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Building Synergy between Regulatory and HTA Agencies beyond Processes and Procedures—Can We Effectively Align the Evidentiary Requirements? A Survey of Stakeholder Perceptions

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ABSTRACT

Objectives: To evaluate the current practice of companies and agencies to assess the changes made in aligning regulatory and health technology assessment (HTA) stakeholders; to identify areas of commonality of evidentiary requirements that could occur; and to identify strategic issues and trends of regulatory and HTA synergy. **Methods:** Two separate questionnaires were developed to assess stakeholders' perceptions on regulatory and HTA alignment, one for pharmaceutical companies and the other for regulatory and HTA agencies. The responses were analyzed using descriptive statistics. **Results:** Seven regulatory and 8 HTA agencies from Australia, Canada, and Europe and 19 international companies developing innovative medicine responded to the survey. This study provided a snapshot of the current regulatory and HTA landscape. Changes made over the past 5 years were reflected in three main areas: there is an increasing interaction between regulatory and HTA agencies; current conditional regulatory approvals are not always linked with flexible HTA approaches; and companies are more supportive of joint scientific advice. Four types of evidentiary requirements were identified as building blocks for better alignment: acceptable primary end points, inclusion of an active comparator, use of patient-reported outcomes, and choice and use of surrogate end point. **Conclusions:** The study showed that the gap between regulatory and HTA requirements has narrowed over the past 5 years. All respondents supported synergy between regulatory and HTA stakeholders, and the study provided several recommendations on how to further improve evidentiary alignment including the provision of joint scientific advice, which was rated as a key strategy by both agencies and companies.

Keywords: drug development, early scientific advice, evidence generation, health technology assessment (HTA), HTA-regulatory synergy, review and reimbursement.

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Introduction

The pathway for bringing a new medicine to the market is dependent on two sequential processes: achieving market authorization from the regulatory agency and reimbursement from a payer [1]. The current health care environment is evolving rapidly; faced with an increasing pressure to control spiraling health care costs [2], payers need to make decisions on the reimbursement of medicines to maximize public health outcomes within limited health budgets. As a result, an important stakeholder has emerged—the health technology assessment (HTA) agency that aims to provide recommendations on reimbursement on the basis of the value of a new medicine [3]. The role of HTA agencies as advisors to the reimbursement decision maker is crucial for application of funding by the health care system, in particular within a single-payer system [4]. Consequently, drug developers seeking to deliver new medicines need to coordinate a development program to generate evidence that meets the needs of both regulatory and HTA agencies.

Pharmaceutical companies have already started to adjust their internal structures and development strategies to meet the goal of demonstrating the efficacy, safety, and cost-effectiveness of a new medicine [5]. Nevertheless, challenges remain in developing evidence that meets the requirements of both regulatory and HTA agencies at the point of launch. The fundamental reasons for these challenges are twofold. First, a regulatory agency focuses on the benefit and risk balance of a medicine, which is based on results from clinical trials provided under ideal circumstances, whereas an HTA agency focuses on effectiveness evaluation of an intervention under the general circumstance of clinical practice. Second, HTA evaluation compares a new medicine against one or more existing treatments. The comparative nature of HTA requires an active comparator trial to demonstrate the value of a new medicine, whereas few regulatory approvals

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are based on the superiority of a new medicine over active comparators [6]. In addition, HTA evaluates the clinical effects and cost over time. Finally, the basic regulatory requirements have been established and standardized via the International Council on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use guidelines. In contrast, HTA evaluates medicines in local clinical context; therefore, the scientific requirements of HTA agencies vary according to local standards of care. This variability introduces uncertainty into drug development decisions and can result in a potential mismatch of regulatory and HTA outcomes.

Numerous studies have assessed the association between regulatory and HTA outcomes across European countries, where significant divergences in the HTA recommendations were identified for medicines approved via the centralized procedure of the European Medicines Agency (EMA) [7–10], resulting in inequitable patient access across countries in Europe. In addition, in response to the increasing demand for new medicines to address unmet medical need, regulatory agencies have developed flexible pathways to speed the review process, including mechanisms such as accelerated and conditional approvals. Nevertheless, there seems to be no association between these flexible regulatory pathways and HTA decisions [11]. This disconnect between regulatory approval and HTA recommendation for products to address unmet medical need may, among other outcomes, lead to false hope from patients in need.

