA process would however bring other benefits to all technologies assessed, such as consistency of evaluation. In the other countries, all products could potentially benefit from EU REA but there are still barriers that need to be overcome (relating to laws and regulations, methodology, regionalisation and lack of support).

Addressing these barriers will require different stakeholders to work together and the benefits of EU REA to be clear to all stakeholders in the countries. There is a recognition that the benefits of EU REA depend on the way it is implemented and how it evolves over time. This will require significant discussions between all the stakeholders affected, these discussions have started but are at an early stage and will need to develop quickly.

6 HTA agencies may also be concerned about reduction of their budget because part of the fees paid by to national HTA agencies may not be due if part of the HTA process is conducted via EUnetHTA.