



**Building quality into HTA/coverage
decision-making processes:**

**What are the features of good
practice in HTA?**

2 – 3 December 2013

HEATHROW, UK

WORKSHOP SYNOPSIS

Synopsis authors

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CIRS - The Centre for Innovation in Regulatory Science - is a neutral, independent UK-based subsidiary company, forming part of the Intellectual Property and Science business of Thomson Reuters. The mission of CIRS is to maintain a leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and HTA policies and processes. CIRS provides an international forum for industry, regulators, HTA and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy through the innovative application of regulatory science. It is governed and operated for the sole support of its members' activities. The organisation has its own dedicated management and advisory boards, and its funding is derived from membership dues, related activities and grants.

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BACKGROUND TO THE WORKSHOP

Health Technology Assessment (HTA) is increasingly used to inform coverage decision making that hinges on whether the additional benefits of interventions are worth their cost. At the same time, HTA agencies are continuously evolving to adopt the best tools and techniques needed in order to make high-quality decisions about the place new medicines will assume in their jurisdiction.

Considerable organisational and methodological variability exists in the HTA appraisal and coverage decision-making processes in different countries. However, consistency across the underlying processes and procedures might be expected among HTA and coverage bodies where remits and scope of function and activities are similar. To this end, discussions have started and initiatives have emerged amongst stakeholders from HTA agencies and other groups such as academia and industry to identify the common methodologies, guidelines, standard processes and good review practices of HTA appraisal.

While HTA agencies are undergoing evolution with regards to their policy, procedures and infrastructure, challenges have also arisen for industry to adjust their submission strategy to align with this progress. In fact, the need for HTA and industry alignment has led to stakeholder discussions to agree on the core factors that would facilitate and positively impact the quality of reviews conducted to support HTA coverage decision making and improve the process of bringing a new medicine to market. It is important, however, that sponsors understand their role in enabling this alignment through the provision of good-quality submissions.

This Workshop continued the work of the [CIRS September 2011 Workshop, *Understanding HTA and Coverage decision-making processes*](#), which focused on the question: what is the key to facilitating transparent access to medicine? It especially dealt with how to build process consistency and quality into both HTA and coverage decision making, as well as on the quality of the submission so as to improve the process of bringing a new medicine to market.

Objectives

- Ascertain companies' and agencies' current perspectives with regard to the quality of HTA/coverage decision-making processes
- Identify and discuss the key aspect of a good-practice process of HTA and coverage decision making
- Identify the key factors that enable companies to prepare a quality submission in an evolving HTA environment
- Recommend which key features should be considered or adopted for best practice in HTA processes and decision making

INTRODUCTION

Day 1 Chair, Prof Hans-Georg Eichler, *Senior Medical Officer, European Medicines Agency* outlined the course of the Workshop which would cover multiple aspects of quality in health technology assessment including meeting stakeholder expectations, communicating decisions, transparency in process and results, measuring quality, developing tools to ensure quality in both HTA submission and review and in measuring the results.

KEY POINTS FROM PRESENTATIONS

SESSION: BUILDING QUALITY INTO THE APPLICATION DOSSIER

The reason that HTA bodies make decisions or recommendations is to improve the efficiency of the health system at delivering value now and in the future and as such there are important implications for HTA decisions for all healthcare stakeholders. Speaking regarding quality in the HTA decision-making process, **Professor Adrian Towse**, *Director, Office of Health Economics* explained that it is possible to identify the key attributes of the process and outcome of HTA decision making, identifying quality issues such as transparency, stakeholder involvement and methods for handling additional research. However, when making decisions regarding the value of new medicines, there are two types of challenges, scientific uncertainty and value judgements that are met through weighting multiple criteria relevant to the decision using deliberative processes and algorithms. The question is, how structured could or should this weighting become?

At F. Hoffmann-La Roche, Switzerland, the Modelling Outcomes Research Statistics and Epidemiology (MORSE) Health Technology Assessment Group, headed by **Marlene Gylmark**, are strategic partners for internal and external stakeholders to deliver innovative credible payer evidence solutions. MORSE proactively provides early systematic literature reviews and health economic evaluations as input to integrated development commercialisation planning and life cycle investment point decisions, identifies unmet medical needs and target populations; provides input for trial designs, including comparators, primary and secondary endpoints and other measures; defines success criteria for developing a "best-in-class" drug and provides inputs into design of patient-reported outcome instruments. MORSE also provides evidence synthesis support, statistical analysis and health economic models to support reimbursement applications and price discussions, delivering fit-for purpose, high-quality, validated health economic models.

At Eli Lilly, those who manage HTA submissions have learned to self-assess their work through an experience-derived understanding of reviewer needs. **Louise Timlin**, *Director, ACE Health Outcomes and HTA, Eli Lilly and Company, UK* detailed those needs as robust, complete, high-quality data – synthesised into a comprehensive and objective overview of the available evidence. A concise well-constructed submission is desirable, in which data are clearly identified, synthesised, analysed and

presented with consistency and integrity of the evidence between text and tables and across sections. Submissions should be straightforward, logical and well written, with data clearly supporting claims and arguments. Maximum advantage must be taken of internal clinical and health economic expertise and cross-functional internal input and review and external advice and assessment from resources such as advisory boards and patient groups, with learnings shared among not only these stakeholders but also across jurisdictions.

