



Understanding HTA and coverage decision-making processes:

**The key to facilitating transparent
access to medicines**

WORKSHOP SYNOPSIS
28-29 September 2011
Surrey, UK

Synopsis authors

Franz Pichler, PhD

Lawrence Liberti, MSc, RPh, RAC

Patricia Connelly, BA, ELS

The Centre for Innovation in Regulatory Science (CIRS) mission is to identify and apply scientific principles for the purpose of advancing regulatory and HTA policies and processes in medicines development.

CIRS is an independent UK-based subsidiary company, forming part of the Intellectual Property and Science business of Thomson Reuters. It is governed pursuant to constitutional documents that assure it is operated for the sole support of its activities. CIRS has its own dedicated management and advisory boards, and its funding is derived from membership dues and related activities.

Centre for Innovation in Regulatory Science (CIRS)
The Johnson Building, 77 Hatton Garden, London, EC1N8JS, UK
Email: Centre@cirsci.org
Website: www.cirsci.org

Report date: November 2011

The following is a high-level summary of key points from a Workshop conducted by the Centre for Innovation in Regulatory Science (CIRS) on 28-29 September 2011, in Surrey, UK. A complete Workshop Report including full presentation summaries and syndicate recommendations will follow.

Background to the Workshop

In general, countries want to improve their population's health by providing medicines that are safe and effective in a timely and efficient manner. Most jurisdictions take a broadly similar approach to providing access to new medicines, whereby the first requirement is the receipt of market authorisation from the regulatory authority based on meeting safety, efficacy and quality criteria. Following market authorisation, a coverage decision is often required to determine how payment for the medicine will be reimbursed. Increasingly, Health Technology Assessment (HTA) is being used to evaluate new medicines and to inform coverage decision making about the added benefits to populations covered, while sometimes also determining whether the new medicine represents added value for money.

There is considerable diversity between countries in the requirements of, the processes for and the extent of transparency in HTA appraisal and coverage body decision making. There is increasing interaction between different HTA agencies to begin to align their requirements and methodologies and also between regulatory agencies, HTA and coverage bodies in defining how to measure relative efficacy, provide shared early advice and otherwise co-ordinate their activities. The diversity of process and transparency represents a challenge to agencies as they try to learn from one another's strengths and capabilities and can hinder understanding and trust between the stakeholders involved.

This Workshop addressed the central question: given the diversity in the processes of HTA evaluation, coverage decision making and reimbursement between countries, *how can the activities of such different systems be compared?*

Workshop Objectives

- **Determine if the different HTA and coverage systems are comparable**
 - *For comparisons to be valid it is important to know on what basis they are made and to understand that the HTA and coverage bodies operate within very different frameworks.*
 - *Can a systematic approach to mapping the processes from regulatory approval to reimbursement provide an understanding of where each process fits into the organisations and health-care systems, the nature of the organisations and hence the meaningfulness of cross comparisons?*
- **Ascertain if there is value in developing HTA-related industry benchmarking**
 - *Companies routinely use internal targets to drive performance, but can comparison between companies in terms of the inclusion of HTA requirements into clinical development and the outcome on the following rollout be used to provide an understanding of the influence of HTA on development plans and rollout?*
 - *Can such benchmarking provide insight into predictability of time or success across jurisdictions?*
- **Establish whether there is value in developing performance indicators for HTA and coverage bodies**
 - *Such indicators could be used for the purpose of measuring ongoing reforms and change, identifying existing procedural facilitators and obstacles and for learning by comparison with peer agencies.*
 - *Is it possible to develop an international set of performance indicators, or should such comparisons be best conducted by region or by similarity of organisation?*

Key points from presentations

Day 1 Chairman, Prof Bengt Jönsson, *Professor of Health Economics, Stockholm School of Economics, Sweden*, initiated the Workshop by remarking that as health technology assessment has evolved over the past several decades to become increasingly important in both policy development and reimbursement decision making, seeking methods to compare and assess diverse international processes has become critical not just for purposes of efficiency and predictability but to stimulate and foster innovation and quality.

SESSION: TRANSPARENCY IN THE EVALUATING NEW MEDICINES FOR COVERAGE DECISIONS SHOULD BE A COMMON GOAL

Published in 2010, the *Rx&D International Report on Access to Medicines* revealed a wide diversity in public coverage for new medicines among the 34 member countries of the Organisation for Economic Cooperation and Development, which ranged from 88% to 19% of new medicines.¹ Although all HTA and coverage agencies are unique and the decisions they make are dependent on a variety of factors, **Dr Brian O'Rourke**, *President and CEO, Canadian Agency for Drugs and Technologies in Health, Canada* said that benchmarking their diverse principles, processes methods and timelines could lead to more consistency and predictability in performance, transparency, value and ultimately, patient access. However, he cautioned that to yield the best results, the benchmarking process should be kept as simple and collaborative as possible.