Over the past decade, a number of initiatives have been established to address the disparities of regulatory and HTA requirements; for example, tripartite discussions among pharmaceutical companies, regulators, and HTA agencies have been launched as a platform to receive parallel scientific advice on drug development plans [12,13]; a collaboration between EMA and European HTA agencies has taken place to improve European public assessment reports in support of the HTA assessment of relative effectiveness [14]; and regional policy-level initiatives, such as the establishment of the European network for Health Technology Assessment, have been undertaken to facilitate the reduction of duplication of effort [15,16]. In addition, research-level initiatives are being conducted to understand decision-making processes and to determine whether divergent decisions between regulatory and HTA agencies are due primarily to differences in the evidentiary requirements or other factors [17]. Despite the growing interest in this area of regulatory and HTA alignment, no studies have assessed the impact of activities focused on improving dialogue and efficiency. Therefore, it is timely to assess the current landscape for the alignment of regulatory and HTA requirements.

The objectives of this study were to evaluate the current practices and procedures of companies and agencies to assess the changes made in aligning the stakeholders, to identify areas of commonality of evidentiary requirements as building blocks of achieving alignment, and to identify the strategic issues and trends for synergy between regulatory and HTA agencies.

Methods

Design and Participants

Two questionnaires were developed with the same aim to assess the perceptions from stakeholders, one for pharmaceutical companies and the other for regulatory and HTA agencies on key topics related to alignment. A pilot industry survey was completed by two companies and a pilot agency survey was completed by one regulatory and one HTA agency to evaluate the clarity and validity of the proposed questions. Feedback was received from the four sources and supported finalization of the questionnaires. Questions were answered by tick-box responses to statements or by using a scale ranging from 1 to 5 (representing "strongly agree" to "strongly disagree"). Free-text comments were optional for each question. The industry and agency questionnaires contained analogous questions where appropriate. Both were organized into three sections: overview of current practice and procedure, evidence and technical requirements, and strategic issues and trends of synergy between regulatory and HTA agencies.

The finalized industry questionnaire was sent to senior management at 25 international pharmaceutical companies, requesting one response from each company's Regulatory Affairs Department and one response from the Health Economics, Outcomes and Research (HEOR) (or equivalent) Department. The companies selected were international companies that develop innovative medicines. The finalized agency questionnaires were sent to contacts holding senior positions within 34 agencies (16 regulatory agencies and 18 HTA agencies) in Australia, Canada, and Europe. Questionnaires were sent via email during July and August 2016; the responses were collected by September 2016.

Data Collection and Processing

Company responses represented a consensus opinion within their department (Regulatory Affairs or HEOR). Agencies responded to the survey as individuals, and the views expressed were those of the respective individuals rather than the general view of the agency. The responses were analyzed using descriptive statistics. Free-text comments were reviewed and manually grouped into key themes according to high concordance responses.

Results

Characteristics of Study Participants

Twenty-nine responses were received from 19 companies including responses from the regulatory departments of 13 companies, the HEOR departments of 12 companies, and joint department responses from 4 companies. These respondents represented a mix of expertise from major companies, and 14 participating companies were categorized as being among the "top 20 companies based on R&D investments" in 2014 [18].

Eighteen of the 34 agencies responded to the survey request; of these, 3 expressed interest but were not able to complete the survey by the deadline, and 15 agencies provided detailed feedback.