SESSION: BUILDING QUALITY INTO THE HTA/COVERAGE REVIEW PROCESS

Although there is no formula for high-quality health technology assessment, **Dr Brian O'Rourke**, *President and Chief Executive Officer of the Canadian Agency for Drugs and Technologies in Health* stated that quality is a journey towards a goal which all health technology assessors strive. At CADTH, quality results from the achievement of the essential attributes of relevance, timeliness, credibility and impact as well as the contributing factors that underpin those qualities: technical competence, engagement, transparency and scientific oversight. This quality leads to the uptake and use of informed HTA decision making that informs clinical and policy decision making, which may result in increased alignment among payers and predictability of process.

Each time a new programme or activity is launched at the National Institute for Health and Care Excellence (NICE), procedural principles are considered that are paramount to its effectiveness: scientific rigour, inclusiveness, transparency, independence, challenge, review, relevance and timeliness. **Meindert Boysen**, *Programme Director, NICE*, explained that these principles centre on the agency's "accountability for reasonableness." The time to attain NICE decisions has significantly decreased in recent years and in 2012, final recommendations for most products were made shortly after marketing authorisation was achieved. However, after it was observed that improvements were required in rates of uptake and implementation of NICE recommendations, the NICE Compliance Regime was introduced to drive up compliance with NICE appraisals at local payer units. In addition, there has been a recent cultural shift at NICE, where the remit of the agency was expanded to fill the gap between health and social care services. Questions as to what constitutes innovation and the effect that adaptive licensing will have on health technology assessment, however, are for future debate.

SESSION: MEETING EXPECTATIONS

Lawrence Liberti, *Executive Director* and **Tina Wang**, *Portfolio Manager, Centre for Innovation in Regulatory Science – CIRS* provided the background and preliminary results for the 2013 CIRS HTA Industry Benchmarking Study. This study is the first focussed effort to benchmark the HTA process by following individual products from research through the payer recommendation, and was initiated to improve the design of pharmaceutical development programmes to address HTA requirements as early and efficiently as possible, defining targets to help focus on ongoing performance improvement initiatives and gaining a better understanding of the HTA system requirements in various jurisdictions. From 2011 through 2013, six companies provided data on nineteen phase III products and nine

companies provided data on thirty developed products. For the majority of products, study participants sought scientific HTA advice, most frequently from company-sponsored advisory boards followed by key opinion leader panels, advice from single HTA agencies and less commonly from multiple agencies simultaneously. Results to date also showed that the majority of products incorporated HTA requirements into phase III trial design, most often, HTA-acceptable endpoints, the inclusion of HTA-relevant comparators, and the use of patient-reported outcomes.

Participation in the CIRS HTA Industry Benchmarking Study has been an important mechanism to achieve Janssen internal process and benchmarking goals including transparency regarding time-sensitive inputs and deliverables. **Shane Kavanagh**, *VP, Health Economics Global Commercial Strategy Organization, Janssen* reported that the CIRS questionnaire was well received by market access colleagues with the organisation and obtaining the input of affiliates for the study has ensured that regional needs are captured in development and that regions are supported in their launch preparation. The data has helped to facilitate internal discussions, and areas of particular interest that emerged included the role and results of early advice, assessor –sponsor interactions during review such as requests for additional data, the use of real-world data in submissions and evaluations and general benchmarking in relation to other companies.

The preliminary results of the CIRS HTA Agency Pilot Benchmarking Study were presented by **Dr Iga Lipska**, *Senior Research Fellow, Centre for Innovation in Regulatory Science*, who discussed the general and product-specific data provided by eight participating HTA agencies from Belgium, Brazil, Canada (Common Drug Review), Canada - Quebec, Croatia, England, Lithuania and Scotland. Some of the initial top-line observations: five of the participating agencies employ fewer than 100 full-time employees and three of the agencies have more than 100; six of eight agencies use universities or academic centres as external resources for their work, five use independent contractors, two use consultancy groups and one agency uses a governmental agency as an external resource. Although the time from HTA submission to HTA recommendation was diverse, the median was 185 days, longer for drugs that were first in indication compared with follow-on therapeutics.

After coming under increasing scrutiny and criticism in response to the divergence between Scottish healthcare policy and that of a much larger and more highly resourced agency, the Scottish Medicines Consortium welcomed the opportunity for participation in the CIRS HTA Agency Study, a mutual, voluntary, fair comparison facilitated by a third-party organisation. **Anne Lee**, *Chief Pharmaceutical Adviser, Scottish Medicines Consortium* informed Workshop participants that SMC found the questionnaire to be straightforward and simple in scope, remit, structure, and outputs. The SMC, which expects to implement significant changes to its process, scope and budget within the next several years, expects to incorporate learnings from the work of other agencies reflected in this data collection project and looks forward to participation in the next phase of the CIRS HTA Agency study.

