WORKSHOP REPORT

Working across regulatory and HTA agencies: collaborative, work-sharing and reliance models – what are the policy implications?

9-10th October 2024
Oatlands Park Hotel, Surrey, UK

CIRS Centre for Innovation in Regulatory Science

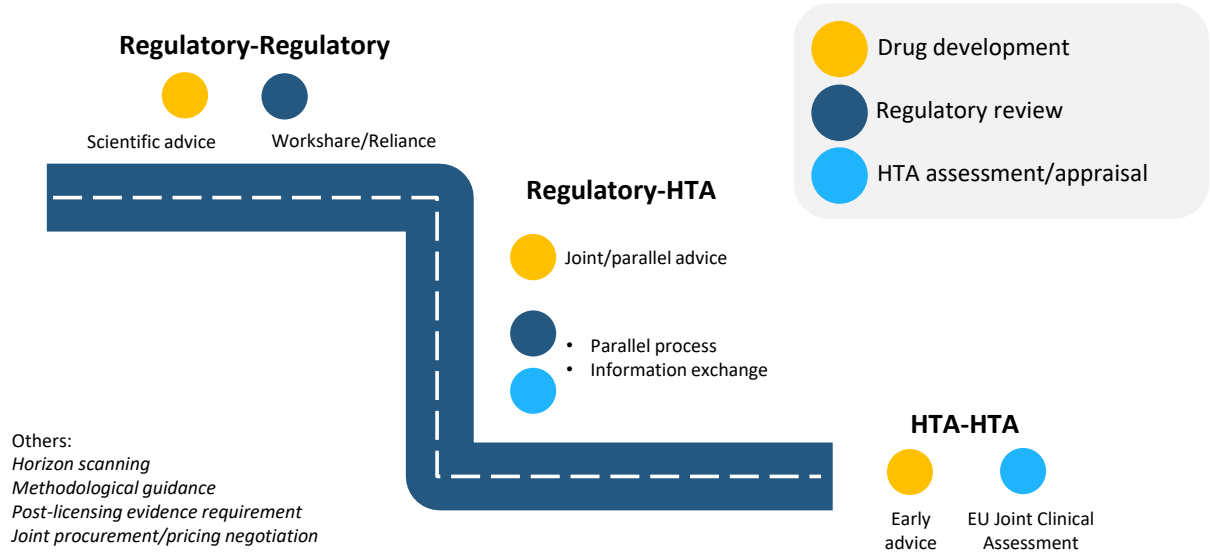
Executive Summary

Background

This workshop was part of a CIRS series looking at new ways of working within and across regulatory and health technology assessment (HTA) agencies to provide a platform for discussion on work sharing, collaborations, reliance and the policy implications and outcomes of such practices on regulatory-HTA alignment and decision making. While regulatory and HTA collaborations were the main focus of this workshop, payer collaborations were also discussed.

There are various dimensions to stakeholder collaboration across the medicine life cycle (see below). There can be a horizontal dimension, where the same type of stakeholders work together e.g. regulatory-regulatory, HTA-HTA etc, as well as a vertical dimension, where different stakeholders (usually within the same jurisdiction) work together e.g. regulatory-HTA. Furthermore, stakeholder collaborations can take place at different stages of the medicine lifecycle and at either a methodological or policy level.

Dimensions of Stakeholder Collaboration Across the Medicine Lifecycle



Regulatory agencies have over the last decade developed review models which build in collaboration e.g. Project Orbis, work sharing e.g. Access Consortium, or reliance routes where one agency can leverage the decision of another trusted agency. There are also collaborative models happening on a regional level such as the various joint assessment initiatives in Africa and the EU centralised procedure.

More recently, formal collaborations have formed among HTA agencies in various jurisdictions. Based on the experiences from EUnetHTA Joint Actions, the European Commission has adopted the HTA Regulation (HTAR), which came into force in January 2025. The new framework covers joint clinical assessments (JCA), joint scientific consultations (JSC) the identification of emerging health technologies, and voluntary cooperation. Outside of Europe, eight HTA agencies from Australia, Canada, New Zealand and the UK have started to plan collaboration on a range of topics and are exploring the feasibility to use each other's HTA information.

Collaboration during development is also being explored across several regulatory and HTA agencies. Indeed, scientific advice during development can help bridge or inform the evidence gap between regulatory and HTA

needs; this tool is evolving with experience. Joint regulatory-HTA advice and joint HTA-HTA scientific advice is evolving both across jurisdictions as well as within them.

These interactions between HTA and regulatory agencies and the networks for collaboration and work sharing are aimed at making HTA and regulation more efficient. However, as agencies are embarking on new ways of working, the actual experiences and practical processes are still being tested. The changing environment in turn impacts companies' development and submission strategies.

In this workshop, CIRS brought together senior representatives from regulators, HTA agencies, pharmaceutical companies, payers, academics and patient organisations to discuss the impact of regulatory and HTA collaborative models and how these should evolve.

Objectives

This multi-stakeholder workshop consisted of a series of sessions (see programme) featuring presentations and panel discussions, as well as three parallel breakout discussions. The objectives were to:

- Assess the impact of different regulatory and HTA collaborative models on development, regulatory review and HTA assessment.
- Understand the experiences and learnings from current regulatory-regulatory, HTA-HTA and regulatory-HTA collaborative models. What can be learnt at regional, national, and international levels? How do these models influence companies' development strategy and jurisdictional roll out?
- Make recommendations on the current and future development of regulatory and HTA collaboration, such as the EU HTA Regulation and its jurisdictional implementation, international initiatives outside of Europe and cross-continent partnerships.

Key points from presentations and open-floor discussions

Regulatory-regulatory collaboration

Regulatory convergence has enabled collaboration

As the regulatory environment has evolved, technical guidelines and review practices have converged to a degree that enables collaborative reviews, work sharing and other models where one agency leverages expertise from another. Various organisations such as the International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH), International Medical Device Regulators Forum (IMDRF) and the International Coalition of Medicines Regulatory Authorities (ICMRA) have helped to promote this convergence over the years.

Further regulatory-regulatory collaboration could be enabled by enhancing transparency, such as improvements to sharing assessment reports and other approval documents, and by using IT platforms to support information exchange between regulators, as well as global company submissions.

Much can be learned from the EMA

The European Medicines Agency (EMA) is one of the oldest forms of regulatory collaboration, which, since 1995, has been coordinating the evaluation and monitoring of centrally authorised products, developing technical guidance and providing scientific advice. While it has helped to build trust between regulators in Member States, which is a key success factor, not all regulators participate in Rapporteur/Co-Rapporteur roles to the same extent. The new Pharmaceutical Legislation provides opportunities for further regulatory-regulatory collaboration within the EU, such as the use of regulatory 'sandboxes' for joint experimentation and learning.

Access and Project Orbis are accelerating regulatory timelines, but could go further

CIRS research has shown that the Access Consortium and Project Orbis are helping to reduce submission gaps, suggesting that these collaborative efforts are supporting efficiency gains. Nevertheless, there is a trade-off between the resources required to make the collaboration successful vs the resources saved as a result; for example, one agency within the Access Consortium found that reviewing one module of a work-share application usually helped to save resources internally but reviewing two modules did not.

From an industry perspective, extending Project Orbis to include additional regulators and other therapeutic areas could make it even more impactful. Regulators should consider promoting better understanding of these collaborative models among companies to improve uptake.

Strong leadership and trust can support mindset change

Without strong leadership, changing the mindsets of reviewers to trust a new collaborative model is difficult. Fostering trust and a culture of learning is key; this can help to prevent potential inefficiencies in a work-sharing arrangement, for example, where peer reviews are conducted multiple times by agencies.

HTA-HTA collaboration

HTA-HTA collaborations are less mature than regulatory-regulatory collaborations

A collaborative culture has been steadily developing and expanding within the HTA community. HTA-HTA collaborations span a wide range of initiatives, each impacting different aspects of the HTA process, from method development and implementation to joint assessment of specific health technologies. However, compared to regulatory collaborations, the maturity and depth of collaborations among HTA agencies are still at a relatively early stage.

The remit of HTA-HTA collaboration can include:

- sharing experiences and best practices, which can be facilitated through various forums such as HTA International (HTAi) and CIRS
- developing approaches for common challenges, such as surrogate endpoints and modelling treatment pathways
- agreeing a standard framework for producing and reporting HTA evidence e.g. EUnetHTA Core Model
- work sharing in the form of joint assessments of new interventions, such as through EU joint clinical assessments (JCAs), the BeNeLuxA initiative and Joint Nordic HTA Bodies (JNHB) collaboration.
- common decision making i.e. making recommendations on the use or funding of new interventions in the respective jurisdictions
- sharing work on horizon scanning.

Mandatory collaboration at the EU level

While the majority of HTA-HTA collaborations are voluntary, the adoption of the EU HTAR has created a mandatory form of HTA-HTA collaboration; HTA agencies are working together through the EU HTA Coordination Group (HTA CG) and its subgroups to prepare for the implementation of HTAR from 2025. While EU JCAs may replace some aspects of joint assessment work already being done within the BeNeLuxA and JNHB initiatives, health economics is not within the scope of JCA and so there will still be value in these collaborations conducting joint pharmacoeconomic assessments.

Joint development takes time

An international collaboration between HTA agencies in Australia, Canada, New Zealand and the UK initially focused on work sharing, horizon scanning, and science and methods advancement. While some areas have had more success than others, the collaboration has enabled the agencies to learn from one another, share best practices and tools, and align in their approaches.

International collaboration is especially important for emerging HTA agencies

International collaborations are important for emerging economies that are developing their HTA systems. For example, the HTA process set up in Taiwan in 2007 drew reference from the HTA programmes of Australia, Canada, and the UK. Engaging with international HTA organisations, such as HTAi and the International Network of Agencies for HTA (INAHTA), and regional networks like HTAsiaLink, are also key to facilitating knowledge exchange and best practices to strengthen local capabilities.

Leveraging the work of other HTA agencies

Adaptive HTA is an umbrella term for a variety of methods used to combine evidence synthesised elsewhere with local adaptation and content. These are often applied in settings with limited HTA capacity, such as in low and middle-income countries, and situations where decisions must be made in a limited timeframe. However, the trade-off for greater speed and efficiency is some sacrifice of accuracy or increase in uncertainty, so caution is required in adjusting and adapting transferred HTA data to the local context. Working with patients and patient groups may help to identify key information in HTA summary reports.

Regulatory-HTA collaboration

Many opportunities but also barriers to overcome

There are many opportunities for regulators and HTA agencies to collaborate, including joint horizon scanning, joint/parallel scientific advice, parallel regulatory and HTA review, IT portals to enable simultaneous management of regulatory and HTA submissions, and aligned post-approval commitments, particularly for medicines with provisional/conditional regulatory approval. Regulatory-HTA collaboration should facilitate understanding of each stakeholder's remits, while maintaining separate roles and decision making. By working together, regulators and HTA agencies can develop innovative methods and solutions to reduce uncertainties.

However, there can be barriers to regulatory-HTA collaboration, such as organisational structures that create silos, concerns that HTA may influence regulatory decisions, and legal constraints in sharing confidential information. From the patient perspective, regulatory-HTA collaboration needs to be strengthened to avoid duplication and accelerate patient access to therapies. Metrics are key to understanding whether closer regulatory-HTA collaboration leads to more medicines being reimbursed and/or faster reimbursement decisions. Patients must consistently be involved across drug development, including in parallel scientific advice.