The agencies that participated represented key stakeholders from a mix of geographical locations: regulatory agencies included Australia's Therapeutic Goods Administration (TGA), Health Canada, EMA, Irish Medicines Board (IMB), Sweden's Medical Products Agency (MPA), Swissmedic, and the Netherlands' Medicines Evaluation Board (MEB); HTA agencies included Australia's Pharmaceutical Benefits Advisory Committee (PBAC), the Canadian Agency for Drugs and Technology in Health (CADTH), Canada's Institut national d'excellence en santé et en services sociaux (INESSS), England's National Institute for Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC), Poland's Agencja Oceny Technologii Medycznych I Tarryfikacji (AOTM), Sweden's Tandvårds-Och Läkemedelsförmånsverket (TLV), and Basque, Spain's Servicio de Evaluación de Tecnologías Sanitarias (OSTEBA).

Part I: Current Practice and Procedures

We first looked at the companies' approaches to addressing regulatory and HTA requirements during development (Fig. 1).

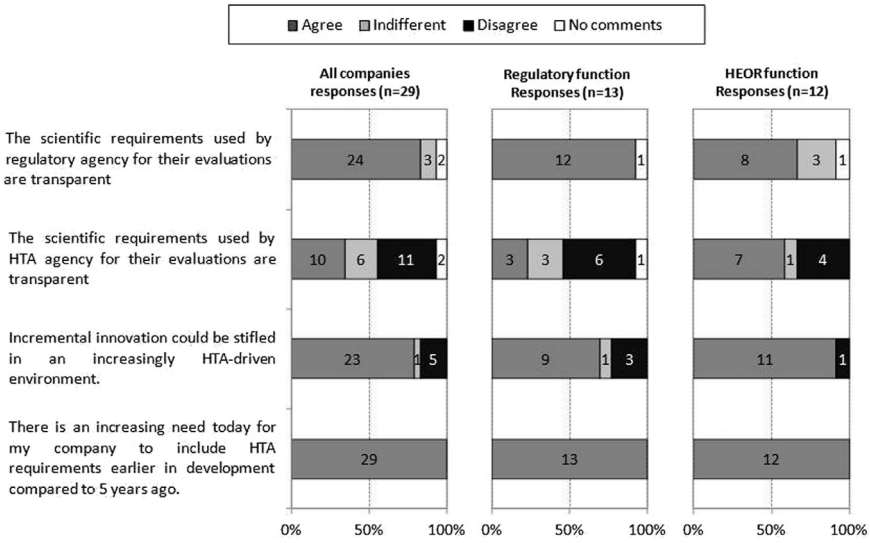

Fig. 1 – Company respondents' views on the regulatory and HTA requirements. HEOR, Health Economics, Outcomes and Research; HTA, health technology assessment.

There were mixed views regarding the transparency of HTA requirements, with 10 company respondents agreeing that these were transparent and 11 stating that they were not. A clear divergence was observed between the responses from regulatory departments and those from HEOR departments. All company respondents felt that there was an increasing need to include HTA requirements earlier in development, with the aim to develop products that are approvable as well as reimbursable. This approach, however, requires efficient coordination across regulatory and HEOR departments in the development decision-making process. Only five respondents confirmed that their company had an integrated approach for the two groups working together and generated evidence on the basis of aligned input. Twenty-three respondents reported that the interactions between the regulatory and HEOR departments took place on an ad hoc basis, and although HEOR input was sought during development, the final decision regarding evidence generation prioritized regulatory requirements.

Several barriers to integrated decision making during development were observed. Internal structure and strategy issues included resource constraints, lack of appropriate infrastructure, lack of awareness of HTA requirements, and development plans being driven by the US market. External uncertainty issues included variation in HTA requirements to be considered and incorporated, rapid changes in clinical practice and standard of care, as well as divergent economic considerations among different markets.

All 29 company respondents provided suggestions to overcome both internal and external barriers, including further communication and training for research and development and regulatory departments to raise awareness of the HTA environment, prioritizing assets that would benefit the most from aligned input from regulatory and HEOR teams, and establishing a project team to coordinate across departments to ensure early interactions and using more consistent decision-making processes. Finally, respondents suggested that seeking early HTA scientific advice would be valuable to improving internal awareness of the importance of HTA as well as to understanding the external requirements to be included in the development plan.