The Canadian Common Drug Review (CDR) was established to standardise the Canadian HTA environment by reducing the duplication of HTA and ultimately, to decrease the time taken for patients to access new and innovative medicines. Because of the differing opinions that have been published regarding the work of the CDR and subsequent Canadian payer decisions, it was suggested that CIRS could provide a nonbiased assessment of the Canadian payer environment that addresses the varying contexts of decision making. Accordingly, *CIRS Research Fellow*, **Nicola Allen** developed a study to identify which factors are most valuable to support the final reimbursement decision for drug products by provincial public payer reimbursement schemes. The study consists of the collection of public domain data for new active substances and major line extensions reviewed between January 2009 to June 2013, from Alberta, British Columbia, Ontario, and Québec, as well as for Australia, Scotland, and England. It also includes a survey for agency information and data regarding six specific drugs and interviews of study participants to provide insights into agency activities and patient input. Final results of this study will be available in late 2014.

Created in 2008, Alberta Health Services (AHS) conflated multiple governance entities to one, comprising 95,000 health professionals and support staff, 15,000 volunteers, 7,400 physicians in practice, serving 4 million Albertans through 98 acute care hospitals. **Dr Don Juzwishin**, *Director, HTA and Innovation, Alberta Health Services, Canada* discussed the Innovation Initiative at AHS, which consists of five programmes: *Assessment and Appraisal*, reviews and makes recommendations on health technologies through the systematic evaluation of global literature; *Reassessment* leads proactive re-assessments of potentially obsolete and/or cost- ineffective technologies; *Access with evidence development* designs and conducts field evaluations, including pilots and trials that collect AHS-specific data on effectiveness and cost effectiveness of new technologies; *Innovation* supports innovations developed within and outside AHS and *knowledge management and translation* acknowledges that the success of evidence-informed decision-making depends on the understanding and dissemination of the principles of HTA.

Day two Chair Meindert Boysen, *Programme Director, Technology Appraisals, National Institute for Health and Care Excellence* remarked that the first day's activities seemed to ascertain that there is value for both industry and HTA agencies in developing HTA-related industry benchmarking and performance indicators for HTA and coverage bodies, although challenges to these developments would include the establishment of a definition of *quality*.

CIRS introduced the Quality Scorecard concept to improve regulatory submissions and regulatory review by providing methodology to enable consistent comprehensive feedback to companies and authorities on the quality of their submissions and review practices; to identify whether there is a sound basis for identifying poor submissions; to facilitate the cross-comparison of reviews of same or similar new drug applications carried out by major regulatory authorities; to identify best practices regarding submissions and reviews and to enable these to be shared with a view to improve the decision-making process and increase efficiency and to provide a basis for an open dialogue between

authorities and companies. **Dr Neil McAuslane**, *Director, Centre for Innovation in Regulatory Science* explained that the Scorecard methodology approach might also provide agencies and companies with systematic standardised, routine feedback regarding their efforts to enhance the quality of HTA submissions and of their review. This approach may help HTA agencies achieve their goal to ensure the availability of cost-effective interventions through a high-quality approval process and help sponsors in their goal to clearly demonstrate how their products add value to patients and the healthcare system.

Dr Wim Goettsch, *Project leader of the EUnetHTA JA2 WP5 Rapid Assessments and Deputy Secretary, Medicinal Products Reimbursement Committee, Health Care Insurance Board (CVZ), The Netherlands* reported on the results of two pilots of rapid relative effectiveness assessment (REA), which were conducted as part of Work Package 5 of the European Network for Health Technology Assessment (EUnetHTA). Dr Goettsch concluded that in general, the quality of the industry submissions was well perceived by the author agencies that were responsible for the pilots and that all stakeholders are fully committed to make these pilots a success. That success, however, may hinge on anticipated changes in industry submissions based on changes in the REA report template and core model, the development of a manufacturer submission template and the conduct of scoping meetings before the start of the assessments to provide well-balanced and relevant submission files.

Recommendations from across the Syndicates

1. Quality item generation: Validate and discuss the potential indicators of quality in health technology assessments specified by this Syndicate with HTA agencies and their partners to develop a list that can then be piloted.
2. Quality in decision making: Explicitly explore quality in decision making separately from submission quality and review quality and develop or identify an instrument to be used to assess the robustness of deliberative processes within HTA agencies.
3. HTA agencies should increase transparency of their requirements and decision-making processes
4. Industry should tell the story clearly within their HTA submissions, highlighting assets and shortcomings and thinking about the relevance and potential use of their product in selected subgroups
5. Industry and HTA agencies should agree on two-way feedback on the quality of the submission and the assessment
6. CIRS should continue to pursue HTA benchmarking programmes and investigate the role of quality decision making in the HTA process.