While **Greg Rossi**, *Vice President, R&D Payer Evidence, AstraZeneca, UK* agreed that transparency and harmonisation in assessments among HTA agencies is possible, current variance in mandates and criteria for assessment will continue to lead to different reimbursement decisions (Figure 1). Nevertheless, the innovative pharmaceutical industry looks to HTAs, that these may facilitate an appropriate benefit for innovation and with the hope that together both stakeholders can build trust in each others' data and rigorous decision-making processes and ensure a clear understanding of the value that innovative products bring to a target population. Harmonisation and transparency among HTA agencies are achievable when assessing the potential effectiveness for new medicines, but transparency and harmonisation in consideration of real-life effectiveness and value are still being debated.

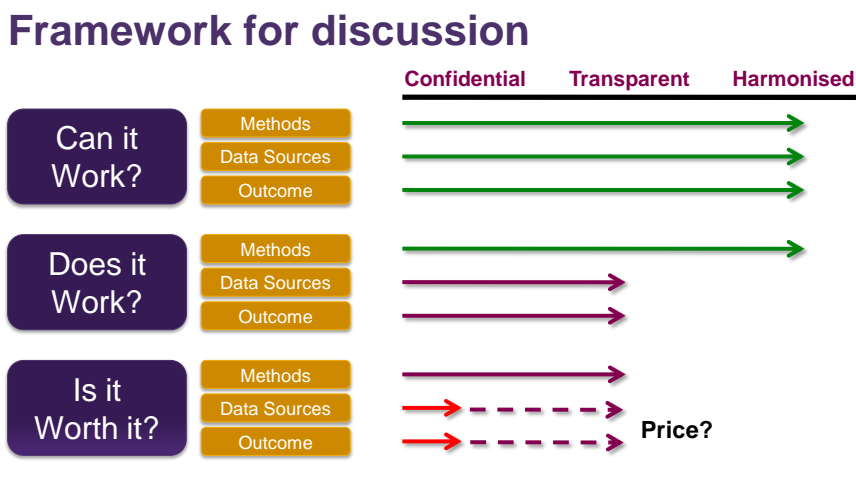


Figure 1. Rossi: The potential for harmonisation and transparency in HTA decision making.

SESSION: HOW ARE TRANSPARENCY, QUALITY AND PREDICTABILITY BUILT INTO DIFFERENT REVIEW SYSTEMS?

Recognising that health outcomes are significantly affected by disparities in clinical judgement and skill and adherence to evidence-based medicine **Dr Marc Berger**, *Executive Vice President & Senior Scientist*,

OptumInsight, UnitedHealth Healthcare Group (UHG), USA, explained that his organisation has been able to positively impact health outcomes through a two-tiered approach of changing clinical behaviour in the treatment of commonplace conditions and ensuring quality treatment through experienced “centres of excellence” for patients with rare, complex conditions. Using information in their data warehouse UHG is able to benchmark performance; analyse practice variation and identify higher quality, higher efficiency providers; provide actionable information to patients and target appropriate patients for care management and referrals to those centres of excellence.

Regulatory agencies have benefitted from the identification of common benchmarking approach and have used the results of independent assessments to identify and implement best practices. For example, since 2006 Swissmedic has successfully met stakeholder expectations for increased efficiency, transparency and consistency with the assistance of external benchmarking and internal indicator systems such as the Advanced Planning and Scheduling System. **Dr Petra Dörr, Head of Management Services and Networking, Swissmedic, Swiss Agency for Therapeutic Products** explained that in addition to increased efficiency, flexibility and adherence to target times, it is expected that this system will optimise transparency in terms of project status and resource utilisation. Experience from the regulatory agencies suggests that a similar approach to benchmarking could be applicable to the activities of seemingly diverse HTA agencies.