Parallel scientific advice needs to evolve

While there is no doubt that regulatory-HTA collaboration has value in optimising evidence development and addressing uncertainties, it may be too early to say whether parallel scientific advice is enabling predictable outcomes for industry. Capacity for parallel advice needs to be built to ensure that advice is provided on time to inform company development programmes. Evolving the parallel advice process to make it less intensive and more efficient would be beneficial to both companies and agencies.

Learnings from the UK Innovative Licensing and Access Pathway (ILAP)

The UK Innovative Licensing and Access Pathway (ILAP) is an example of vertical (regulatory-HTA-payer) and horizontal (HTA-HTA) collaboration aiming to provide earlier patient access to innovative medicines. First established in 2021, ILAP has been relaunched to address capacity and governance challenges faced first time round. The refreshed pathway will operate under an improved governance system that will hopefully overcome the complexities of working across organisational boundaries. Other learnings from the first ILAP include the need for all partners to align on a shared vision and for constant evolution towards a successful and sustainable pathway.

Disconnect between expedited regulatory decisions and HTA

Expedited timelines from regulatory-regulatory collaborative initiatives like Project Orbis have highlighted a longer submission gap to HTA agencies following regulatory approval. This is particularly evident with products granted

Orbis Type A approvals in Australia and Canada, where the regulatory review is concurrent with FDA with simultaneous submission (less than 30 days from FDA submission) (see CIRS R&D Briefing 96). Vertical collaborations and information sharing among stakeholders, along with coordinated preparations for upcoming pipelines within companies, may help to bridge this gap between regulatory and HTA decisions.

Collaboration on RWE needs to be across the healthcare system

While progress has been made in real-world evidence (RWE) generation and utilisation, there are still data challenges i.e. data quality, completeness, linkage etc, and stakeholder-related challenges, such as the capability to collect and interpret real-world data (RWD), and the acceptability of RWE. The value of RWE goes beyond just regulatory and HTA decisions; it should be integrated into healthcare decision making through a collaborative environment where industry, regulators, HTA agencies, healthcare providers, patients, and researchers work together.

Payer collaborations

HTA-payer collaboration is not a pre-requisite

Collaboration between the HTA agency and payer in a jurisdiction can help to promote value-based and evidence-based decision making, reduce fixation on budget costs and give more flexibility in payer negotiations, as the HTA advice for implementation can be better tailored to the tools payers employ. However, HTA agencies and payers can exist independently, as close HTA-payer collaboration is not a prerequisite to the existence of either entity. Higher political involvement and functional variation within payers can mean fewer opportunities for HTA-payer collaboration. Jurisdictions with non-comprehensive or very diverse payer arrangements for their healthcare systems, with no or limited HTA, or with a mismatch between the level of the payer and the HTA agency e.g. central HTA and regional payer, are less likely to have close HTA-payer collaborations.

Payer collaborations take various forms

Payers can collaborate across jurisdictions through networks such as the Pharmaceutical Pricing and Reimbursement Information (PPRI) network, BeNeLuxA initiative and the Medicine Evaluation Committee (MEDEV). Information relating to pricing and upcoming pharmaceutical products can be shared via the European Integrated Price Information Database and International Horizon Scanning Initiative Database, respectively. Common challenges that European payers can tackle include communication of public needs, such as sustainability and affordability of medicines; pharmaceutical policy developments, such as the upcoming HTAR and General Pharma Legislation; joint negotiation or purchase; and advancing the European Health Data Space so the use of RWD in payer decision making can be improved.

Recommendations from breakout discussions

HTA collaborative models – What are the key considerations or frameworks that enable the construction and delivery of an efficient and effective model?

Recommendations for moving HTA collaborative models forward:

- Introduce **product agnostic early dialogue -** a forum for regulators, HTA bodies, payers, industry, patients and clinicians to come together to discuss/explore unmet need and national health priorities. This could take place at a jurisdictional level and be linked to pipeline/portfolios rather than specific products.
- Promote **mutual learning on regulatory/HTA science and methodologies** – there could be mutual benefit in regulators and HTA agencies learning from each other, for example, for HTA agencies to understand how regulators came to an indication decision.
- Encourage **HTA convergence on methodologies** – there is more opportunity for HTA-HTA collaboration with the goal of mutual learning.
- Identify opportunities for **adapting other agencies' reports in decision making** - Regulatory and HTA agencies should 'look in their neighbourhoods' to identify where they can adapt other agencies' reports to the local context (if timelines and legal frameworks allow).
- Discuss the **management of potential conflicts of interests of patient experts** – this could be a topic of discussion at the 2025 CIRS workshop on patient involvement. While conflicts of interests must be managed, they should not become a barrier for representative patient and patient group input into HTA processes e.g. EU joint scientific advice and joint clinical assessment.

Changing mindsets – How can this best be achieved within companies and agencies to enable work-sharing collaborative models?

Recommendations for changing mindsets to enable work-sharing collaborative models:

- Identify **case study examples** of successful work sharing or collaborations with demonstratable outcomes.
- Provide **clarity on the benefits of optional collaborative models** to help potential users understand the added value of these models.
- Ensure the success of collaboration is an **organisational priority**. For example, senior leaders could have a KPI related to the success of collaboration.
- Identify **interim short-term goals** of the collaboration to demonstrate success and create momentum.
- Explore the concept of an **ICH-type organisation for HTA agencies.** ICH provided a common framework within which regulatory collaborations could work; is a similar framework for HTA required/useful?
- Expand **awareness and acceptance** of collaborations through dissemination activities, such as external conferences.
- Establish internal **peer champions** to be advocates for collaborations.

Good collaborative practices for companies and agencies – What needs to be in place to move from principle to implementation?

Recommendations for key elements of good collaborative practices:

- Start with a clear, aligned **purpose and vision**, which is mutually beneficial and understood by all parties. There must be clear goals and definition of who are the actors and beneficiaries of the collaboration. Support from senior leadership is key.
- Establish good **project leadership and management.** There needs to be clear roles and responsibilities as well as a framework for decision making, including closing/sunsetting. Reviewing best practices from existing collaborative models would be helpful.
- Develop appropriate outcome **assessments/metrics**. These should ideally be agreed upfront, considering the views of different stakeholders.

Next steps/research needed to support the above:

- **Identify** use cases for successful and unsuccessful collaborations.
- **Generate** combined outputs from each of the breakout groups.
- **Research** appropriate assessments and metrics.

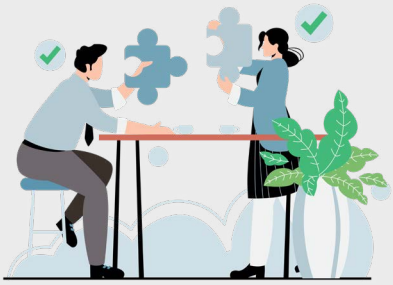
INFOGRAPHIC SUMMARY

CIRS brought together regulators, HTA agencies, pharmaceutical companies, payers, academics and patient organisations to discuss how **regulatory and HTA collaborative models** should evolve.

KEY RECOMMENDATIONS

Align and define

Start with a clear, aligned vision for the collaboration, with agreement on how to measure success.



Changing mindsets

Ensure the success of collaboration is an organisational priority, with senior leadership buy-in.

Look in your neighbourhood

Identify opportunities to adapt regulatory and HTA assessment reports for decision making.

Product agnostic early dialogue

Explore a new forum for stakeholders to discuss unmet need and national health priorities.

Workshop Programme

Please click on a section of interest to find that section in the report.

Day 1: Wednesday 9th October 2024

Session 1: Embedding collaborative ways of working as part of the regulatory and HTA toolkit – How is the landscape changing for the review and assessment of new medicines?	
09:00	**Chair's welcome and introduction** **Niklas Hedberg,** Chief Pharmacist, TLV, Sweden
09:10	**Current implementation/utilisation of different collaboration models within and across regulators and HTA agencies – How is this changing the review and HTA assessment landscape?** **Dr Tina Wang,** Associate Director, HTA Programme and Strategic Partnerships, CIRS
09:25	**Discussion**
09:30	**Collaboration between regulators in the development and review of new medicines – How has this evolved and what are the key learnings, challenges, and opportunities?** **Prof Ton de Boer**, Chair, Medicines Evaluation Board, The Netherlands
09:45	**Discussion**
09:50	**Regulatory collaborative models in practice - Panel discussion** *5-10 minutes reflection on the following questions:* – *How are collaborative models in development, such as scientific advice or FDA-EMA cluster activities, aiding agencies and companies? What are the key learnings?* – *Are worksharesuch as Access or collaborative review models such as Orbis and Open improving quality of reviews, capacity and timeliness of medicines availability?* – *What were the challenges and what mindset changes were/are needed internally to gain benefit from such working practices?* – *Can such models be duplicated for other therapeutic areas (Orbis) or other regions (Access)?* **Shannon Thor,** Deputy Director, Europe Office, Food and Drug Administration **Dr Eveline Trachsel,** Head of Medicinal Product Authorisation and Vigilance, Swissmedic **Company Perspective – Jeffrey Francer,** Vice President, Head of Global Regulatory Policy and Strategy, Eli Lilly, USA
10:30	**Discussion**
10:45	**Break**
11.15	**Collaboration between HTA agencies in the assessment and development of new medicines – How has this evolved to where it is now and what are the key learnings, challenges, and opportunities?** **Meindert Boysen,** Chair, Health Technology Assessment International Global Policy Forum
11:30	**Discussion**

	Regional/transregional HTA collaborative models - What can be learnt and how could these evolve?
11:35	**Joint Nordic HTA Collaboration** **Niklas Hedberg**, Chief Pharmacist, TLV, Sweden
11:50	**Beneluxa HTA Collaboration** **Dr Marc Van de Casteele,** Coordinator, Pharmaceutical Expertise, Department of Pharmaceutical Reimbursement, Belgian Health Care Institute RIZIV-INAMI, Belgium
12:05	**AUS-CAN-NZ-UK collaboration** **Dr Farah Husein,** Director Science and Methods, Canada's Drug Agency
12:20	**Discussion, followed by lunch**
Session 2: Focus on Regulatory-HTA collaborations – Are these helping to bridge the regulatory-HTA gap?	
13:35	**Chair's introduction** **Dr Michael Berntgen,** Head of Scientific Evidence Generation Department, European Medicines Agency
13:40	**Regulatory HTA alignment - Successes, failures and lessons learnt** **Prof John Skerritt**, Enterprise Professor for Health Research Impact, University of Melbourne, Australia
14:00	**Discussion**
14:05 14:25	**Integrated jurisdictional regulatory-HTA alignment during development – Is this building a better model for the future?** **UK Innovative Licensing and Access Pathway – Innovative access pathways** **Jeanette Kusel,** Director, NICE Advice, National Institute for Health and Care Excellence (NICE), UK and **Louise Knowles**, Deputy Director, Innovation Accelerator and Regulatory Science, Medicines and Healthcare Products Regulatory Agency (MHRA), UK **Company perspective - James Ryan,** Director, Global HTA Policy, HTA and Modelling Science, AstraZeneca, UK
14:40	**Discussion**
14:45	**Regulatory-HTA collaboration during development in providing scientific advice – Panel discussion** *5-10 minutes reflection on the following questions:* – *What is the value add of regulatory-HTA early scientific advice?* – *Is it enabling improved evidence generation and predictable outcomes?* – *Does it need to evolve?* **Company perspective – Dr Nicole Kubitz,** Senior Director, HTA & Decision Science**,** Johnson & Johnson Innovative Medicine, Germany **Patient perspective – Josephine Mosset,** Policy Officer, Cancer Patients Europe, Belgium **Regulatory perspective - Karen Reynolds,** Director General, Pharmaceutical Drugs Directorate, Health Canada
15:20	**Discussion, followed by break**