We further asked the agencies to comment on their current practice in terms of interactions with peer agencies in the same jurisdiction. Interactions between regulatory and HTA agencies were observed across different stages of the product life cycle. Three HTA agencies (TLV, NICE, and OSTEBA) and four regulatory agencies (EMA, IMB, MEB, and MPA) that participated in the survey currently provide joint scientific advice to companies during drug development. Two HTA agencies (CADTH and PBAC) accept a submission while the medicines are still under review by the respective regulatory agencies. NICE can also start its process before EMA authorization; it is, however, not a formal parallel procedure. Information sharing between regulatory and HTA agencies during the postauthorization period occurred in four HTA and four regulatory agencies. The collaboration between regulatory and HTA agencies was mainly driven by the increasing demand for faster patient access to new medicines (Fig. 2). Regulatory agencies also indicated that information sharing to reduce duplication of work was a key driver, and HTA agencies were keen to support relevant evidence generation during drug development.

Nevertheless, barriers to regulatory and HTA agencies working together were identified, including organizational issues, resource limitations, working culture challenges, legislative issues, and, importantly, divergences in assessment methodology and evidentiary requirements. The details are listed in Appendix Table 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2017.11.003.

Part II: Divergences Observed and Potential Alignment of Evidentiary Requirements

Company respondents indicated that the two main areas in which regulatory and HTA divergences have been observed related to products for which there was a high level of clinical uncertainty, for example, oncology products, orphan drugs, and products receiving conditional and accelerated approval. Furthermore, economic concerns from high-cost and high-budget-impact medicines contributed to divergences.

Both companies and agencies were asked to review a list of evidentiary requirements and identify the areas in which divergences have been observed and potential alignment could occur. The results are detailed in Appendix Table 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2017.11.003. The areas in which divergences were frequently perceived among all three stakeholders were as follows: acceptable primary end points, inclusion of an active comparator arm in the trial, and

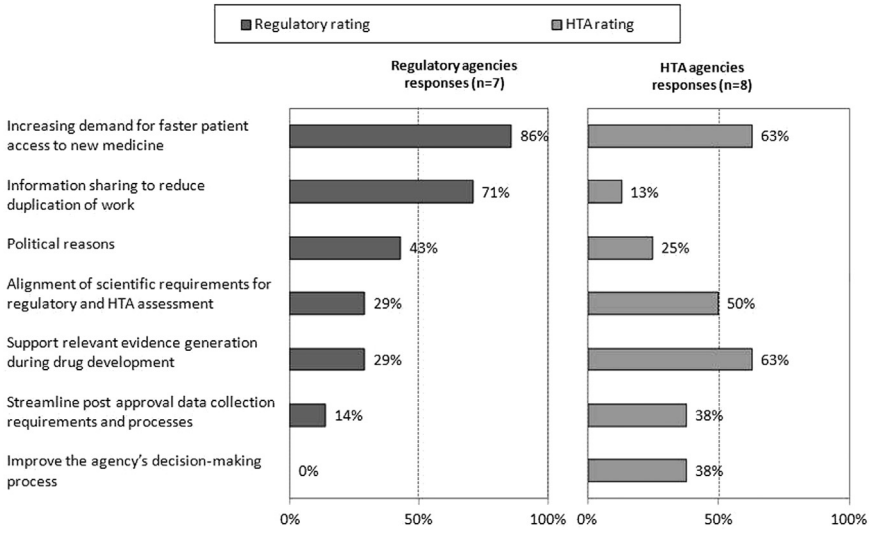

Fig. 2 – Main drivers for regulatory and HTA agency collaboration. HTA, health technology assessment.

choice and use of surrogate end points. Areas of evidentiary requirements in which commonality could occur were also evaluated. Overall, companies were more positive than regulatory or HTA agencies in their perceptions of potential evidentiary alignments. For example, companies were positive about the alignment of health-related quality-of-life measures (82% of respondents). In contrast, only 57% of regulatory respondents and 50% of HTA respondents agreed for that requirement (Table 1).

