Impact of EMA clinical trial transparency policies on HTA decisions in Germany

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Background

The European Medicines Agency (EMA) has two policies that govern access to clinical trial data.

Policy 070

• Requires trial overviews, summaries, and clinical study reports (CSRs) from centrally authorized market authorization applications to be published on the EMA’s clinical data website.1
• Stipulates that trial data should be published 60 days after the European Commission decision on the publication of the European Public Assessment Report (EPAR).
• Came into effect in January 2015 for license extensions and in July 2015 for new indications.

Policy 043

• Allows anyone to request CSRs.2
• Applies to applications and data submitted before Policy 070 came into effect, and to non-centrally authorized products.

Implications and potential use of data available under these policies

Manufacturers already provide health technology assessment (HTA) agencies with additional, unpublished data, and authorities can request additional analyses for appraisals. However, HTA agencies could use data published under Policy 070 to gain a more complete view of the evidence and competitor landscape, rather than published trials and summaries of product characteristics (SmPCs).

Methods

• The EMA clinical data publication website was searched for medicines with published clinical data (cut-off 31 August 2018) and for the EPAR publication data launch.
• The IQWiG website was searched for assessments of these drugs. The reference lists were then extracted (cut-off 31 August 2018) and for the EPAR publication date/launch date.
• The EMA clinical data publication website was searched for medicines with published clinical data submitted in 2015 and 2016.

Results

A total of 121 applications had clinical data published up to the cut-off date; the documents identified included 69 initial applications, 39 indication extensions, and 11 applications that were subsequently withdrawn (see Figure 1).

When generics were excluded, there were 73 initial applications or extensions and two workshare applications (not included in the analysis), of which 24 had been assessed by IQWiG (see Figure 3).

IQWiG reports (for drugs without orphan status) were published between 42 and 110 days after publication of the EPAR. IQWiG assessment reports were published before the publication of clinical data for all of the drugs; these were published an average of 372 days (range: 249–513 days) before the data were available.

We found no evidence that IQWiG considered the data published under Policies 070 or 043 when assessing applications for new indications, extensions or workshare applications. However, we found that IQWiG considered the data published under Policies 070; this could be due to the following:

1. IQWiG strongly supported Policy 070 in a document summarizing the agency’s comments on the draft policy. It stated: “There is overwhelming evidence, that so far publicly available trial data are insufficient to provide a complete and unbiased picture of a given healthcare intervention. HTA needs additional independent and high quality data sources.”

2. The EMA conducted an online survey in mid-2017, in part to determine the roles of the people involved in the EMA clinical data publication process. It stated: “There is overwhelming evidence, that so far publicly available trial data are insufficient to provide a complete and unbiased picture of a given healthcare intervention. HTA needs additional independent and high quality data sources.”

Discussion

Pushback from some manufacturers

Manufacturers have highlighted that providing clinical data under Policy 070 may make additional data from other companies available, which they may consider to be a competitive disadvantage. In the second survey, it was clear that some companies who wanted to prevent trial data being made available under Policy 070 had a primary aim of preventing their competitor products.

Issues with implementation

• We were not surprised to find that IQWiG did not appear to have used the data available through Policy 070; this could be due to the following:
  - Data were not available when the assessments were conducted.
  - Implementation of the policy is still in its early stages, and clinical data can be published up to 618 days after publication of the EPAR.
  - Publishing the clinical data closer to the target of 60 days after the EPAR could allow these data to be considered in the HTA process, although the time between EPAR publication and IQWiG’s decisions was often short, on one occasion only 42 days.

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Utility of the clinical data site

• The EMA conducted an online survey in mid-2017, in part to determine the roles of the people accessing the data.

• Interestingly, HTA agency affiliation was reported by 1% of the respondents, but we do not know which agencies they were affiliated with.

Global trend towards more transparency of data in regulatory decisions

• There appears to be a global trend towards transparency in regulatory decision-making and clinical trials:
  - EMA – hosted delegates and visiting experts from the US Food and Drug Administration (FDA), Health Canada, and the Japanese Ministry of Health, Labour and Welfare to enhance international cooperation on clinical data publication, enabling sharing of best practices and development of standardized processes.
  - Health Canada – the Protecting Canadians from Unsafe Drugs Act (also known as Vanessa’s Law) is under development.
  - FDA – a pilot program, known as the Clinical Data Summary Pilot (started in January 2018).

EMA priorities

• As of 1 August 2018 the EMA has suspended all new activities related to clinical data publication under Policy 070.
• Clinical data submitted by the end of July 2018 will still be processed but no new data packages will be processed until further notice.

Conclusions

• The EMA clinical trial data publication site is a key resource that is being underutilized in HTA; this is likely to be due to delays in the publication of clinical data submitted in 2015 and 2016.
• A potential limitation of the study is that we would not have detected the use of the published clinical data in systematic reviews submitted by manufacturers.
• The introduction of similar schemes by other regulatory agencies suggests a global trend towards increased transparency.

References


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