	HTA/regulator engagement and collaboration on better leveraging RWE in health technology assessments and regulatory decision making
16:00	**Agency perspective – Dr Anja Schiel,** Senior Adviser, Lead Methodologist in Regulatory and Pharmaeconomic Statistics, Norwegian Medical Products Agency
16:15	**Company perspective – Laetitia Mariani,** Director, HTA Collaborations, International Market Access & Pricing, AbbVie, Switzerland
16:30	**Discussion**
Session 3: Breakout discussions	
16:40	**Introduction to breakout sessions**
	Topic A: HTA collaboration models – What are the key considerations or frameworks that enable the construction and delivery of an efficient and effective model? **Chair: Dr Nick Crabb,** Chief Scientific Officer, National Institute for Health and Care Excellence (NICE), UK **Rapporteur: Marie Eckart,** Europe Joint HTA Lead, Takeda, Switzerland
	Topic B: Changing mindset – How can this best be achieved within companies and agencies to enable workshare collaborative models? **Chair: Dr Sean Tunis,** Senior Fellow, Tufts Center for the Evaluation of Value and Risk in Health, USA **Rapporteurs: Dr Antonia Morga,** Senior Director, Global HEOR and HTA Strategy Lead, Astellas, UK, and **Adrian Griffin,** Vice President for HTA Policy, Janssen, UK
	Topic C: Good collaborative practices – Companies and agencies – what needs to be in place moving from principle to implementation? **Chair: Dr Alicia Granados,** Global Head, Scientific Advocacy and Insights, Sanofi, Spain **Rapporteur: Dr Esteban Herrero-Martinez,** Director, Regulatory Intelligence and Policy, AbbVie, UK
18:00	**End of day one**
19:00	**Reception and dinner**

Day 2: Thursday 10th October 2024

Session 4: Breakout discussions and feedback	
08:30	**Breakout sessions resume**
10:15	**Break**
11:00	**Chair's introduction** **Prof John Skerritt,** Enterprise Professor for Health Research Impact, University of Melbourne, Australia
11:05	**Feedback of Syndicate discussions and participants' viewpoints**

Session 5: Payer collaborations – How do these improve access to medicines?	
12:00	**Jurisdictional payer-HTA collaboration – What are some examples and why is payer – HTA collaboration needed?** **Prof Andrew Mitchell,** Honorary Professor, Department of Health Economics Wellbeing and Society, The Australian National University, Australia
12:15	**Cross jurisdictional payer collaborations – What are the benefits and why is this needed?** **Dr Robert Sauermann,** Head, Department of Pharmaceutical Affairs, Austrian Federation of Social Insurances
12:30	**Discussion**
12:45	**Lunch**
Session 6: Evolution of collaboration and workshare in the review and HTA assessment of new medicines	
13:45	**Chair's introduction** **Dr Brian O'Rourke,** Chair, CIRS HTA Steering Committee
13:55	**Adaptive HTA – A novel method for efficient application of HTA methods and principles** **Dr Dan Ollendorf,** Chief Scientific Officer and Director of HTA Methods and Engagement, Institute for Clinical and Economic Review, USA
14:10	**HTA strengthening and capacity building - New initiative in Taiwan** **Dr Li Ying (Grace) Huang,** Senior Director, Division of HTA, Center for Drug Evaluation, Taiwan
14:25	**Discussion**
14:35 14:50	**Next generation of collaborative, workshare and or reliance models - What are the next steps and key considerations?** **Academic perspective - Prof Lotte Steuten,** Deputy Chief Executive, Office of Health Economics, UK **Patient perspective - François Houÿez,** Director of Treatment Information and Access, EURORDIS - Rare Diseases Europe, Belgium
15:05	**Next generation of collaborative, workshare and or reliance models - What are the next steps and key considerations? Panel discussion** **HTA-HTA collaborations - Dr Yot Teerawattananon**, Secretary General, HITAP, Ministry of Public Health, Thailand **Regulatory-Regulatory collaborations – Dr Supriya Sharma,** Chief Medical Adviser, Health Canada **Reg-HTA collaborations – Dr Michael Berntgen,** Head of Scientific Evidence Generation Department, European Medicines Agency **Payer collaborations – Prof Hans-Georg Eichler,** Consulting Physician, Association of Austrian Social Insurance Institution
15:50	**Discussion**
16:15	**Chair's summary and close of meeting**

Session summaries

Please note that the following summaries represent the views of the individual presenters and do not necessarily represent the position of the organisation they are affiliated with. The slide featured in each of the following summaries is attributed to the individual presenter and has been reproduced with their permission.

Session 1: Embedding collaborative ways of working as part of the regulatory and HTA toolkit – How is the landscape changing for the review and HTA assessment of new medicines?

Implementation and utilisation of collaborative models within and across regulatory and HTA agencies: How is this changing the regulatory and HTA landscape?

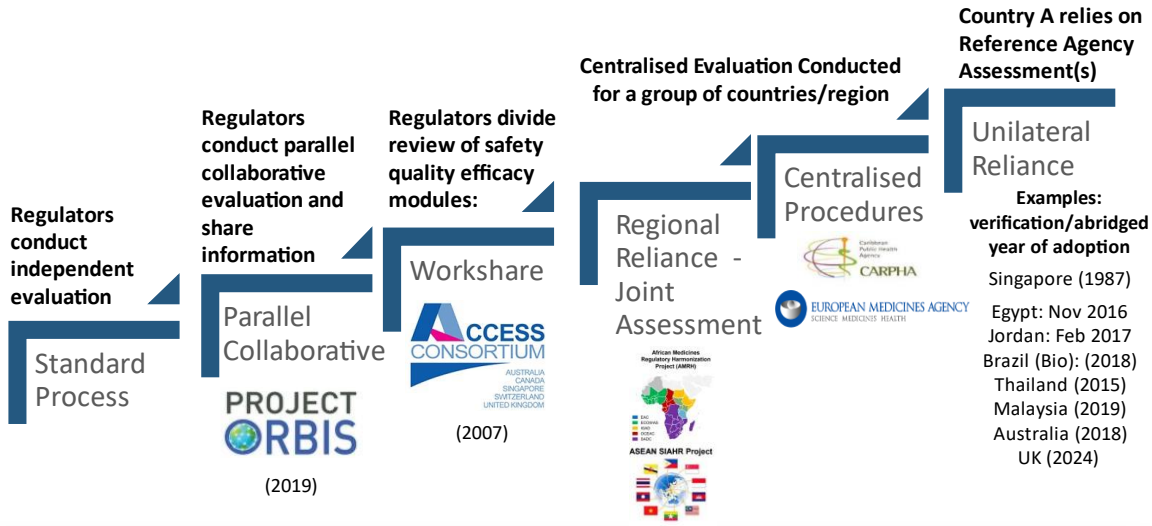
Dr Tina Wang, Associate Director, HTA Programme and Strategic Partnerships, CIRS

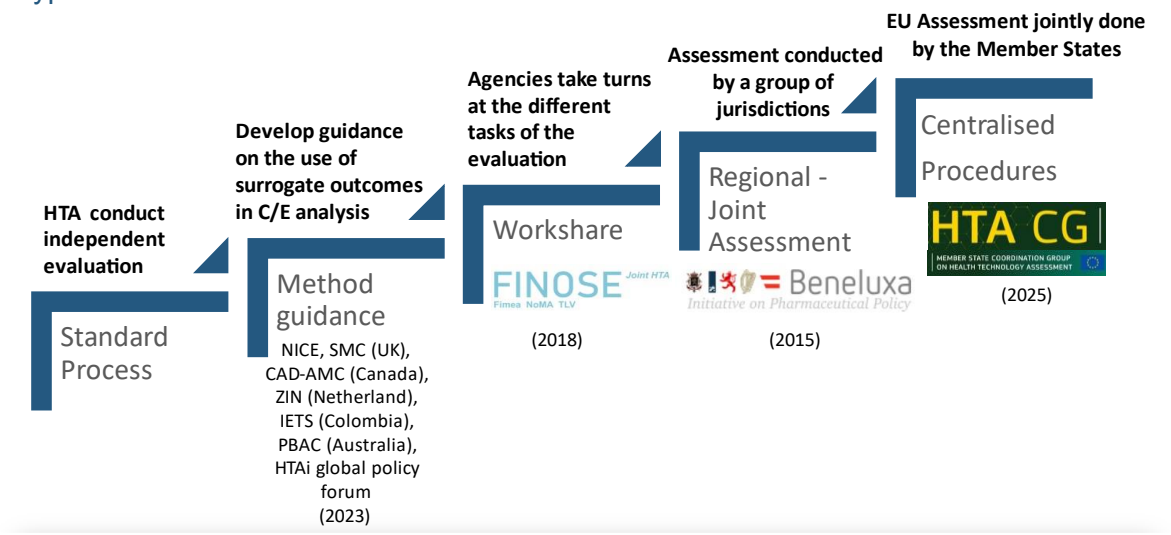
Dimensions of stakeholder collaboration

There are various dimensions to stakeholder collaboration across the medicine life cycle. There can be a horizontal dimension, where the same type of stakeholders work together e.g. regulatory-regulatory, HTA-HTA, as well as a vertical dimension, where different stakeholders (usually within the same jurisdiction) work together e.g. regulatory-HTA. Furthermore, stakeholder collaborations can take place at different stages of the medicine lifecycle and at either a methodological or policy level.

Many regulators, irrespective of maturity and resources, are actively implementing different types of collaborative approaches as part of their toolkit (see below). Some similar collaborations exist between HTA agencies but not to the same extent; for example, leveraging models like unilateral reliance are not widely used by HTA agencies.

Types of models of regulatory collaboration





Measuring success of collaboration

CIRS has been monitoring and evaluating stakeholder collaborations for over a decade through a series of multi-stakeholder workshops and research studies. For example, CIRS research has shown that Project Orbis and the Access Consortium are helping to reduce submission gaps, suggesting that these collaborative efforts are supporting efficiency gains. A recent CIRS workshop has suggested several potential measures that could be used to assess the efficiency and effectiveness of joint clinical assessment in the EU. With regards to HTA early advice, a survey of CIRS member companies showed that measuring the impact on evidence generation, internal learnings and jurisdictional submission strategy were key to demonstrating the success of HTA advice internally.

Summary

Stakeholders are actively piloting and implementing collaborative approaches, with CIRS conducting research, providing tools and facilitating dialogue to support stakeholders. Different collaboration models are applied across development, regulation and HTA processes; regulatory collaborations are showing a more mature approach while HTA collaborations are progressing. Timely access to medicine is a measurable benefit, alongside other qualitative metrics that demonstrate the effectiveness and efficiency of collaboration. Evolving stakeholder collaboration requires active measures, the development of good practices and a mindset shift to enable further progress.

Collaboration between regulators in the development and review of new medicines – How has this evolved and what are the key learnings, challenges and opportunities?