WORKSHOP PROGRAMME

DAY 1: 2 DECEMBER 2013

SESSION 1: BUILDING QUALITY INTO THE APPLICATION DOSSIER	
Chairman's introduction	Prof Hans-Georg Eichler , <i>Senior Medical Officer, European Medicines Agency</i>
The quality of decisions and the decision-making process for HTA assessment	Prof Adrian Towse , <i>Director, Office of Health Economics, UK</i>
Quality management in an industry HTA department	Marlene Gyldmark , <i>Head of Modelling, Outcomes Research, Statistics and Epidemiology, F. Hoffmann-La Roche, Switzerland</i>
Critical self-assessment: What companies can learn from analysing their own HTA experience	Louise Timlin , <i>Director, ACE Health Outcomes and HTA, Eli Lilly and Company, UK</i>
SESSION 2: BUILDING QUALITY INTO THE HTA/COVERAGE REVIEW PROCESS	
Building quality into the HTA review process.	Dr Brian O'Rourke , <i>President and Chief Executive Officer of the Canadian Agency for Drugs and Technologies in Health (CADTH)</i>
Process or data? A HTA perspective on the keys to quality HTA recommendation	Meindert Boysen , <i>Programme Director, Technology Appraisals, National Institute for Health and Care Excellence</i>
SESSION 3: MEETING FUTURE EXPECTATIONS	
Chairman's introduction	Prof Hans-Georg Eichler , <i>Senior Medical Officer, European Medicines Agency</i>
Measuring industry HTA performance: CIRS study	Lawrence Liberti , <i>Executive Director, CIRS</i> Tina Wang , <i>Manager, HTA Programme, CIRS</i>
Study discussant – Industry perspective	Shane Kavanagh , <i>VP, Health Economics, Janssen Pharmaceutica, Belgium</i>
Measuring agency HTA performance: CIRS study	Dr Iga Lipska , <i>Senior Research Fellow, CIRS</i>
Study discussant – HTA/coverage perspective	Anne Lee , <i>Chief Pharmaceutical Adviser, Scottish Medicines Consortium</i>
The Canadian HTA process project	Nicola Allen , <i>Research fellow, CIRS</i>
Discussant – Canadian process project	Dr Don Juzwishin , <i>Director HTA and Innovation. Alberta Health Services, Canada</i>
SESSION 4: SYNDICATE DISCUSSIONS	
Introduction to the Syndicate discussions	
Syndicate A: Is it possible to develop an international set of performance indicators to measure the quality of the review process? What process and procedures would an ideal agency adopt?	Chair: Prof Robert Peterson , <i>Executive Director Drug Safety Effectiveness Network, Canadian Institutes of Health</i> Rapporteur: Deven Chauhan , <i>Strategy Director, Global Health Economics, GlaxoSmithKline, UK</i>
Syndicate B: What are the key elements of a quality dossier or submission that can enable the HTA/coverage review process and decision-making? What process and procedures should companies be adopting?	Chair: Prof Bruno Flamion , <i>Professor of Physiology and Pharmacology, University of Namur, Belgium</i> Rapporteur: Julia Chamova , <i>Director of Operations – EUnetHTA Secretariat, Danish Health and Medicines Authority</i>

DAY 2: 3 DECEMBER 2013

SESSION 4: SYNDICATE DISCUSSIONS <i>continued</i>	
Chairman's remarks	Meindert Boysen , <i>Programme Director, Technology Appraisals, National Institute for Health and Care Excellence</i>
Syndicate feedback and discussion	All participants
Panel discussion HTA perspective - Europe HTA perspective - USA Industry perspective	Dr Wim Goettsch , <i>Project Leader of the EUnetHTA JA2 WP5 Rapid Assessments, Health Care Insurance Board (CVZ), The Netherlands</i> Dr Sanjay Gupta , <i>Executive Director and Head, Health Economics and Outcomes Research, Daiichi Sankyo Inc, USA</i> Dr Thomas Lönngren , <i>Independent Strategy Advisor, Pharma Executive Consulting</i>
Measuring quality of the regulatory review process – Can this be a useful model for HTA agencies?	Dr Neil McAuslane , <i>Director, CIRS</i>
What has been the EUnetHTA experience with the pilot industry submissions project?	Dr Wim Goettsch , <i>Project leader of the EUnetHTA JA2 WP5 Rapid Assessments, Health Care Insurance Board (CVZ), The Netherlands</i>
Chairman's summary	Meindert Boysen

SYNDICATE DISCUSSIONS

Syndicate Discussion A

Syndicate A: Is it possible to develop an international set of performance indicators to measure the quality of the review process? What process and procedures would an ideal agency adopt?

Chair	Prof Robert Peterson , <i>Executive Director Drug Safety Effectiveness Network, Canadian Institutes of Health</i>
Rapporteur	Deven Chauhan , <i>Strategy Director, Global Health Economics, GlaxoSmithKline, UK</i>

Background

At the 2011 CIRS Workshop *Understanding HTA and coverage decision-making processes: The key to facilitating transparent access to medicines* it was recommended that CIRS should:

- Find mutually acceptable solutions and seek gradual improvement in the quality of HTA methods, assessments, and decision processes
- Assess HTA quality in the context of internationally accepted principles.
- Refine the definition of quality in the context of HTA
- Establish the elements of a quality dossier and a quality review
- Evaluate the Quality Scorecards system developed by CIRS for the regulatory field to assess the quality of dossier submissions and their reviews in the context of HTA

This Syndicate was asked to focus specifically on the area of the HTA review process and procedures and to identify potential performance indicators against which an agency could be evaluated and which relate to building quality into the process and procedures.