In considering the criteria for choice of a surrogate end point, companies and regulatory agencies revealed similar views. Nevertheless, the most disparity in viewpoints in this area occurred between respondents from companies and HTA agencies. Most company respondents (93%) suggested that they would choose a surrogate end point that was previously used by an HTA agency. Surprisingly, HTA agency respondents indicated a low acceptance (25%) of this approach and specified rather that surrogate end points need to be clinically relevant and related to local context and would therefore be considered on a case-by-case basis rather than be based on precedent choice (Fig. 3). All company respondents commented that, ideally, regulatory and HTA agencies should work together to develop a joint list of acceptable and validated biomarkers and surrogate end points.

Part III: Strategic Issues and Trends of Synergy between Regulatory and HTA Agencies

Early scientific advice was suggested by companies as a key strategy for drug development. Company respondents were positive about their joint scientific advice experiences. Two-third of the respondents, however, revealed that early scientific advice had not yet reached its full potential to align regulatory and HTA requirements. Company respondents pointed out that the input from the current joint advice meetings was more regulatory-focused and advice received was diverse rather than an aligned view from both stakeholders.

Agencies recognized that joint scientific advice would be of great value, especially for conditional approvals. Benefits include clearer strategies for earlier and controlled release of new medicines, commitment by all stakeholders for postmarketing evidence development, and maximization of the ongoing postapproval assessment of new medicines. For agency respondents, joint scientific advice would add value to the development plan in the areas of use of patient-reported outcomes, agreeing on acceptable primary end points, defining unmet medical need, agreeing on health-related quality-of-life measures, analysis methodology, and choice and use of surrogate end points. Nevertheless, four areas in which regulatory and HTA agencies hold important different opinions were defining the size of the trial (100% regulatory rating

Table 1 – Top areas where potential alignment across regulatory and HTA requirements could occur.

Evidentiary requirements	Companies (n = 28)	Regulatory agencies (n = 7)	HTA agencies (n = 8)
Acceptable primary end points	86%	86%	75%
Inclusion of an active comparator arm in the trial	86%	71%	75%
Use of patient-reported outcomes	86%	71%	75%
Health-related quality-of-life measures	82%	57%	50%
Choice of and use of surrogate end points	79%	86%	75%
Criteria considered in choice of comparator: therapeutic	79%	86%	63%
Use of subgroup analyses	75%	71%	63%
Inclusion and choice of secondary efficacy parameters	75%	100%	63%
Definition of unmet medical need	75%	86%	63%
Use of biomarkers to monitor patient outcomes	75%	86%	63%

HTA, health technology assessment.

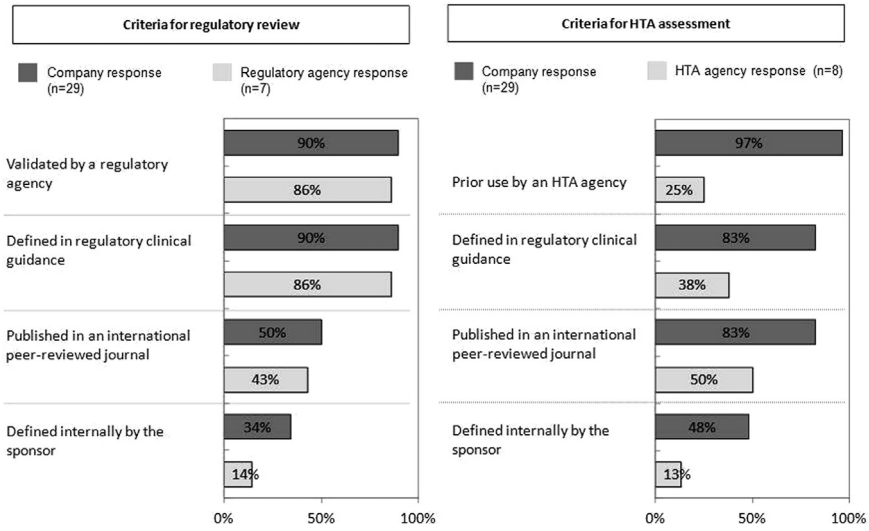

Fig. 3 – Key criteria considered for the choice of a surrogate end point. HTA, health technology assessment.

vs. 50% HTA rating), use of subgroup analyses (100% regulatory rating vs. 63% HTA rating), pharmacological criteria considered in the choice of comparator (43% regulatory rating vs. 88% HTA rating), and potential needs for diagnostics (0% regulatory rating vs. 63% HTA rating), suggesting uncertainty of joint advice outcomes regarding these requirements.