Prof Ton de Boer, Chair, Medicines Evaluation Board (MEB), The Netherlands

The European Medicines Agency (EMA) is one of the oldest forms of regulatory collaboration, which, since 1995, has been coordinating the evaluation and monitoring of centrally authorised products, developing technical guidance and providing scientific advice. EMA's scientific committees and working parties are made up of experts from national regulatory authorities within the European Union (EU) and European Economic Area (EEA). A key success factor to this collaborative way of working is the existence of common regulatory framework supported by International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines.

Centralised procedure

Under the centralised authorisation procedure, companies submit a single marketing authorisation to EMA, which, if successful, allows them to market the medicine throughout the EU. The EMA Committee for Medicinal Products for Human Use (CHMP) conducts a scientific assessment of the submission, with two countries taking the lead on the assessment (they are referred to as the Rapporteur and Co-Rapporteur). Not all countries take up Rapporteur/Co-Rapporteur roles to the same extent, which may be due to differences in the capacity and capability of each country's assessors. Multinational assessment teams have been launched to support broader involvement of national regulatory authorities in EMA assessments, allowing expertise to be built up while still maintaining high-quality scientific work.

Scientific advice

In addition to centralised scientific advice from EMA, regulatory collaboration is being fostered through simultaneous national scientific advice (SNSA). SNSA allows sponsors to obtain scientific advice from two or more national regulatory authorities, helping to optimise resources and improve consistency of advice.

EMA's Scientific Advice Working Party (SAWP) is collaborating with HTA agencies through parallel scientific advice. The number of parallel advice procedures has been declining in recent years, which may be due to challenges with HTA capacity. Future collaboration between the SAWP and HTA agencies is expected to be more intense under the new HTA Regulation; joint scientific consultation formally starts from 2025, where HTA agencies will provide joint scientific advice with EMA.

New Pharma Legislation

The reform of the EU Pharmaceutical Legislation has specific objectives related to timely patient access, security of medicine supply, supporting innovation and environmental sustainability. It provides the opportunity for regulatory 'sandboxes', where regulators can jointly advance regulation through proactive learning and experimentation, for example, to find the best means to regulate innovations at a very early stage of development. This could be especially valuable in the context of digitalisation and the use of artificial intelligence in the life cycle of medicinal products.

Summary

Much can be learned from EMA; its collaborative way of working has helped to facilitate regulatory convergence, information sharing and building trust between Member States. However, not all regulators take up Rapporteur/Co-Rapporteur roles to the same extent, so efforts are ongoing to support broader participation. The new EU Pharmaceutical Legislation provides opportunities for further regulatory-regulatory collaboration within the EU, such as the use of regulatory 'sandboxes' for joint experimentation and learning.

Regulatory collaborative models in practice - Panel discussion

Each participant was asked to provide their reflections on the following questions:

- How are collaborative models in development, such as scientific advice or FDA-EMA cluster activities, aiding agencies and companies? What are the key learnings?
- Are workshares such as Access or collaborative review models such as Orbis and Open improving quality of reviews, capacity and timeliness of medicines availability?
- What were the challenges and what mindset changes were/are needed internally to gain benefit from such working practices?
- Can such models be duplicated for other therapeutic areas (Orbis) or other regions (Access)?

Shannon Thor, Deputy Director, Europe Office, Food and Drug Administration (FDA)

- To foster regulatory dialogue and collaboration, FDA has a physical presence in several locations, with offices in China, India, Costa Rica, Mexico, Chile and Belgium, and new ones planned to open in Rwanda and Brazil.
- The FDA Europe Office in Brussels, Belgium, conducts policy analysis looking at emerging issues throughout Europe to identify areas where regulatory convergence or alignment would be beneficial.
- Collaborations between FDA and EMA are encouraged by the presence of an FDA/EMA liaison within each of the agencies. FDA collaborates with EMA on several activities such as information-sharing 'clusters' (which often grow to involve other regulators) and parallel scientific advice.
- Mutual Recognition Agreements between FDA and other regulators allow reliance on each other's GMP inspections for human and animal drugs.
- Trust is the foundation of collaboration; confidentiality commitments are key to enabling robust scientific discussions between regulators.

Dr Eveline Trachsel, Head of Authorisation, Swissmedic

- The Access Consortium and Project Orbis are helping to reduce submission gaps, which is especially important for smaller markets like Switzerland.
- There is often a trade-off between the resources required to make the collaboration successful vs the resources saved as a result; for example, Swissmedic found that reviewing one module of an Access work-share application usually helped to save resources internally but reviewing two modules did not.
- Challenges facing regulatory collaborative models include:
    - Limited company uptake – Working with trade associations on the communication of the models' benefits, as well as collecting feedback on companies' experiences, could be potential solutions.
    - Lack of shared IT platform for efficient information exchange (though work is being done to set one up within Access)

- Mindset change – Fostering trust and a culture of learning is key; this can help to prevent potential inefficiencies in a work-sharing arrangement, for example, where an agency may conduct an additional internal peer review of their own work before sharing it externally with partnering agencies for their peer review.

Jeffrey Francer, Vice President, Head of Global Regulatory Policy and Strategy, Eli Lilly, USA

- Global regulatory collaboration is essential given the increasing pressure on regulators due to:
  - Limited number of reviewers
  - Exponential growth in the complexity of medicines
  - Increasing need for regulatory science skill specialisation (which also applies to companies).
- Regulatory collaboration through ICH has contributed to more consistent regulatory guidelines and practices, thus aiding global company development strategies.
- Extending Project Orbis to include additional regulators and therapeutic areas beyond oncology could make it even more impactful.
- Further regulatory-regulatory collaboration could be enabled by enhancing transparency, such as improvements to sharing assessment reports and other approval documents, and using IT platforms to support information exchange between regulators as well as global company submissions.

Collaboration between HTA agencies in the assessment and development of new medicines – How has this evolved and what are the key learnings, challenges and opportunities?

Findings from the 2024 HTAi Global Policy Forum

Meindert Boysen, Chair, HTA International (HTAi) Global Policy Forum

The HTAi Global Policy Forum is a group of 39 members from non-profit and for-profit organisations that meet each year to discuss a key topic of interest. In 2024, the chosen topic for the Policy Forum was 'Designing collaborations involving HTA: Finding the rhythm for success'. Collaboration was defined as the act of working together to develop a common approach, which is more resource intensive than coordination (getting aligned) and cooperation (sharing best practices).

Why do HTA agencies collaborate?

There are several reasons for HTA agencies to collaborate, which may vary depending on the maturity of the HTA organisation involved. For example, increasing efficiency and quality or increasing credibility may be the main driver for a less mature HTA agency. Other reasons to collaborate could be to share knowledge and leverage expertise across organisations, or improving timeliness with collective (rather than individual) effort. The Policy Forum found that collaborators do not always know why they are collaborating; the purpose of the collaboration should be made clear before it starts.

Who, what and how to collaborate?

HTA agencies collaborate with a range of stakeholders including industry, clinicians, regulators, payers, policy makers and patients. Collaborations with other HTA agencies (HTA-HTA) can be national e.g. Spanish HTA system, regional e.g. EUnetHTA, or international e.g. INAHTA. HTA-HTA collaborations focus on various HTA activities over the technology lifecycle, such as horizon scanning, scientific consultation, clinical assessments, economics/pricing (though this is less likely), post-HTA and disinvestment.

There are several ways to support collaborations, starting with infrastructure (making it possible to collaborate), followed by user experience (making it easy), communities (making it normative), incentives (making it rewarding) and finally policy (making it required). Collaborations are enabled by trust, strong leadership and clear scope/goals (see below). Barriers to collaborating include conflicts of interest, legal constraints and imbalanced engagement.

	Enablers	Barriers
The 'Who'	• Trust and Respect • Communication • Commitment • Balance • Strong leadership and political will/support	• Conflicts of interest • Diversity or unaligned value sets • Legal and jurisdictional constraints • Cultural misunderstandings • Imbalance of engagement
The 'What'	• Clear scope and goals • Topic of shared importance • Clarity on terminology • Defined outcome measures	• Competing/conflicting/changing priorities • Lack of transparency • Lack of willingness /ability to change practices • Resource-intensive legal overview
The 'How'	• Sufficient and sustainable resources • Clear governance, roles, responsibilities • Open and transparent processes • Working together over time	• Insufficient staff time • No dedicated point contact • Limited expertise/experience in the area • Insufficient external communication

Recommendations for HTA-HTA collaborations

The HTAi Global Policy Forum had six breakout groups that looked at various aspects of collaboration. The group that discussed collaborations involving HTA agencies concluded that the following elements were important for success: efficiency gains by sharing work; enabling joint methods development and alignment; alignment (and possibly consistency) across HTA agencies on principles for patient involvement, value perspectives and evidence requirements; and enhancement of the purpose of HTA.

Summary

- Determining the collaboration purpose is essential but may be dynamic, changing over time.
- Choosing the collaboration topic takes time, requiring upfront investment and stakeholder mapping.
- Inviting the right participants and treating them equally is important, including those who can impact HTA, those who will be impacted by HTA and those who bring new information.
- Collaborations need clear governance, defined roles, responsibilities, metrics, and case study/pilots can be a useful operational model.
- Resourcing collaborations sustainably is a challenge – the time, people, and money required are often under-estimated.
- Undertaking continual, iterative learning reviews ensures ongoing value and impact of collaborations.

Regional/transregional HTA collaboration models – What can be learnt and how could these evolve?

Joint Nordic HTA collaboration

Niklas Hedberg, Chief Pharmacist, Dental and Pharmaceutical Benefits Agency (TLV), Sweden

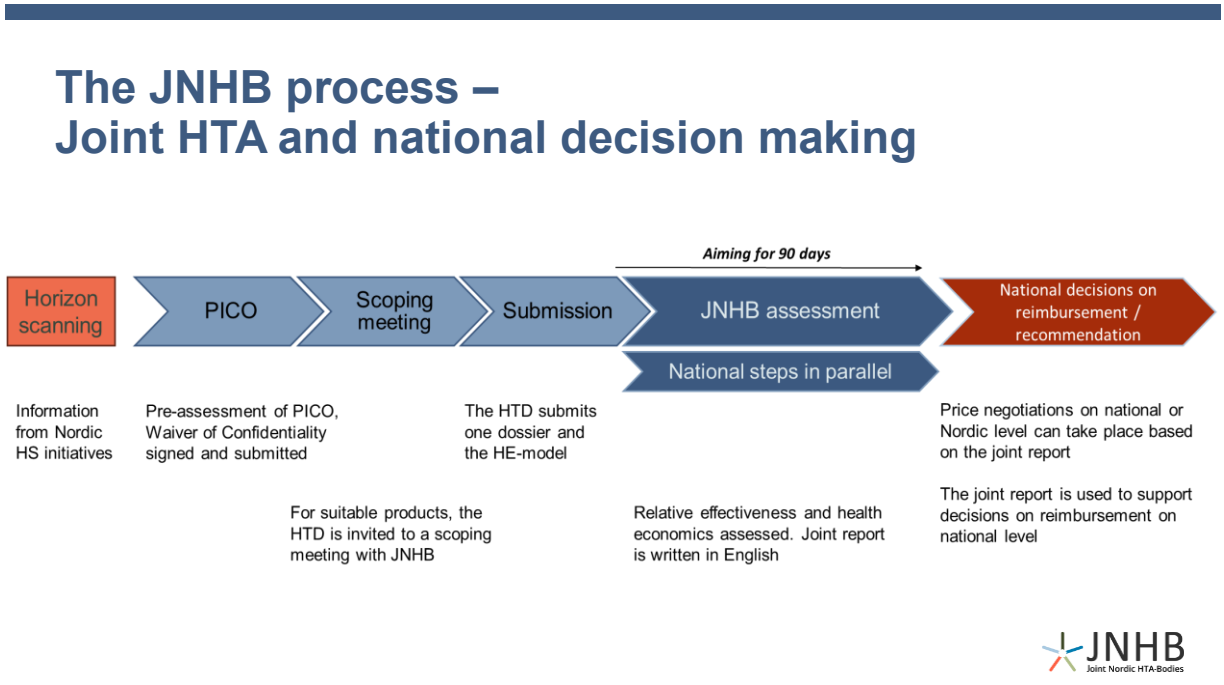
The Joint Nordic HTA-Bodies collaboration (JNHB, formerly known as FINOSE) was launched by HTA agencies in Finland, Norway and Sweden in 2018 to address resource constraints and the increasing complexity of assessments. Denmark and Iceland joined the collaboration in 2023 and 2024, respectively. A Memorandum of Understanding between the five HTA agencies defines the JNHB collaboration in terms of its scope, legal basis, roles, responsibilities and open formulations to give freedom to develop the collaborations.