Although the definition of *quality* is difficult to establish, it is possible to identify parameters that can ensure a quality process. The questions this Syndicate was asked to discuss are “Is it possible to develop an international set of performance indicators to measure the quality of the review process? What process and procedures would an ideal agency adopt?”

Objectives

The objectives of this Syndicate were to:

- Identify the common elements of a review and the processes and procedures that ensure a quality review process
- Discuss which of these could be key performance measures of the review
- Recommend the elements that could be measured across agencies as indicators of a quality review process

Questions for consideration

- What are the common elements that underpin the HTA review?
- Which are the key areas that could be used to measure or provide feedback to an agency on the quality of its review?
- How could this information aid agencies as they evolve their processes and procedures?

The Syndicate was provided additional information to act as a starting point for discussions.

Key Performance Indicators that are considered important from a company's perspective with regard to quality of the HTA review process and procedures

- Availability of pre-submission advice
- Scientific advice (if appropriate)
- Process timeliness
- Consistency of the HTA interactions during the review
- Professional and scientific competence of the HTA authority
- Nature of the questions asked by the authority (Relevance, clarity)
- The quality of the assessment report as whether it is readily available
- The recommendation
- The extent and nature of communications and overall transparency
- Overall assessment of the review process

What might agencies see as other areas that can be used to measure the quality of the review either internally or with external feedback from the companies?

Measuring the agency process and procedures: Possible suggestions

Items to be considered	Types of areas that could be measured or a company could provide feedback on that would directional indicate areas where quality of the review maybe lacking
Pre-submission dialogue	<ul style="list-style-type: none"> a) Overall view on the pre-submission meeting b) The general approach taken by the authority in delivering the advice during the pre-submission meeting was ... c) The extent to which the provided advice was useful for the submission of the dossier d) The extent to which the provided advice was useful in avoiding / reducing objections being raised by the authority during review e) The extent to which the HTA was consistent in relation to previous advice given in a pre-submission meeting

Scientific advice (if appropriate)	<ul style="list-style-type: none"> a) Overall the provided scientific advice was . . . b) The general approach taken by the authority in delivering the scientific advice was ... c) The extent to which the provided scientific advice was useful to the development of the product d) The extent to which the provided scientific advice was useful in avoiding / reducing objections being raised by the authority during review e) The extent to which the HTA authority was consistent in relation to previous scientific advice given
Consistency of the HTA during the review	<ul style="list-style-type: none"> a) The extent to which the HTA authority was consistent in following its own guidelines and procedures b) The extent to which the guidelines were sufficient to address the type of application c) The extent to which the HTA was consistent in keeping in line with previous precedents when reviewing similar products
Professional and scientific competence of the regulatory authority	<ul style="list-style-type: none"> a) The knowledge and experience of the HTA authority in the therapeutic area of this reviewed product was . . . b) If HTA outsourced, knowledge and experience of the HTA authority in the therapeutic area of this reviewed product
Questions asked by the authority	<ul style="list-style-type: none"> a) The extent to which the questions asked during the process were relevant b) The extent to which the questions asked during the process were clear c) The timeframe stipulated by the authority for the provision of responses was . . . d) Were any of the questions asked based on misinterpretation or misunderstanding of the dossier? e) Were there any questions which were inappropriate and did not address a particular scientific deficiency in the data?
The assessment report	<ul style="list-style-type: none"> a) the Clinical Assessment b) the Economic Assessment
The recommendation	<ul style="list-style-type: none"> a) The extent to which the ultimate recommendation decision on the product was driven by science. b) The extent to which the decision-making process was open c) The opportunity for discussion and negotiation with the HTA in order to reach the optimal product decision
Communication	<ul style="list-style-type: none"> a) Overall, the quality of communication of the HTA authority was b).The extent to which the staff in the HTA authority were accessible c) The professionalism of the HTA authority was d) The transparency of the HTA authority was . . .
Timeliness	Did the HTA meet its own target time for completion of the assessment
Overall assessment of the review process	<ul style="list-style-type: none"> a) Overall, how would you rate the quality of the review process?

Additional information for consideration: Feedback from Syndicate discussion at the 2011 CIRS HTA Workshop: *Beyond benchmarking time and process: can we assess quality?*

Quality in the context of HTA: the syndicate developed a working definition of quality as “meeting expectations”, in this case, the expectations of the companies in relation to the quality of an HTA review and of the agencies in relation to the quality of the HTA submission. The group discussed other factors included in the determination of quality, including the stakeholder’s unique perspective, the transparency and timeliness of the process, and the manner in which to best present and consider relevant information. Furthermore, there was consensus that the quality of submissions directly relates to their solid scientific content. Ultimately, however, it was agreed that a complete and comprehensive definition of quality as it relates to HTA processes would require further analysis and refinement.

Elements of a quality dossier and review: listed by the syndicate in order of importance, the quality of a dossier to support a submission for HTA depends upon the robustness of the data that supports the reimbursement decision and the inclusion of all relevant information. The integrity of the data within the dossier is also critical; that is, the data must be consistent between tables and text and between clinical effectiveness analysis and economic evaluation or budget impact analysis. Finally, the physical dossier should be a logically structured, well written compilation using a clear format. Also named in order of importance, a quality review of an HTA submission must be transparent, scientifically sound, and scientifically consistent, that is, the same as for other drugs within the same therapeutic area, legally consistent by jurisdiction, address relevant needs such as societal values, be procedurally predictable, and within time targets.