Five HTA agency respondents indicated that conditional reimbursement schemes could be applied to products that have received regulatory conditional approvals, but companies reported that conditional approvals were not currently aligned with conditional reimbursement. Most company respondents (17 of 27) and HTA agencies (5 of 7) stated that the HTA processes currently used to assess conditional approvals were no different to standard approvals. Company respondents, however, pointed out that the HTA recommendations were different as a result of a higher level of scrutiny for conditional approvals by HTA agencies. Most of the regulatory (57%) and HTA (75%) respondents indicated that joint scientific advice discussions on selection of compounds for accelerated assessment would be beneficial in achieving mutual understanding of an unmet medical need and in identifying compounds that would offer clear value for health care systems.

Regarding the future trends, most of the company and regulatory agency respondents suggested that HTA agencies should seek to rely on regulatory public assessment reports to minimize duplication of work, whereas HTA agencies held a more tempered view on this approach. The involvement of regulatory agencies in the assessment of cost-effectiveness of new medicines was indicated as a possibility by both HTA agency and company respondents; all regulatory agency respondents, however, disagreed with this option (Fig. 4).

Discussion

The two sequential processes of regulatory and reimbursement decision making have resulted in a degree of uncertainty regarding patient access to new medicines. HTA requirements for relative and cost-effectiveness are often referred to as the "fourth hurdle of market access" [19]. Over the past decade, interest has

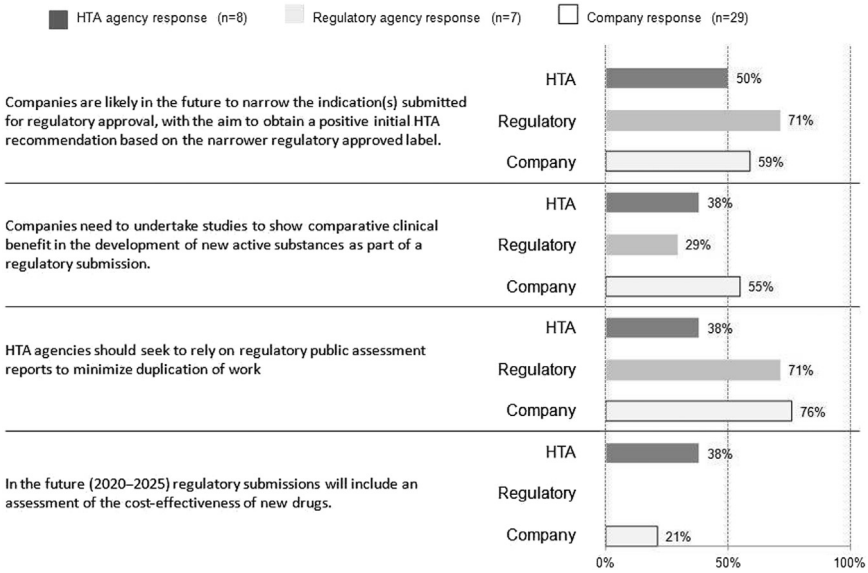

Fig. 4 – Perceptions regarding future trends in regulatory HTA collaboration. HTA, health technology assessment.

risen in the growing body of research comparing regulatory and HTA decisions, stimulating calls for more effective alignment between the two bodies [7,9,11,20]. A stakeholder survey conducted in 2012 by Liberti et al. [21] was the first effort to explore the stakeholder perceptions of regulatory and HTA interactions. Our study assessed the current practices and perceptions of companies and agencies regarding the synergy of regulatory and HTA activities and the changes in this area to date. Compared with the 2012 study, our study respondents perceived that the gap between regulatory and HTA stakeholders has narrowed, and all companies and agencies that responded to our survey supported the synergy of regulatory and HTA activities. The current environment was reflected in three main areas in this study: 1) there is increasing interaction between regulatory and HTA agencies; 2) current conditional regulatory approvals are not always linked with flexible HTA approaches; company respondents pointed out that the HTA recommendations were different as a result of a higher level of scrutiny for conditional approvals by HTA agencies; and 3) companies show more willingness and support of joint scientific advice.