The aims of the JNHB collaboration are to:

- Share resources and knowledge to facilitate high quality assessments
- Facilitate less divergence in HTA methodologies and evidence requirements
- Support timely and equal access for Nordic patients
- Adapt to the joint clinical assessment (JCA) process in the upcoming HTA Regulation (HTAR)
- Support joint Nordic price negotiations
- Be a flexible system beneficial for both companies and HTA agencies, acting as a single point of contact.

JNHB process

The JNHB Process Guideline describes the JNHB process (see below), including the PICO proposal, scoping meeting, how to build and send the dossier, assessment timelines, and roles and responsibilities. The JNHB also has a submission dossier template outlining the core requirements for a joint Nordic HTA, including differences between the HTA agencies that may require country-specific input e.g. discount rates, patient time and indirect costs, calculation of severity of the disease etc. The JNHB process aims to work in parallel with national processes as much as possible, so the JNHB report and national appendices are finalised simultaneously.



Supporting price negotiations

To support joint Nordic negotiations for products assessed through JNHB, the JNHB and New Expensive Drugs (NED) section of the Nordic Pharmaceutical Forum have entered a collaboration. There are several points of contact between JNHB and NED throughout the HTA and negotiation process, including during horizon scanning, before and during JNHB assessment, and at the end of NED price negotiations.

Adapting to the HTAR

In line with the intention expressed in the HTAR, JNHB will consider JCA reports as valid documents in a JNHB submission and is committed to avoiding duplicative requests to developers. While JCAs may replace some aspects of joint assessment work already being done within JNHB, health economics is not within the scope of JCA and so there will still be value in JNHB conducting joint pharmacoeconomic assessments.

Several JNHB members have had prominent roles in the work of EUnetHTA and all members are actively involved in the implementation of the HTAR through the HTA Coordination Group and its sub-groups. JNHB has been a practice ground for pragmatic PICO discussions, so joined participation of JNHB members in the HTAR PICO scoping process should facilitate alignment among the Nordic countries to the best possible extent.

Summary

The JNHB offers efficient joint HTAs of medicinal products in the five Nordic countries, supporting timely and equal access for Nordic patients. Better communication/promotion of the JNHB and streamlining the JNHB process could help to improve uptake among companies. The extensive experience of JNHB members will help to ensure that the JNHB is well prepared for the implementation of the HTAR in 2025.

Beneluxa initiative

Dr Marc Van de Casteele, Coordinator, Pharmaceutical Expertise, Department of Pharmaceutical Reimbursement, Belgian Health Care Institute RIZIV-INAMI, Belgium

In response to a mismatch between incentives supporting marketing authorisations and issues with the affordability of pharmaceutical products, the Belgian and Dutch health ministries formed the Belgium-Netherlands collaboration in April 2015. Since then, Luxembourg, Austria and Ireland have joined the collaboration, which is now known as the Beneluxa initiative.

The Beneluxa initiative aims to achieve sustainable access to, and appropriate use of medicines in the participating countries by conducting the following activities:

- Anticipating national health challenges by horizon scanning
- Increasing the efficiency of HTA by exchanging expertise and conducting joint HTAs
- Sharing policy expertise and best practices
- Improving the payers' position in the market:
    - by improving their knowledge on products, usage and markets
    - by joint (price) negotiations for specific products
- Improving transparency on pricing between the collaborating countries.

Joint HTA pilots

Beneluxa countries are exploring 're-use' of each other's HTA reports, where parts of the reports are adapted to the local context, as well as joint writing of HTA reports, where a company makes a single submission to two or three countries and a joint report containing clinical, economic and budgetary assessment for those countries is produced. So far, there has only been one case of re-use of an HTA report (which did proceed onto a joint negotiation), and joint report writing has been conducted for seven products.

A regional collaborative procedure called mutual recognition and adoption is also being investigated. This is where a company submits to one country who prepares the HTA report, which is then shared and adopted by other countries in a parallel process. However, this procedure has not yet been used due to legal constraints and the perception that national stakeholders are excluded from the decision making.

Key learnings

A key learning from Beneluxa is that countries must have a good knowledge of each country's procedures before collaborating on joint HTA work. Exchanging expertise and sharing the reasons for positive or negative reimbursement with peers is also important. Countries considering setting up regional collaborations should conduct careful legal checks to see whether/how far cross border work is possible.

Summary

The Beneluxa initiative is conducting a range of activities to help increase patients' access to high quality and affordable treatments, from horizon scanning to joint HTA reports. Countries considering setting up regional collaborations should ensure that they 'know each other' in terms of their HTA procedures and legal frameworks. Next steps for Beneluxa include joint negotiations, use of the International Horizon Scan Initiative (a spin-off of Beneluxa collaborative work) and incorporation of the EU HTA Regulation into its work. While joint clinical assessments under the HTA Regulation may replace some aspects of joint assessment work already being done within Beneluxa, health economics is not within the scope of JCA and so there will still be value in Beneluxa conducting joint pharmacoeconomic assessments.

What are the key learnings ?

- Voluntary collaboration
  Even within Beneluxa collaboration voluntary opt-in opt-out
- Knowing each other
  " stakeholder consultations outside your borders
- Have 'some idea' on what procedures in other jurisdictions are like
- Expertise exchange on complex medicines
- Justify to your peers why/why not reimburse ?

Beneluxa
Initiative on Pharmaceutical Policy

AUS-CAN-NZ-UK collaboration

Dr Farah Husein, Director, Science and Methods, Canada's Drug Agency (CDA-AMC)

In 2022, HTA agencies from Australia (PBAC), Canada (CDA-AMC) and the UK (NICE, SMC and HTW/AWTTC) started collaborating on shared priorities to identify solutions to common challenges they face. In 2023, the collaboration was expanded to include agencies from New Zealand (PHARMAC) and Quebec (INESSS), bringing these international HTA partners to collaborate on selected focus areas. Key priority areas for the AUS-CAN-NZ-UK collaboration are work sharing, horizon scanning and science and methods advancement.

Joint development takes time

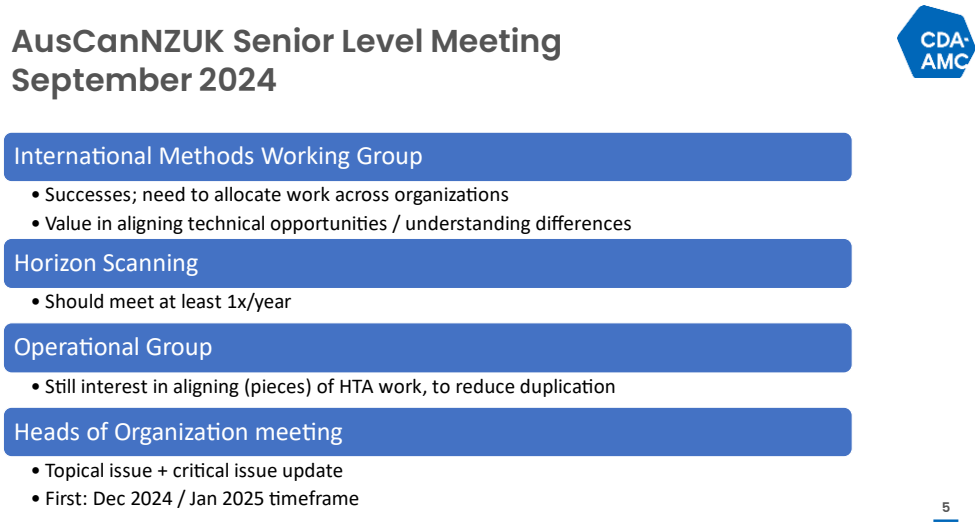
The AUS-CAN-NZ-UK collaboration has enabled the participating agencies to learn from each other and share best practices, methods, processes and tools. However, there have been challenges, such as different focuses for horizon scanning, difficulties sharing HTA work including differences in market-relevant comparators or indications, lack of common IT infrastructure, etc. Projects resulting from this collaboration include a joint paper on the use of surrogate endpoints in cost-effectiveness analysis, piloting a framework for the assessment of an AI-enabled digital health technology, and input to inform the development of CDA-AMC's Methods Guide.

Scientific advice

Over the last decade, CDA-AMC has been running parallel scientific advice programmes with Health Canada and NICE. While these programmes have benefitted the agencies involved, companies often go to HTA agencies other than CDA-AMC for their early scientific advice. CDA-AMC is now evolving these programmes to include the later pre-submission and even post-submission phases to focus less on optimising the clinical development programme and more on real-world evidence plans and modelling approaches, where CDA-AMC feels there is more added value for the sponsors and the agency.

Summary

While the collaboration initially focused on work sharing, horizon scanning and science and methods advancement, some areas have had more success than others. The collaboration has enabled the agencies to learn from one another, share best practices and tools, and align in their approaches.



Session 2: Focus on regulatory-HTA collaborations – Are these helping to bridge the regulatory-HTA gap?

Regulatory-HTA alignment – successes, failures and lessons learned

Prof John Skerritt, Enterprise Professor for Health Research Impact, University of Melbourne, Australia

Closer collaboration between regulators and HTA agencies has several potential benefits such as reducing the time between regulatory and reimbursement decisions (and potentially the speed of patient access to new medicines), minimising duplication of work for both agencies and companies, informing the evidence gap between regulatory and HTA needs, and aligning requirements for post-licensing studies. Nevertheless, it is essential that the roles and decision-making responsibilities of regulators and HTA agencies remain separate.

How could regulatory-HTA coordination be improved?