SESSION: CASE STUDIES OF PERFORMANCE INDICATORS FOR A NATIONAL HTA AGENCY

According to **Prof Lloyd Sansom, Emeritus Professor, Division of Health Sciences, University of South Australia**, because of international differences in legally available public information, benchmarking HTA processes from public domain data may be challenging. However, readily available performance indicators for the Pharmaceutical Benefits Advisory Committee (PBAC) of Australia demonstrate that approximately 90% of new drugs are recommended for coverage in Australia within 5 years of first submission to the agency (Figure 2). These data indicate that for many drugs, however, multiple resubmissions and data reanalyses are required and PBAC is committed to using the results of this type of benchmarking project to enhance international dialogue and cooperation with all stakeholders to optimise the efficiency and effectiveness of the HTA process.

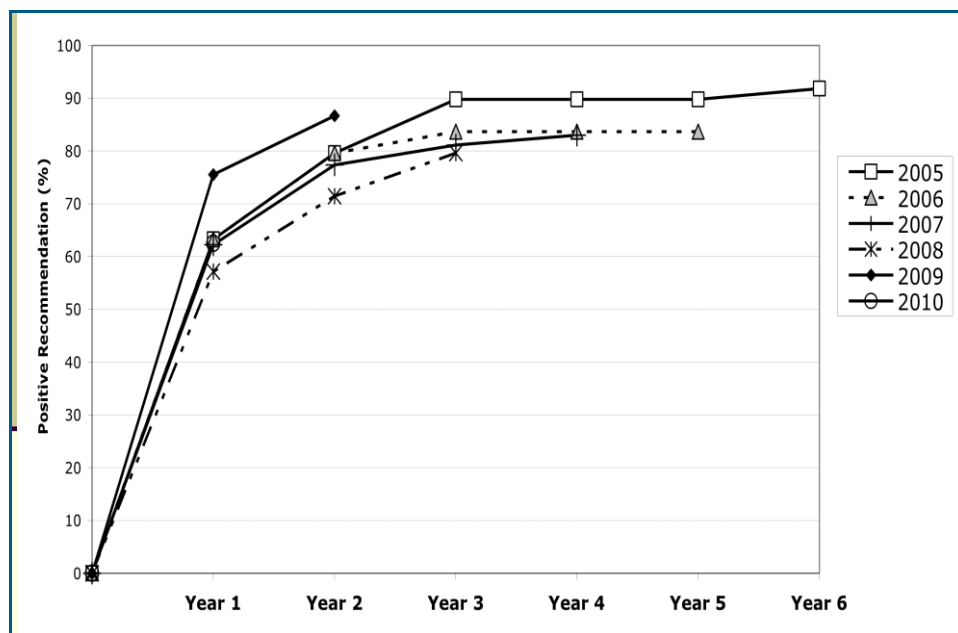


Figure 2. Sansom: Cumulative PBAC recommendation percentage for initial major submissions.

Since its beginnings in March 2000, the National Institute for Health and Clinical Excellence (NICE) has issued guidance on 232 new medicines. **Nina Pinwill**, *Associate Director, Centre for Health Technology Evaluation, NICE, UK* explained that during that time, NICE has adjusted its processes and methods to meet the expectations of a broad group of shareholders, and this adaptation will continue with the implementation of value-based pricing for new medicines beginning in January 2012. Although significant changes are underway in the National Health Services, NICE is expected to continue to remain at the centre of new policies to improve access and innovation in medicine.

SESSION: CAN COMPARISON, PERFORMANCE INDICATORS AND BENCHMARKING USED TO ENABLE SHARED LEARNING?

In 2008, the International Working Group for HTA Advancement published *Key principles for the improved conduct of health technology assessment for resource allocation decisions*.² Day 1 Chair **Prof Bengt Jönsson**, *Professor of Health Economics, Stockholm School of Economics, Sweden*, reported that a subsequent investigation into the use of and support for those principles showed that while no health technology organisation implemented all fifteen of the principles, support for this approach is positive among European agencies.³ Publications on HTA benchmarking and principles for comparative effectiveness research are currently underway.

Because member companies of the CIRS HTA Programme indicated that CIRS could add value by undertaking a programme to determine the impact of HTA requirements on the development of new products, CIRS has initiated a pilot for a benchmarking database that tracks individual products through their development and rollout. Although assessing the comparison of the impact of diverse HTA systems represents a significant challenge, **Dr Franz Pichler**, *Manager, HTA Programme, CIRS*, detailed the preliminary results derived from observations on twelve products across eight jurisdictions that support the feasibility of the proposed CIRS benchmarking process, provided an indication of individual insights to come, identified new areas of investigation and highlighted the need to contextualise the results (Figure 3).