Agency respondents recognized increasing interactions between regulatory and HTA agencies within their jurisdictions, driven mainly by the increasing demand for faster patient access to new medicines. Collaboration between the two stakeholders within their jurisdiction was observed in the study, mostly related to providing joint scientific advice to companies during development and early submission to HTA agencies during the regulatory review process. Although coordinated data collection postauthorization was perceived by respondents as being of great value, in particular for products that were approved under conditional or accelerated pathways, the level of collaboration during postauthorization was confined to interagency information sharing. A number of international platforms facilitate the collaboration between regulatory and HTA agencies, such as the HTA international's interest group HTA-Regulatory Interactions and Conditional Coverage and the European network for Health Technology Assessment.

The increasing overlap in activities between agencies was mirrored in the more integrated approach between regulatory and HEOR departments within companies. This encouraging development in companies may be related to the increasing awareness and understanding of HTA requirements through knowledge and capacity building as well as to learning from interactions with HTA agencies through early scientific advice. Nevertheless, because regulatory division respondents rated the transparency of HTA requirements to be lower than those from HEOR divisions, it showed that more internal education may improve the understanding of regulatory and HTA evidentiary requirements across functions.

Conditional approvals are granted to allow early access to medicines such as anticancer drugs that fulfill an unmet medical need. The 2012 study raised an open question as to how the conditional approvals were associated with HTA decisions for faster patient access [21]. Our survey showed that companies felt that the processes that HTA agencies currently use were no different to those used for standard approvals. Although conditional reimbursement schemes existed in certain HTA systems, these were not believed to be aligned with conditional approvals. This is supported by the findings by Lipska et al. [11] and Desjardins and Conti [22] where no association was found between the type of EMA approvals and HTA decisions within selected European Union countries. These results raised questions regarding the benefit of conditional approvals as an early access route to patients. It is therefore important for regulatory and HTA agencies to work in a more aligned way on the process of reviewing conditional approvals. For countries where there is no current conditional approval (e.g., Australia, at the time of this study), a collaborative approach may be worth considering when setting up a formal procedure for applying for flexible regulatory routes.

Further to understanding the processes and procedures, company respondents pointed out that the evidentiary requirements from HTA agencies on conditional approvals showed the biggest divergence compared with regulatory requirements. Because conditional regulatory approvals are normally granted on the basis of less comprehensive data compared with standard approvals, companies experienced a higher level of scrutiny by HTA agencies for products approved through these pathways. This divergence leads to the challenge for companies to find the right balance between timely access and optimal reimbursement, and to generate a data package that will be acceptable to both regulatory and HTA agencies as soon as possible.

These results were supported by the study from Liberti et al. [23] in which HTA agencies were seen as being less committed to flexible approaches than were regulatory agencies, and recommended that one of the building blocks to a successful flexible regulatory pathway is a streamlined approach to align regulatory and HTA requirements. Our survey respondents suggested that the requirements need to be aligned not only at the initial approval stage but also during postauthorization to best fulfill the follow-up evidentiary requirements of regulatory and HTA agencies. A recent study by Ruof et al. [24] assessed the postauthorization data request from EMA and the German HTA body Der Gemeinsame Bundesausschuss (G-BA), and found that G-BA made additional requests with less clear instructions compared with those made by the EMA.