- **Joint horizon scanning** - It is critical that evaluators within regulatory and HTA agencies have the capacity and capability to evaluate new technologies effectively. To upskill their evaluators and avoid duplication, regulatory and HTA agencies could potentially organise joint workshops to learn from R&D experts, as well as joint pipeline meetings where a company presents on their product pipeline and the technologies behind them.
- **Greater alignment of evidentiary requirements** – While some evidentiary requirements are specific to either regulation or HTA, it should be possible to develop an inclusive package that recognises these differences. Joint discussion of regulatory and HTA evidentiary requirements with sponsors could be particularly helpful in certain scenarios e.g. novel types of therapies, products undergoing expedited review pathways, alternative trial designs etc.
- **Greater use of patient-reported outcomes and real-world evidence** (RWE) – Regulators could learn much from HTA agencies around the use of patient input and patient outcomes data. Closer regulatory-HTA collaboration could also help to improve the quality, quantity and oversight of RWE.
- **Joint scientific advice during development** – While joint advice programmes are evolving e.g. EU Joint Scientific Advice (JSC), relaunched Innovative Licensing and Access Pathway (ILAP), several challenges remain. These include agency and company capacity for provision of receipt and joint advice, and understanding the impact of joint advice on evidence generation activities, outcomes and probability of regulatory approval and positive HTA recommendations.
- **Joint pre-submission meetings** after completion of clinical trials in the lead up to regulatory submission are available in some countries and can provide advice on facilitated regulatory and early access pathways, which is particularly useful for products with high uncertainty.
- **Shared IT (product submission) portals** – These would enable simultaneous management of regulatory and HTA submissions, thus reducing administrative burden on companies.
- **Clinical and safety evaluations** – There could be more information exchange between regulators and HTA agencies about safety and effectiveness, but how much would be appropriate? It is important to avoid duplication of roles and the potential for conflicting messages about safety.
- **Parallel regulatory and HTA review** – CIRS data has shown that parallel review helps to reduce the time to reimbursement decision but does not necessarily lead to a greater number of positive reimbursement decisions.

- **Aligned post-approval commitments** – It should be possible to align many regulatory and HTA requirements and avoid two sets of parallel post-approval trials. This is particularly important for medicines with provisional/conditional regulatory approval and medicines approved with small or non-randomised controlled trial (RCT) data. There needs to be a framework established for post-licensing data sharing between regulators and HTA agencies.

Barriers to regulatory-HTA cooperation

Organisational structures force regulatory and HTA functions in many companies and governments into separate silos, making interaction and collaboration more challenging. There can also be cultural barriers to regulatory-HTA cooperation, such as agency and company perceptions of HTA influencing regulation (and vice versa), and legal constraints and concern from companies about sharing confidential information between regulatory and HTA agencies.

Summary

Regulatory-HTA collaboration should facilitate understanding of each stakeholder's remits, while maintaining separate roles and decision making. By working together, regulators and HTA agencies can develop innovative methods and solutions to reduce uncertainties in medicine development. However, there are organisational, cultural and legal barriers to regulatory-HTA collaboration that need to be overcome. Metrics are key to understanding whether close regulatory-HTA collaboration leads to more medicines reimbursed and/or faster reimbursement decisions.

Conclusions – There are many opportunities!

- **Better collaboration** can potentially lead to improved decisions, while maintaining separate roles and decision -making between regulatory and HTA agencies
- A larger number of processes could **address both regulatory and HTA requirements**
- Need to **formalise HTA-regulator collaboration processes** rather than rely on *ad hoc* cooperation
- **Metrics will be needed** on whether closer collaboration leads to more medicines reimbursed and/or faster reimbursement decisions
- **Some recent changes** in Europe and the UK Innovative Licensing and Access Pathway (ILAP) could provide a model for other countries

Integrating regulatory-HTA alignment during development – Innovative access pathways

HTA/Regulatory agency perspective

Jeanette Kusel, Director, National Institute for Health and Care (NICE) Advice, NICE, UK, and

Louise Knowles, Deputy Director, Innovation Accelerator and Regulatory Science, Medicines and Healthcare Products Regulatory Agency (MHRA), UK

Innovative Devices Access Pathway (IDAP)

Aims and potential benefits

With increasing pressures within the UK healthcare system and a varied, complex MedTech sector, IDAP was launched as an end-to-end pathway linking key steps and partners in the route to market for an innovative MedTech device. These partners are MHRA, NICE, Health Technology Wales, the National Health Service (NHS) England, the Office for Life Sciences and the Scottish Health Technologies Group.

The aim of IDAP is to enable and improve patient access to innovative and transformative medical devices by providing an integrated and enhanced regulatory and access pathway to developers. Successful applicants receive non-financial support from a team of experts to develop a tailored roadmap called the Target Development Profile, which outlines regulatory and access touchpoints across the product's development. Examples of support available through IDAP includes system navigation advice, a fast-tracked clinical investigation review, joint scientific advice, safe-harbour meetings with key stakeholders to discuss product realisation, Exceptional Use Authorisation granted by the MHRA and an assigned Health Innovation Network.

Learnings so far

IDAP has been piloted with eight technologies to test the main elements of the pathway and provide informative learning and feedback that will help shape the future IDAP.

Learnings from the pilot so far are:

- Collaborative programmes take a long time to plan
- Good governance and programme management is key
- Developers benefit from early joint dialogue with both regulators and HTA.

Innovative Licensing and Access Pathway (ILAP)

Aims and benefits

The aim of ILAP is to reduce the time to market for transformative medicines by providing a single integrated platform for sustained collaborative working between the developer, HTA bodies, MHRA, and more recently, the NHS. Developers first apply for an Innovation Passport and then, like IDAP, work with partners to develop a Target Development Profile roadmap for delivering early patient access. Developers can benefit from access to tools such as joint scientific advice, innovative and flexible licensing routes, and the ILAP Access Forum, where the NHS, HTA bodies and the developer come together to discuss market access challenges and potential solutions.

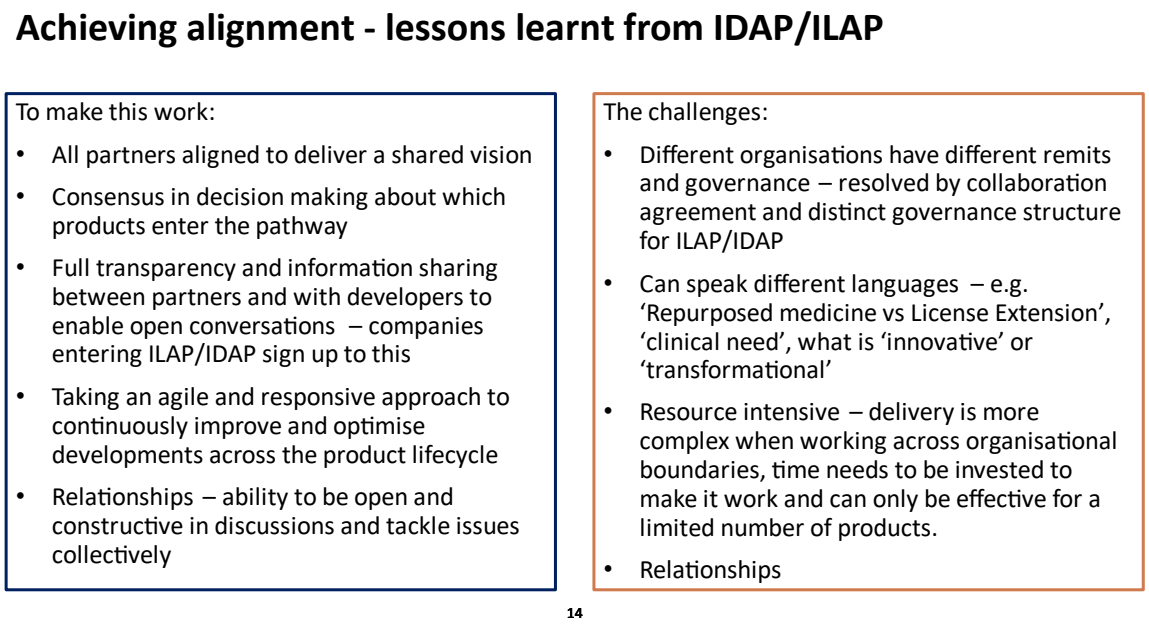
Learnings from ILAP

Since its first launch in January 2021, ILAP has received an unprecedented number of applications, with 166 Innovation Passports being awarded. Of those, 28 have had Target Development Profile roadmaps, 12 had ILAP Access Forums and 24 received marketing authorisations.

ILAP has recently been relaunched to address capacity challenges and feedback from stakeholders. The new ILAP includes more focused entry criteria and directly involves the NHS to support timely adoption of ILAP products.

Key learnings from the first version of ILAP are:

- All partners need to be aligned to a shared vision
- Good governance and programme management are key
- Constant evolution is required to develop a successful and sustainable pathway.



Company perspective

James Ryan, Director, Global HTA Policy, HTA and Modelling Science, AstraZeneca, UK

Global clinical development

Industry must balance the needs of multiple stakeholders across and within regions, constantly making decisions on evidence packages. Evidence development comes at an opportunity cost, as evidence for one medicine is traded off against evidence for another. Prioritisation is essential, so key populations, outcomes and comparators must be identified with consideration of various factors including ethical issues.

Value in collaboration

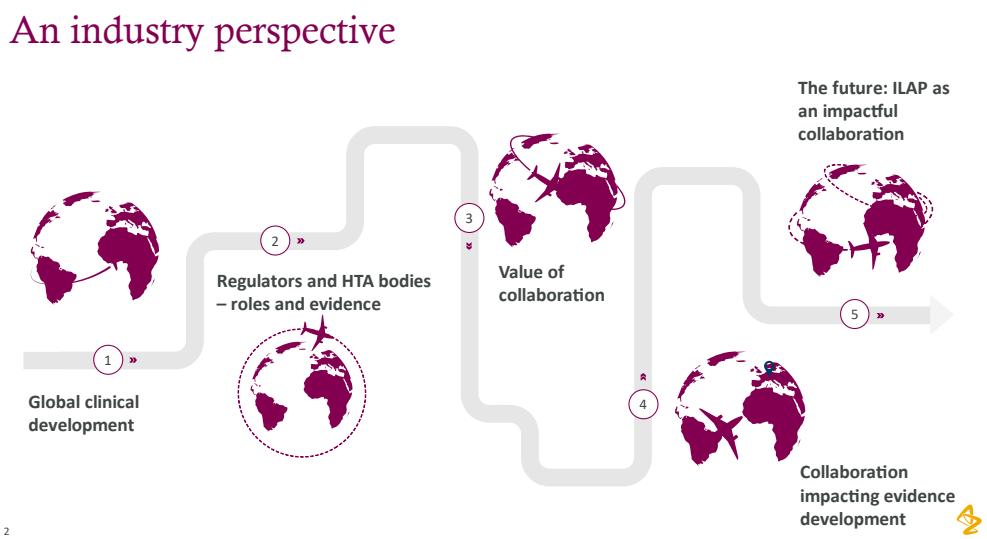
Regulatory-HTA collaboration is important for mutual understanding of decision remits, whether that's within a company or between two agencies. Secondly, it has an important role in developing innovative methods and solutions, such as different forms of evidence, which are needed to keep up with evolving science and technologies.

Innovative Licensing and Access Pathway (ILAP)

Industry has appreciated being able to share its experiences of the UK Innovative Licensing and Access Pathway (ILAP) to help shape the next version of the pathway. To ensure that innovative health technologies can be disseminated into the healthcare system, stakeholder engagement in ILAP needs to be expanded so that MHRA, HTA bodies, NHS England, patients etc are actively involved. Industry participants of ILAP must also be committed to providing resource and support to get the best out of the pathway; demonstrating the impact of ILAP in terms of medicines funded, as well as its potential relevance beyond the UK, would help to enable this.

Summary

For industry, regulatory-HTA collaboration has value in helping to optimise evidence development and address uncertainties. Integrated pathways such as ILAP hold great potential for delivering transformative medicines to patients but need better stakeholder engagement and commitment to be truly impactful.