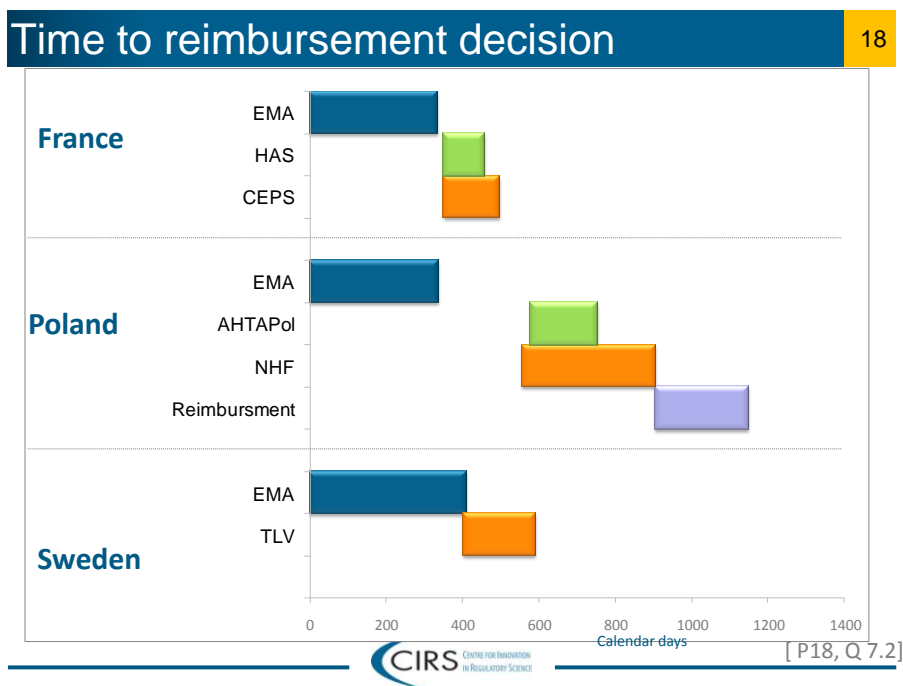


Figure 3. Pichler: Preliminary results from the CIRS HTA database feasibility study highlight the need to contextualise data.

Day 2 Chairman, Prof Adrian Towse, *Director, Office of Health Economics (OHE), UK* introduced the second day's presentations by remarking that the process developed for and lessons learned from the ongoing benchmarking of regulatory agencies in Europe can and should be successfully translated for use in an HTA context.

SESSION: BUILDING QUALITY THROUGH CREATION OF A COMMON TECHNICAL DOCUMENT FOR HTA

As *Director of the Secretariat, European Network of Health Technology Assessment (EUnetHTA)* **Prof Finn Børlum Kristensen** reported on the development and implementation of good practice principles for assessing relative effectiveness based on the EUnetHTA HTA Core Model, a pool of structured information categorised into nine chapters or “domains” which permit a consistent presentation of information deemed necessary to inform an HTA decision. The core model has been developed as an online tool. Dr Kristensen noted that although there are more similarities than differences underlying the scientific assessment of relative effectiveness across jurisdictions, in EUnetHTA's development of the framework for a common European methodology, both the differences between countries and the context for those differences are considered.

SESSION: TIMELINESS, QUALITY, PREDICTABILITY AND TRANSPARENCY IN HTA/COVERAGE: A VIEW FROM OTHER KEY STAKEHOLDERS

Considering how transparency and comparison of systems will benefit HTA-regulator interaction, **Prof Hans-Georg Eichler**, *Senior Medical Officer, European Medicines Agency, (EMA), UK* stated that because the move toward increased transparency by regulators is unavoidable and independent comparisons of regulatory activities are already underway, HTA organisations should work towards facilitating open discussion about the scientific basis for their decisions especially when diverse coverage decisions for the same new medicine occur across jurisdictions. Approaches can include the alignment of methodology and evidence standards, the explanation of divergent decisions on the basis of credible differences in regional healthcare environments and the anticipation and management of high-profile variances in decision outcomes.

Speaking on behalf of industry stakeholders, **Ed Godber**, *Vice President, Access to Medicines Centre of Excellence, GlaxoSmithKline, UK* suggested four concepts that can help optimise innovation through health technology assessment; predictability of the value of a new medicine can be best attained through linking the assessment to the medicine's performance in the health system; transparency through a commitment to review the product's performance through the use of sound scientific approaches; quality through “value mapping” the evidence-generation process ensuring precision to address evidence throughout the product's life cycle and timeliness through an ongoing dialogue and scientific exchange to support the alignment of evidence with public and patient value expectations.