The measurement of quality: according to this syndicate, of inputs, processes and outputs, quality is most easily measured in processes. Tools to ensure quality or to support good quality process such as internal and external peer-reviews, audits, the use of standard operating procedures and procedures for learning and feedback should be in place and followed.

The continuous improvement of quality: the Syndicate agreed that the impact of HTA decisions should be evaluated and built into future decision-making paradigms. Furthermore, quality HTA systems should be flexible and responsive, for example, to new data and evidence standards and should become even more adaptable in light of the growing prospect of international information exchange.

Transparency: documents related to HTA submission and review should be available in the public domain although confidentiality, particularly as it relates to patient-level data may be an issue. In the course of involving all stakeholders in dialogue all conflicts of interest should be disclosed.

Syndicate results: Critical issues

The Syndicate agreed that the regulatory framework for quality decision making could be translated for use for health technology assessment with some modifications. Caveats include the fact that not all agencies have the capacity to provide pre-submission dialogue or scientific advice and this element therefore may not be a legitimate point of comparison among agencies. In addition, compared with regulatory review, HTA involves complex issues in the management of multiple stakeholders and arguably, an even greater need for transparency and disclosure of assessment intricacies that are associated with the potential need for comparison with a plethora of comparators. Finally, an important difference between regulatory and health technology assessments is the need for HTA agencies to introduce advice on pharmacoeconomic modelling often with quite limited data being available.

There was consensus that the indicators of quality in HTA review as cited by Dr O'Rourke in his presentation were especially relevant. **Timeliness** was considered to be a key factor and the most measurable indicator of quality focused on whether adequate prioritisation techniques were employed by HTA agencies in their queue management systems and on the ways in which parallel reviews expedited results. Robust methods must be used to establish agency **credibility** and predictability of process and one credibility indicator might be the availability of guidance documents detailing HTA processes and the establishment of fora for stakeholder dialogue to iteratively improve the processes. An awareness of public health priorities and a dispute management procedure should also be included in HTA decision-making processes.

Agency **relevance** should be maintained through a customer focus that includes engagement with patients, payers and industry to ensure that all stakeholder viewpoints are represented. This representation includes the need for adequate patient education and an acknowledgement of the status of taxpayers as healthcare stakeholders. It was also questioned whether there might be a methodology to assess the quality of agency clarification questions and to monitor the amount and effect of unplanned agency-industry interactions.

Transparency in decision making is critical, particularly the communication of the attributes taken into account in the deliberative process and it was suggested that posting relevant documents on agency websites may be a potential method to enhance this communication, although the protection of intellectual property in some countries remains a concern.

It was questioned whether assessing the **impact** of HTA assessments is currently feasible. As implementation of the assessments is a statutory requirement, it is only possible to evaluate their impact on society as a whole, even though it is important to understand the impact of HTA on the actual payer. One potential method for assessing impact of an agency's technology evaluation, might centre on evaluating its expertise to diffuse that technology. Finally, it is important to remember that

the quality of the HTA review and decision are ultimately dependent on the quality of the HTA submission.

Critical issues

<p>TIMELINESS</p> <ul style="list-style-type: none"> • Timeliness is a key measurable indicator – if not met needs justification of delay • Industry perspective quality of review should not be hindered - clock stops? • Queue system – are the most important medicines being prioritised? 	<p>RELEVANCE</p> <ul style="list-style-type: none"> • Requests for clarification • Number of interactions with agencies • Two way feedback companies and agencies • Transparent communication of decisions • Transparency – list of available documents? • Forum for dialogue to improve processes • Who are the right stakeholders – patient versus public? Are they adequately educated
<p>CREDIBILITY</p> <ul style="list-style-type: none"> • Dispute management/ arbitration process • Consistency of decision-making processes • Unmet need and public health priorities encompassed in decision-making • Guidance documents on process and methods • Inclusion of all relevant evidence • Comparator/ standard of care 	<p>IMPACT</p> <p>How feasible is impact assessment? Implementation of TAs a statutory requirement</p> <p>Impact also around the expertise to diffuse technology</p> <p>Important to understand the impact of HTA on the actual payer</p>

Figure 1. Syndicate A outlined the factors in a quality review of health technology assessment.

Recommendations

- Quality item generation: Validate and discuss the potential indicators of quality in health technology assessments specified by this Syndicate with HTA agencies and their partners to develop a list that can then be piloted.
- Quality in decision making: Explicitly explore quality in decision making separately from submission quality and review quality and develop or identify an instrument to be used to assess the robustness of deliberative processes within HTA agencies.