Regulatory-HTA collaboration during development in providing scientific advice

Panel discussion

Each participant was asked to provide their reflections on the following questions:

- What is the 'value add' of regulatory-HTA early scientific advice?
- Is it enabling improved evidence generation and predictable outcomes?
- Does it need to evolve?

Company perspective – Dr Nicole Kubitz, Senior Director, HTA & Decision Science, Johnson & Johnson Innovative Medicine, Germany

- By taking early regulatory-HTA scientific advice, industry hopes for enhanced predictability for regulatory approval and downstream HTA/payer decision making, as well as greater time efficiency by receiving simultaneous consolidated feedback and early insights on areas of convergence/divergence between regulatory and HTA.
- Early scientific advice is also important for mutual understanding and sharing knowledge of the complexities of particular programmes e.g. cell and gene therapies.
- While there is no doubt that regulatory-HTA collaboration has value in optimising evidence development and addressing uncertainties, it may be too early to say whether parallel scientific advice is enabling predictable outcomes for industry.
- There needs to be more agency capacity for parallel advice and a greater degree of flexibility to ensure that advice is provided on time to inform company development programmes.

Patient perspective – Josephine Mosset, Policy Officer, Cancer Patients Europe, Belgium

- Regulatory-HTA collaboration can lead to faster patient access to therapies, more patient-centred evidence, predictable pathways and reduced inequality in access across the EU.
- However, there are challenges that can create delays for patients, such as fragmented assessments across EU Member States, insufficient patient involvement and misaligned data requirements between regulators and HTA agencies.
- There are several ways for regulatory-HTA collaboration to evolve to meet patient needs:
    - Stronger EMA and HTA collaboration.
    - More frequently and consistently involving patients across drug development, including in parallel scientific advice.
    - Use of real-world evidence and patient-reported outcomes to reflect real life experiences.
    - Reducing inequalities through efforts at the EU level.

Regulatory agency perspective – Karen Reynolds, Director General, Pharmaceutical Drugs Directorate, Health Canada

- Regulatory-HTA early scientific advice provides opportunity to give guidance on the Canadian context and to discuss clinical considerations with external medical experts early in the drug review cycle. In addition, these meetings are a unique opportunity to have both the HTA and regulator providing advice at one table. However, it is too early to observe long term outcomes of these meetings.
- Uptake of parallel scientific advice in Canada has been limited (only seven meetings since 2019, of which Health Canada participated in five), which may be due to the time and resources required.
- Evolving the parallel advice process to make it less resource intensive and more efficient would be beneficial to both companies and agencies.
- There also needs to be further clarification on the roles of external experts vs regulatory staff, as well as a clearer distinction between parallel advice and Health Canada pre-submission meetings.

HTA/regulator engagement and collaboration on better leveraging RWE in health technology assessments and regulatory decision making

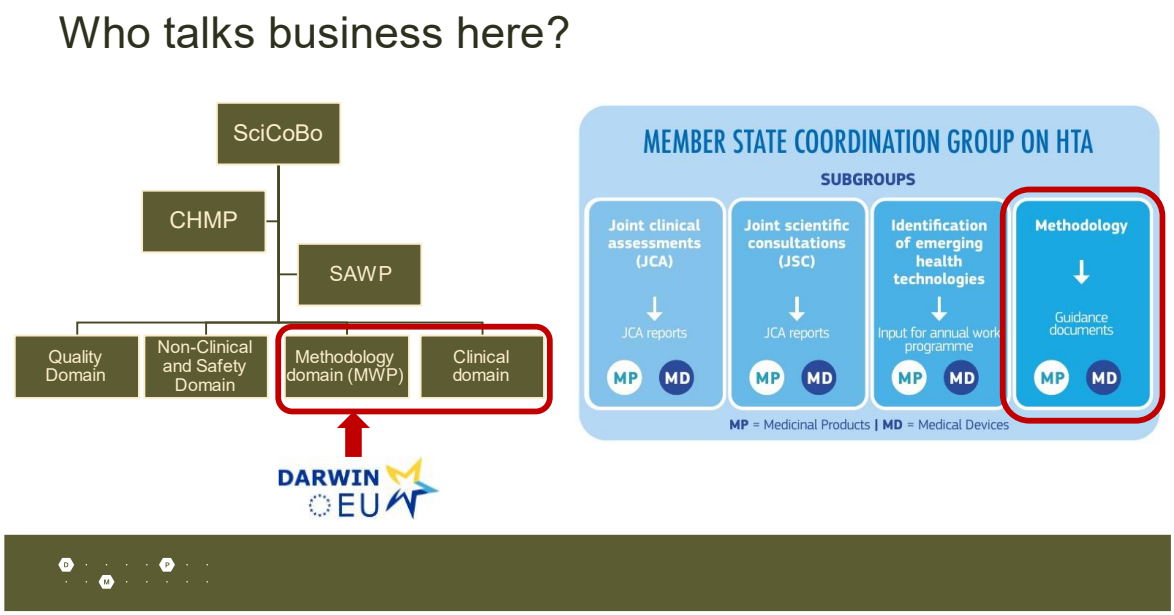
Agency perspective

Dr Anja Schiel, Senior Adviser, Lead Methodologist in Regulatory and Pharmacoeconomic Statistics, Norwegian Medical Products Agency (NOMA)

Who are the key players in leveraging RWE?

In the EU, there are many groups of regulatory and HTA experts with different tasks and perspectives (see below). However, communication and collaboration between these groups has been limited, which may be due to the high pressure of delivering the EU HTA Regulation (HTAR).

The EMA Methodology Working Party (MWP) was established by the Committee for Medicinal Products for Human Use (CHMP) as a source of expertise in biostatistics, modelling and simulation, pharmacokinetics, pharmacogenomics and RWE. This group also help to support the Data Analysis and Real World Interrogation Network (DARWIN-EU).



DARWIN-EU

DARWIN-EU was created to enable EMA and national regulatory agencies to access and analyse healthcare data from across the EU. The latest progress report from DARWIN-EU shows that 20 data partners from 13 European countries have been onboarded since 2022 and approximately 10 data partners are expected to be added each year going forward. While this collectively represents a wealth of RWD, there are still challenges relating to agencies' capability to generate and interpret RWD, data quality, data completeness and linkage between data sources.

Learnings from DARWIN-EU have also highlighted the difficulty in asking the 'right' research question to fit the available data sources. Out of 60 research topics proposed between February 2023-February 2024, only 31 (52%)

were found to be feasible and 21 topics (35%) were not feasible. It also remains unclear how EMA and EU regulators are using the RWE reports generated to complement other evidence when assessing medicines.

DARWIN-EU has only conducted two HTA-focused studies, which is not surprising given the data quality issues and lack of patient-reported outcome data. The general lack of HTA guidelines on RWE may reflect the need for flexibility in HTA decision making, which comes with a trade-off of predictability. RWE may not be the highest priority in the HTA community right now, given the upcoming HTAR.

Summary

While the benefits of RWE will primarily be for patients, they go beyond medicines regulation to the wider healthcare system. DARWIN-EU is helping improve understanding of what is possible with RWD, though there are challenges around data quality, completeness and linkage. It is important to be realistic about what RWE can achieve and ensure a learning-by-doing approach. As DARWIN-EU progresses alongside the HTAR, there is room for improvement in communication, alignment and collaboration between key players in the regulatory and HTA community in the EU.

Company perspective

Laetitia Mariani, Director, HTA Collaborations, International Market Access & Pricing, AbbVie, Switzerland

Opportunities to use RWE

To meet evidence requirements, industry use complementary data streams from RCTs and RWE. RWE is used in each phase of the product lifecycle, from discovery right through to post HTA. For regulators, the main role of RWE is to inform long-term safety and effectiveness, while for HTA agencies, in addition to clinical outcomes RWE helps to better understand the patient population, treatment pathways and comparators, and economic outcomes. As the EU HTA Regulation comes into force in 2025, there is an opportunity to use RWE to address PICOs as part of the JCA process.

Key success factors for RWE

Many HTA agencies prefer local comparative effectiveness data reflecting their country's health system. While some countries have rich data sources that can be leveraged to answer multiple questions, for others without such infrastructure, using suitable data from other countries may be the solution. The 'transportability' of comparative effectiveness evidence from one country to another is an important research topic that could help to drive acceptability and expand the benefits of RWE.

Good science principles are key to the successful conduct of non-interventional studies. For example, there must be an appropriate research design for the research question being considered, as well as valid, fit-for-purpose, traceable data.

Early experiences of DARWIN-EU have demonstrated the need for shared confidence and trust in RWE used for regulatory and healthcare decision making across stakeholder groups including health professionals and patients. A common framework for generating fit for purpose evidence, irrespective of who is generating the evidence, is key. It is also important that sponsors have the opportunity to review protocols and interpret evidence being generated using DARWIN-EU.

Summary

The value of RWE goes beyond just regulatory and HTA decisions; it should be integrated into healthcare decision making through a collaborative environment where industry, regulators, HTA agencies, healthcare providers, patients, and researchers work together. As medical product development is global, there needs to be greater convergence on approaches to RWD and harmonisation of requirements globally. Early planning, adherence to good scientific principles, and predictability and trust in the acceptance of RWE are key to success.

Conclusions

To meet evidence requirements, we use complementary data streams

- RWE is used in each phase of the product lifecycle, addressing evidence needs of multiple stakeholders
- Medical Product Development is a global effort - increasing international convergence on acceptability of RWE is a key enabler for predictability and uptake.

Different dimensions of uncertainty have different levels of relevance depending on context.

- E,g, industry and HTA agencies to collaborate on RWE to address uncertainty
- EUHTA as enabler for RWD to complement RCTs

Meeting expectations for evidence generation requires dialogue and greater predictability

- Critical to build alignment on fitness for purpose of data, methodologies and analytical approaches.
- Greater predictability for sponsors will be facilitated by guidance development (e.g. ICH M14 as a starting point).

Shared confidence and trust in real-world evidence

- A common framework for generating fit for purpose evidence irrespective of who is generating the evidence.
- A collaborative, principled approach with engagement opportunity for the sponsor to review protocols and interpretation of evidence being generated (ie; DARWIN EU)

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Sessions 3 & 4: Breakout discussions

Workshop participants were assigned to a breakout group and provided with a background document developed by CIRS, containing information and questions for discussion. The Chairs and Rapporteurs of each breakout were asked to facilitate and document the discussion, respectively. The Rapporteurs then fed back to all workshop participants in the main plenary session.

Breakout A: HTA collaborative models – What are the key considerations or frameworks that enable the construction and delivery of an efficient and effective model?

Chair: Dr Nick Crabb, Chief Scientific Officer, NICE, UK

Rapporteur: Marie Eckart, Europe Joint HTA Lead, Takeda, Switzerland

The group considered the following questions to help generate discussion and the development of a set of recommendations:

- Types of HTA collaboration – What makes them effective and efficient?
- Stakeholder engagement – What strategies help to ensure meaningful and continuous involvement of diverse stakeholders in HTA processes?
- Methodological standardisation – Are standardised methodologies an aim of collaboration and if so, how can this be achieved?
- Robust and timely collaboration – What are best practices and do these differ depending on the type of collaboration?
- Resource allocation – What are the challenges and how could these be addressed?