References

1. Wyatt Health Management. *The Rx&D International Report on Access to Medicines*. Available at http://www.patientscomefirst.ca/inc/pdfs/RxD_InternationalReport_2010_en.pdf; accessed October 2011.
2. Drummond MF, Schwartz J, Jönsson B. Key principles for the improved conduct of health technology assessment for resource allocation decisions. *Int J Technol Assess Health Care*. 2008;24:244-258.
3. Neumann PJ, Drummond MF, Jönsson B. Are key principles for the improved conduct of health technology assessment supported and used by Health Technology Assessment organizations? *Int J Technol Assessment Health Care*. 26: 71–78.

Syndicate Discussions

Key Points from Syndicate Discussion 1

Can milestones be identified to allow for meaningful comparison between different HTA or coverage bodies?

- **Which HTA and/or payer organisations should be benchmarked?** Members of this Syndicate recommended benchmarking not only individual agencies but also the entire HTA and payer system. With self-improvement as a goal, these stakeholders were advised to initiate a circle of voluntary mutual comparisons leading to gradual overall progress, before financially pressed local governments intervene. The focus in this process should be on identifying value-added steps and improving process efficiency, and identifying dimensions such as medical need that can be compared across countries.
- **What to benchmark?** The scientific and technical aspects of HTA assessment should be mapped and understood for purposes of comparison and benchmarking. These maps must be explicit and fully transparent with the goal of reducing unintentional random variations among processes. Although the societal values implicit in appraisals, pricing, and reimbursement decisions should also be mapped and understood, they are not yet amenable to benchmarking. Rather, the foundation must be laid for a stepwise, bottom-up, long-term convergence of decision-making processes.
- **Expectations, goals and incentives of different stakeholders:** In addition to efficiency and speed, the pharmaceutical industry seeks predictability and consistency from HTA and payer agencies in their dealings with scientific evidence. For their part, healthcare decision makers want accountability affordability equity, value for money and to some degree, synergy between agencies. Total quality improvement and improved patient access are shared but still distant goals, with healthcare systems and budget silos often acting as negative incentives.
- **The Donabedian framework and the 15 principles for quality improvement:** It was this group's consensus that the combination of the well-established "Donabedian model" of examining the input, process and outcome of a system specially to evaluate healthcare services together with the 15 key principles for the improved conduct of health technology assessment cited by Professor Bengt Jönsson in his presentation should serve as an excellent foundation for HTA process enhancement. Of the input aspects of the model, the Syndicate identified agency planning and prioritisation as particularly key; whilst consolidating HTA models was deemed an essential process and the planned and thoughtful dissemination of results was identified as one of the most important aspects of HTA outcomes. It was recognised, however, that the infrastructure to evaluate those dimensions on a regular basis would require substantial resources.
- **Dimensions and efficacy:** To avoid redundancy in efforts to establish the various elements of efficacy in HTA assessment such as comparators, pharmacoeconomic studies and disease-specific guidelines, the Syndicate advocated synergies and the use of existing models among the various groups examining HTA improvement such as the International Network of Agencies for Health Technology Assessment and the European Network for Health Technology Assessment.
- **Time and timeliness indicators:** The Syndicate suggested that although the total timing of a coverage assessment is important, an examination of time to achieve interim milestones would likely be of more practical utility, and the trade off between the timing and quality of HTA-sponsor interactions is a vital consideration.

Key Points from Syndicate Discussion 2

Removing barriers to patient access to new medicines

- **National barriers:** It was this group's consensus that barriers to patient access include inter-country differences such as existing legislation and bureaucracy, social philosophy, economics, treatment practices, clinical trial endpoint preferences, current expectations of benefit-risk and clinical benefit and comparative or relative effectiveness and the influence of patient-relevant outcomes.
- **History of change:** Although acceptance of the Common Technical Document (CTD) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and for the Centralized Authorisation procedure of the European Medicines Agency took more than a decade, it was hoped that the speed of innovation can facilitate faster acceptance of common HTA standards and processes. It was further anticipated that the work of the European Network for HTA, CIRS and other HTA organisations will contribute to the recognition of this standardisation behind decision making.
- **The importance of dialogue:** Dialogue, that is, the improved communication and collaboration among stakeholders, was determined to be the key to HTA enhancements that would accelerate patient access to medicines. A common lexicon is already being developed and its continued thoughtful development will be necessary for this communication to grow. Industry should communicate, potentially through publication, the learnings in both process and outcomes from parallel submissions to multiple HTA bodies and from HTA and regulatory agencies. Stakeholder consensus on pharmacoeconomic models should also be published. All of these communications should be enhanced by engagement with patients or patient advocates.