Joint scientific advice has been suggested by survey respondents as a platform for input from regulatory and HTA agencies regarding the evidence generated during development and postauthorization. The 2012 survey results [21] showed a reluctance from companies to seek joint advice because of the uncertainty about its benefits. Changes to this perception were observed in our study and all company respondents agreed that their joint scientific advice experiences have been helpful. Nevertheless, the respondents still felt that the current advice meetings did not reach their full potential and issues raised in this regard included more focus on regulatory questions rather than a balanced input, diverse advice across agencies, and the unbinding nature of advice, which resulted in uncertainty regarding outcome. A previous study [25] also showed similar opinions for joint advice meetings regarding a predominantly regulatory focus as well as the perception that joint advice meetings could be better used to reach a more aligned and better outcome.

Questions discussed during joint scientific advice meetings are prepared by companies and normally submitted before the meeting in a briefing book or structured template [26]. Therefore, preparing the right questions to be addressed is crucial for maximizing the benefit of joint advice. In our survey results, the type of topics identified as being of most value included the use of patient-reported outcomes, acceptable primary end points, health-related quality-of-life measures, analysis methodology, and surrogate end points.

Because our survey results suggested that HTA agencies are less likely to rely on precedents in the choice of surrogate end points, it is critical for companies to understand HTA requirements for acceptance of these end points during early interaction. A recent study by Tafuri et al. [13] reviewing EMA and HTA agencies' parallel scientific advice meeting minutes also demonstrated the need to discuss the choice of surrogate end point, because some HTA agencies requested demonstration of a correlation of the surrogate end point with clinical outcomes and quality of life. Tafuri et al. also found disagreement among HTA agencies regarding the choice of comparator. The definition of unmet medical need was also viewed as one of the important topics to be discussed during joint advice meetings, particularly regarding the selection of products for conditional or accelerated regulatory routes of review. In fact, in

Table 2 – Recommendations to improve synergy between regulatory and HTA stakeholders.

Category	Area	Recommendations
Practice	Company internal practice	• Seek early scientific advice with HTA agencies • Raise awareness of access environment outside the United States • Increase skills and capabilities of staff • Establish a project/brand team with aligned input from regulatory and HEOR functions • Prioritize assets that will benefit the most from aligned approach
	Agency practice	• Understand the advantages of alignment and use political will to promote interaction • Align on timelines/review process between regulatory and HTA • Conduct a rolling review of valid new evidence and better understanding of uncertainties • Seek continuous joint scientific advice and early dialogue to improve mutual understanding • Focus on unmet medical need
Evidentiary requirements	Area for alignment	• Have acceptable primary end points • Include an active comparator arm in the trial • Discuss choice and use of surrogate end points
	Strategy	• Focus alignment of evidence generation on efficacy/effectiveness • Align on minimum thresholds for clinical trials • Align where appropriate and acknowledge national differences • Use real-world evidence to support relative effectiveness assessment
Future trend	Opportunities	• Achieve aligned views on end point and outcome • Enable adequate and effective data collection • Continue evolvement of joint advice process • Share information on patient input • Improve transparency in decision making • Conduct joint evaluation or share assessment of clinical context • Align on postmarketing evidence generation • Establish joint registry

HEOR, Health Economics, Outcomes and Research; HTA, health technology assessment.

2015, EMA issued guidance that recommended that companies seek joint scientific advice with HTA agencies for products intended for conditional approval.

Study Limitations

Although our research is international in nature, we excluded jurisdictions with maturing HTA systems because of their different capacity levels and focused on jurisdictions with mature HTA agencies, including Australia, Canada, and selected European countries that use cost-effective assessment in the HTA review. Therefore, respondents in the survey represented jurisdictions with regulatory and HTA agency interaction experience, potentially leading to more positive perspectives regarding awareness of and readiness for alignment.

Conclusions

On the basis of the findings of this study, recommendations are suggested to continuously improve synergy (Table 2). This study identifies the current practices and perceptions from stakeholders and showed progress made in this area. In addition, we explored the stakeholders' perceptions of where alignment of requirements could occur as building blocks to better alignment. The next step of this research will be to investigate the synchronization of regulatory and HTA decisions by assessing the respective review times and access outcomes, to help quantify the changes made to patient access.

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Supplemental Materials

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