Syndicate Discussion B

What are the key elements of a quality dossier or submission that can enable the HTA/coverage review process and decision-making? What process and procedures should companies be adopting?	
Chair	Prof Bruno Flamion , <i>Professor of Physiology and Pharmacology, University of Namur, Belgium</i>
Rapporteur	Julia Chamova , <i>Director of Operations –EUnetHTA Secretariat, Danish Health and Medicines Authority</i>

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- Refine the definition of quality in the context of HTA
- Establish the elements of a quality dossier and a quality review
- Evaluate the Quality Scorecards system developed by CIRS for the regulatory field to assess the quality of dossier submissions and their reviews in the context of HTA

This Syndicate was asked to focus specifically on the area of the HTA dossier and submission and to identify potential performance indicators against which a company could be evaluated which relate to the quality of the dossier so that companies could build quality into the process and procedure for dossier compilation and submission. Although the definition of *quality* is difficult to establish, it should be possible to identify parameters that can ensure a quality dossier and submission. The questions this Syndicate was asked to discuss were *What are the key elements of a quality dossier or submission that can enable the HTA/coverage review process and decision making? What process and procedures should companies adopt?*

Objectives

The objectives of this Syndicate group were to:

- Identify the common elements of a quality dossier and submission and indicate which of these could be key performance measures of a quality dossier/submission
- Discuss internal processes and procedures that companies should consider to ensure they build quality into the process for dossier submission and construction
- Recommend the elements that could be measured across companies as indicators of a quality dossier

Questions for consideration

- What are the Common elements which underpin a quality dossier/submission?
- Which are the key areas that could be used to measure or provide feedback to a company on the quality of the dossier?
- **How** could this information aid companies to provide quality submissions to HTA agencies?

The Syndicate was provided additional information to act as a starting point for discussions.

Areas that could be considered in regard to measuring the quality of the dossier/submission:

Application format: The presentation and construction of the dossier

Summaries/Overviews: Whether the reviewer feels that the company drew out and addressed the important issues, placing emphasis on the more critical areas

Use of pre-submission advice and/or guidelines: Whether the applicant had followed the advice provided

Technical content: The extent to which the supporting data for each section (Clinical analysis, economic analysis) of the application supported the proposed label

Response to questions: The way in which the company responded to issues raised during the review and the speed with which they provided additional data to the reviewer

Communication: The extent and value of the communication between the two parties throughout the review and whether those involved understood, and provided, what was needed:

Procedural operation: Measures of how well the review procedures had been followed

Outside of these other areas would agencies see as key areas for measuring the quality of the submission?

Measuring the sponsors dossier and submissions: Possible suggestions

Items to be considered	Types of areas that could be measured or a HTA could provide feedback on that would directional indicate areas where quality of the dossier/submission maybe lacking
Pre-submission advice Guidelines	a)The extent to which the advice/guidelines provided was followed
Application format	a) The format of the dossier and the logical order of the data was. b) The presentation of the dossier was (e.g. appropriate font size, layout, clear visuals and graphs) c) Ease of navigation through the dossier was d) The clarity of the language used in the dossier was... (e.g. was it clear and unambiguous) e) The completeness of the data set in the dossier was... (e.g. all necessary graphs and tables were included in the dossier Did the format of the dossier cause delays

Dossier and content Could be broken down into Clinical analysis Economic analysis	Summaries and overviews a) Overall rating on the quality of the summaries in each section The amount of detail in the summaries The extent to which the summaries reflect the supporting data The extent to which the major issues were addressed in the summaries and highlighted to assist the review The extent to which the summaries and overview are linked to other parts of the dossier Technical content B) Overall rating on the quality of the technical content The extent to which the technical guidelines were followed The extent to which the discussion addresses the consistency and inconsistency of results The extent that the data supports the proposed indication Completeness of the data in the dossier Is the data sufficient to support the cost and clinical effectiveness decisions
Communication	Overall the quality of communication of the company was... The extent to which the company contact was available The professionalism of the company contact was The transparency of the company was
Response to questions asked by the authority	The quality of the company's responses to questions raised was... The time taken to respond to the questions raised was ...
Competence of the company	The knowledge and experience of the company in the therapeutic area of this reviewed product was
Overall Quality Clinical assessment Economic assessment	Overall, how would you rate the quality of the dossier

Syndicate results: Critical issues

Syndicate members agreed that certain issues needed to be highlighted before a discussion of the quality of the dossier. These issues included the diversity among HTA agencies' requirements for the critical content of a quality dossier in different jurisdictions. This diversity adds further complexity to the ongoing challenge in designing clinical trials that satisfy both regulatory and HTA requirements and the agreement as to a core or standard set of content requirements would make life considerably easier for industry.

The group agreed that some subjectivity in judgement will always come into play in the process of HTA decision making, highlighting the importance of transparency regarding HTA requirements and decision-making processes in order for companies to build quality into their HTA submissions. Interaction and dialogue between an HTA agency and a company is also critical to HTA dossier quality, including early dialogue on pipelines and scientific advice at pre-submission meetings.

Strategies

The four elements of a quality dossier that were provided to the Syndicate from the 2011 CIRS HTA Workshop were still considered valid in December 2013. The robustness and relevance of the scientific data in the dossier; the dossier's completeness, that is, all relevant information is included; its integrity or consistency; and its logical structure and clear format. To these elements the group added that the dossier should "tell the story well" making it locally relevant and appealing or convincing. In addition, it was discussed that companies should be transparent and proactive in addressing the shortcomings and assets of the product, showing exactly where the most benefits will be relevant in this particular context; lay out and explaining assumptions made behind dealing with uncertainties.