Key Points from Syndicate Discussion 3

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 perspective, the transparency and timeliness of the process and the consideration of all available information, and there was consensus that the quality of submissions directly relates to solid scientific content. Ultimately, however, it was agreed that a complete and comprehensive definition of quality would require further analysis and refinement.
- **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, standard operating procedures and procedures for learning and feedback should be in place and followed

- **Elements of a quality dossier:** 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 match between tables and text, 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.
- **Elements of a quality review:** Also named in order of importance, a 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, include all relevant information such as societal values, be procedurally predictable, within time targets and follow correct format and structure.
- **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.
- **The continuous improvement of quality:** The Syndicate agreed that the impact of HTA decisions should be evaluated and built into future decision-making. Furthermore, quality HTA systems should be flexible and responsive; for example to new data and evidence standards and should increase due to international information exchange.

Conclusions

The role of health technology assessment in the delivery of quality and cost-effective healthcare continues to evolve. National differences in economies, politics, standards of treatment and expectations of benefit and risk will continue to result in disparate HTA decisions, but elements of a high-quality HTA procedure and underlying decision methods are quantifiable and amenable to international alignment.

Although the harmonisation of regulatory submission and the centralisation of regulatory review in Europe took place over a period of decades, it is anticipated that based on this work, similar alignment in the field of health technology and reimbursement may be achieved more expeditiously. Anticipating this alignment, HTA and payer agencies may wish to identify and benefit from regional best practices by comparing and benchmarking their own procedures and performance against one another or against the established model of examining the input, process and outcomes to evaluate their activity.

This self-benchmarking, the establishment of a common lexicon, the continued dialogue among stakeholders and the synergy of ongoing efforts by multiple outside groups such as the European Network for Health Technology Assessment, CIRS and others will all be essential elements in the ongoing enhancement of the predictability, transparency, quality and timeliness of health technology assessment.

SPECIAL THANKS TO

The Workshop Chairs

Prof Bengt Jönsson, *Professor of Health Economics, Stockholm School of Economics (SSE), Sweden*

Prof Adrian Towse, *Director, Office of Health Economics (OHE), UK*

Presenters

Dr Brian O'Rourke, *President and CEO, Canadian Agency for Drugs and Technologies in Health (CADTH), Canada*

Professor Hans-Georg Eichler, *Senior Medical Officer, European Medicines Agency, (EMA), UK*

Greg Rossi, *Vice President, R&D Payer Evidence, AstraZeneca, UK*

Ed Godber, *Vice President, Access to Medicines Centre of Excellence, GlaxoSmithKline, UK*

Dr Marc Berger, *Executive Vice President & Senior Scientist, OptumInsight, UnitedHealth Group, USA*

The Syndicate Chairs

Dr Petra Dörr, *Head of Management Services and Networking, Swissmedic, Swiss Agency for Therapeutic Products*

Syndicate 1: Prof Bruno Flamion, *Chairman, Belgian Committee for Reimbursement of Medicines (CTG/CRM), Belgian National Institute for Health and Disability Insurance (INAMI-RIZIV)*

Prof Lloyd Sansom, *Emeritus Professor, Division of Health Sciences, University of South Australia*

Syndicate 2: Katrine Frønsdal, *Senior Researcher, Norwegian Knowledge Centre for the Health Services (NOKC), Norway*

Nina Pinwill, *Associate Director, Centre for Health Technology Evaluation, National Institute for Health and Clinical Excellence (NICE), UK*

Syndicate 3: Barbara Sabourin, *Senior Executive Director, Therapeutic Products Directorate (TPD), Health Canada*

Prof Bengt Jönsson, *Professor of Health Economics, Stockholm School of Economics (SSE), Sweden*

The Syndicate Rapporteurs

Dr Franz Pichler, *Manager, HTA Programme, CIRS*

Syndicate 1: Pierre Sagnier, *Vice President, Development Projects, Global Market Access, Bayer Health Care Pharma, Germany*

Prof Finn Børlum Kristensen, *Director, European Network of Health Technology Assessment (EUnetHTA)*

Syndicate 2: Angus Grant, *Vice President, Business Development and Global Strategic Alliances, Celgene Corporation, USA*

Syndicate 3: Dr Iga Lipska, *Senior Research Fellow, CIRS*