Industry may also wish to consider including how scientific advice was incorporated into the dossier or justifications for not taking the advice. Subgroup analyses should be supported and the quality of support detailed. Other dossier suggestions included the specification of its overall quality and robustness of evidence and answers to questions as to whether societal needs were addressed adequately, cost-effectiveness well proven, justification for quality of life surrogates provided, the patient perspective presented and shortcomings highlighted.

The group agreed that there were three different "levels" of quality for HTA submissions: 1) meeting the requirements of an HTA agency proactively from the start and answering all concerns when expressed: 2) objective measures such as scientific quality, use of comparators, clarity, robustness and relevance of methodology and 3) "connecting all the dots" or telling the story well. Regarding this last point, it may be helpful to industry if HTA agencies would provide feedback regarding dossier "stories that were well-told."

Although the exact methodology of how to measure quality is still elusive, CIRS benchmarking, coupled with more experience from the continuing interaction between companies and HTA agencies will further inform and bring improvement to the process and quality of the dossier development as well as the HTA review process.

Recommendations

- HTA agencies should increase transparency of their requirements and decision-making processes
- Industry should tell the story well within their HTA submissions, highlighting assets and shortcomings and thinking about the relevance and potential use of their product in selected subgroups
- Industry and HTA agencies should agree on two-way feedback on the quality of the submission and the assessment
- CIRS should continue to pursue HTA benchmarking and investigate the role of quality decision making in the HTA process

APPENDIX: WORKSHOP ATTENDEES

Reimbursement, payer and care provider and regulatory agencies		
Meindert Boysen	<i>Programme Director, Technology Appraisals</i>	<i>National Institute for Health and Care Excellence, UK</i>
Julia Chamova	<i>Director of Operations – EUnetHTA Secretariat</i>	<i>EUnetHTA Secretariat, Danish Health and Medicines Authority</i>
Dr Don Juzwishin	<i>Director, HTA and Innovation</i>	<i>Alberta Health Services, Canada</i>
Prof Hans-Georg Eichler	<i>Senior Medical Officer</i>	<i>European Medicines Agency</i>
Dr Wim Goettsch	<i>Deputy Secretary</i>	<i>Medicinal Products Reimbursement Committee, Health Insurance Board, the Netherlands</i>
Anne Lee	<i>Chief Pharmaceutical Adviser</i>	<i>Scottish Medicines Consortium</i>
Dr Brian O'Rourke	<i>President and Chief Executive Officer</i>	<i>Canadian Agency for Drugs and Technologies in Health (CADTH)</i>
Prof Robert Peterson	<i>Executive Director</i>	<i>Drug Safety and Effectiveness Network, Canadian Institutes of Health Research</i>
Prof Adrian Towse	<i>Director</i>	<i>Office of Health Economics, UK</i>
Academic Institutions		
Prof Bruno Flamion	<i>Professor of Physiology and Pharmacology</i>	<i>University of Namur, Belgium</i>
Dr Anke Hövels	<i>Assistant Professor</i>	<i>Utrecht University, the Netherlands</i>
Pharmaceutical companies and consultancies		
Ali Azough	<i>Head of Health Economics</i>	<i>Amgen Limited, UK</i>
Michael Chambers	<i>Head, Reimbursement and Value Demonstration</i>	<i>GlaxoSmithKline, UK</i>
Deven Chauhan	<i>Strategy Director, Global Health Economics</i>	<i>GlaxoSmithKline, UK</i>
Dr Sanjay Gupta	<i>Executive Director and Head, Health Economics and Outcomes Research</i>	<i>Daiichi Sankyo Inc, USA</i>
Marlene Gyldmark	<i>Head MORSE – HTA Group</i>	<i>F Hoffmann-La Roche, Switzerland</i>
Shane Kavanagh	<i>Vice President, Health Economics</i>	<i>Janssen Pharmaceutica, Belgium</i>
Dr Thomas Lönngren	<i>Independent Strategy Advisor</i>	<i>Pharma Executive Consulting, UK</i>

Dr Jan Georg Moeller	<i>Director, Access Insights Speciality Medicine</i>	<i>Bayer HealthCare Pharmaceuticals, USA</i>
Dr Franz Pichler	<i>Director, Global Public Policy</i>	<i>Eli Lilly and Company, UK</i>
Louise Timlin	<i>Director, ACE Health Outcomes and HTA</i>	<i>Eli Lilly and Company, UK</i>
Dr Viktoriia Tymoshenko	<i>Communication and Change Manager, Global Market Access</i>	<i>Bayer Pharma, Germany</i>

Centre for Innovation in Regulatory Science

Nicola Allen	Doctoral candidate
Magda Bujar	Research Analyst
Patricia Connelly	Manager, Communications
Lawrence Liberti	Executive Director
Dr Iga Lipska	Senior Research Fellow
Dr Neil McAuslane	Director
Adam Somauroo	Senior Research Analyst
Prof Stuart Walker	Founder
Tina Wang	Portfolio Manager, HTA Programmes