Recommendations to support the evolution of collaborative HTA models

1) **Introduce product agnostic early dialogue**

The group agreed that more multi-stakeholder conversations are needed to better define and understand unmet needs and national health priorities. They suggested that a new type of early advice or multi-stakeholder forum should be explored, which would allow regulators, HTA bodies, payers, industry, patients and clinicians to discuss pipelines/portfolios (before phase II) rather than specific products. This could take place at a jurisdictional level, or potentially cross-jurisdictionally for certain diseases e.g. rare diseases, paediatric. It was hoped that this sort of forum could give opportunity to discuss rough pricing levels and society's "ability to pay", helping to set expectations and potentially facilitate alignment between payers.

2) **Promote mutual learning on regulatory/HTA science and methodologies**

The group agreed that there should be mutual benefit in regulators and HTA agencies learning from each other. For example, for HTA agencies to understand how regulators came to an indication decision, and for regulators to understand the impact of indication wording on HTA. It is also important that industry is kept informed of advances in regulatory/HTA science to ensure understanding of what goes into regulatory/HTA considerations.

3) Encourage HTA convergence on methodologies

The group discussed whether standardising HTA methodologies should be a goal of HTA-HTA collaboration. While high-level HTA principles could potentially be harmonised, the group agreed that it is more important to focus on mutual learning and trust building between HTA agencies, which could facilitate convergence on methodologies, rather than standardisation or harmonisation. Nevertheless, there could be an opportunity for more HTA-HTA collaboration on innovations where national methodologies have not been set yet. The group also discussed whether convergence on HTA methodologies would lead to a better quality of HTA assessment but concluded that quality is too difficult to define.

4) Identify opportunities for adapting other agencies' reports in decision making

The group agreed that regulatory and HTA agencies should "look in their neighbourhoods" to identify where they can adapt other agencies' reports to the local context (if timelines and legal frameworks allow). There has been success for doing this in the context of regulatory reliance; could there be cross-learnings for the HTA community? The group agreed that adapting other agencies' reports must be a voluntary activity and that transparency is key, though it can be difficult to share unredacted reports.

5) Discuss the management of potential conflicts of interests of patient experts

The group discussed conflict of interest management for patient experts, which has been a key issue in the implementation of the HTA Regulation. While conflicts of interests must be managed, they should not become a barrier for representative patient and patient group input into HTA processes. The group recommended that CIRS include this as a topic of discussion at the 2025 multi-stakeholder workshop on patient involvement.

Breakout B: Changing mindsets – How can this best be achieved within companies and agencies to enable work-sharing collaborative models?

Chair: Dr Sean Tunis, Senior Fellow, Tufts Center for the Evaluation of Value and Risk in Health, USA

Rapporteurs: Dr Antonia Morga, Senior Director, Global HEOR and HTA Strategy Lead, Astellas, UK, and **Adrian Griffin,** Vice President for HTA Policy, Janssen, UK

The group considered the following numbered questions. Key points from the discussions are summarised below.

1) Identify the **key needs** for mindset change/cultural transformation for the utilisation of workshare collaborative models by companies and agencies in global submission/assessment of new medicines.

- Trust/relationship building between partners
- Identifying a framework to supporting cultural change including:
    - Awareness for business reason for change
    - Belief in desire/need for change
    - Continuous communication and encouragement on need and benefits of change.
- Start by assuming 'best intent'
- Create incentives (organisational and individual) – recognising the need to explain "what's in it for me?"

2) Identify **practical approaches** that need to be addressed in the short and long term to achieve cultural transformation that enables utilisation of collaborative workshare models.

Practical approaches for adoption of workshare models	Short term	Long term
Ensure all partners engaged in collaboration are aligned on the reason for change; shared objective / common ground	X	
Success of collaboration needs to be a key objective (KPI) for all organisations' senior leaders.	X	
Recognise barriers/boundaries – be explicit on the scope of collaboration	X	
Clear governance structure for long-term success of collaboration; leaders should have responsibility for success beyond their organisation.		X
Continuous communication & encouragement on the need for change	X	X

3) Discuss potential **challenges and solutions** to utilising the approaches identified above in Q2.

Challenges	Solutions
Optional collaborative models may not be used by the target stakeholder e.g. Access, Project Orbis	Clear communication of the benefits/value of the model e.g. to industry
Difficulty engaging partners within the collaboration	Identify common goals and ensure clear consistent messaging
Lack of common framework within which HTA-HTA collaborations can work	Explore concept of ICH-type organisation for HTA agencies - is this required/useful?
Adequate resources – managing change likely needs short-term input	Make organisational priority

4) Suggest potential **measures** to identify the success of collaborative work-sharing efforts.

- Measuring decision timeframes with/without collaboration
- Measuring submission lag with/without collaboration
- Organisational throughput (capacity)
- Measuring impact of regulatory collaborations (e.g. Access Consortium, Project Orbis) on HTA activity e.g. Do regulatory collaborations make HTA easier or harder?
- Growth of agencies engaged in collaboration over time
- Growth of assessments in collaborations over time

Recommendations for changing mindsets to enable work-sharing collaborative models

- Identify **case study examples** of successful work sharing or collaborations with demonstratable outcomes.
- Provide **clarity on the benefits of optional collaborative models** to help potential users understand the added value of these models.
- Ensure the success of collaboration is an **organisational priority**. For example, senior leaders could have a KPI related to the success of collaboration.
- Identify **interim short-term goals** of the collaboration to demonstrate success and create momentum.
- Explore the concept of an **ICH-type organisation for HTA agencies**. ICH provided a common framework within which regulatory collaborations could work; is a similar framework for HTA required/useful?
- Expand **awareness and acceptance** of collaborations through dissemination activities, such as external conferences.
- Establish internal **peer champions** to be advocates for collaborations.

Breakout C: Good collaborative practices for companies and agencies: What needs to be in place to move from principle to implementation?

Chair: Dr Alicia Granados, Global Head, Scientific Advocacy and Insights, Sanofi, Spain

Rapporteur: Dr Esteban Herrero-Martinez, Director, Regulatory Intelligence and Policy, AbbVie, UK

The group considered the following questions. Key points from the discussions are summarised below.

1) Definition of good collaborative practices – What are **common elements** irrespective of the collaborative model?

- Start with an aligned, mutually beneficial (and understood) vision, with clear goals and benefits as well as end/completion.
- Implement agreements and ensure there is clear governance including around communications, work products and platforms.
- Start small (pilot), aiming for 'low hanging fruit' to build confidence and trust. Then consider iterations/continuous evolution.
- Relationships are key – need to have clear internal and external communications
- Independence and separate remits need to be maintained e.g. regulator vs HTA agency.
- Mutual understanding/trust, facilitated by:
    - Listening/learning from each other on individual and organisational level – including understanding others' legal limitations/restrictions and ways of working
    - Training and upskilling
    - Common terminology.
- Tether to sustainable practices because relationships can change e.g. individuals leave/retire.

2) How should good collaborative practices be **measured**?

- There were mixed views among the group as to whether good collaborative practices can/should be objectively measured.
- There were also mixed views on the value of qualitative (softer) measures.
- Challenges for measuring collaborative practices:
    - Cannot have a single measure e.g. final outcome vs process measures.
    - Difficult to factor in trade-offs in addition to metrics e.g. one meeting vs another.
    - Difficult to measure outcomes and success of multi-year initiatives.
- Potential measures:
    - Process measures (time/on time/budget)
    - Employee satisfaction/retention.
- Important to consider how to measure the end of a collaborative initiative.
- May want to use a third party to evaluate to avoid potential bias.

Recommendations for key elements of good collaborative practices:

- Start with a clear, aligned **purpose and vision**, which is mutually beneficial and understood by all parties. There must be clear goals and definition of who are the actors and beneficiaries of the collaboration. Support from senior leadership is key.
- Establish good **project leadership and management**. There needs to be clear roles and responsibilities as well as a framework for decision making, including closing/sunsetting. Reviewing best practices from existing collaborative models would be helpful.
- Develop appropriate outcome **assessments/metrics**. These should ideally be agreed upfront, considering the views of different stakeholders.

Next steps/research needed to support the above:

- Identify use cases for successful and unsuccessful collaborations.
- Generate combined outputs from each of the breakout groups.
- Research appropriate assessments and metrics.

Session 5: Payer collaborations

Jurisdictional payer-HTA collaboration – What are some examples and why is payer-HTA collaboration needed?

Andrew Mitchell, Honorary Professor, Department of Health Economics Wellbeing and Society, Australian National University, Australia

Collaboration between the HTA agency and payer in a jurisdiction can help to promote value-based and evidence-based decision making, reduce excessive fixation on budget costs alone and give more flexibility in payer negotiations, as the HTA advice for implementation can be better tailored to the tools payers employ. However, higher political involvement and functional variation within payers can mean fewer opportunities for HTA-payer collaboration.

Close collaboration examples

Australia is an example of close payer-HTA collaboration. Listing onto the Pharmaceutical Benefits Scheme (PBS) (administered by the Australian Government, the payer) is a two-step legal process involving first the Pharmaceutical Benefits Advisory Committee (PBAC) (the HTA agency), then the Minister for Health. This legal framework in Australia means that PBAC has a 'pre-veto' power, so nothing can be listed onto the PBS without a recommendation to do so from PBAC. PBAC can either recommend on the basis requested by the company – including with respected to price, or with non-binding conditions that guide post-PBAC negotiations. The PBAC HTA process is uniquely embedded in the PBS, enabling close collaboration and trust between PBAC and the Minister; misalignments between the two have been ultra-rare.

Other examples of close HTA-payer collaboration include the Netherlands, which established HTA agency ZIN to support regulated private health insurance, and England, Wales, Scotland, Sweden and Canada, which have established close HTA-payer collaboration to reduce geographical variation in reimbursement and/or promote national negotiation.

Poor collaboration examples

The US healthcare landscape is made up of a multiplicity of payers, and unlike many developed countries, there is no central, national HTA agency. There has been a long history of resistance to the federal government having a role in pricing and 'full' HTA. The influence of HTA on non-federal government payers varies, and the transparency of this influence also varies.

Other examples of poor HTA-payer collaboration are:

- Jurisdictions with non-comprehensive payer arrangements for their healthcare systems.
- Jurisdictions with no or developing HTA.
- Jurisdictions with a mismatch between the level of the payer body and the level of the HTA body.
    - For example, cross-national versus national versus sub-national.
- Regions with a mismatch between the cross-jurisdictional collaborations across payer bodies and across HTA bodies.

Summary

Collaboration between the HTA agency and payer in a jurisdiction can help to promote value-based and evidence-based decision making, reduce excessive fixation on budget costs alone and give more flexibility in payer negotiations. However, HTA agencies and payers can exist independently, as close HTA-payer collaboration is not a prerequisite to the existence of either entity. Jurisdictions with a very diverse payer landscape, with no or limited HTA, or with a mismatch between the level of the payer and the HTA agency, are less likely to have close HTA-payer collaborations.

Why is HTA-payer collaboration needed?

- Promotes value-based decision-making
  - incremental health benefits, health system cost off-sets
- Reduces fixation on budget costs
  - incremental cost-justification
- Promotes evidence-based decision-making
  - rigour, transparency, consistency, defensibility
- Enables some independence from political variation
  - protects politicians from individual decisions
- Encourages and informs helpful flexibility in payer negotiations

7

Cross jurisdictional payer collaborations – What are the benefits and why is this needed?

Dr Robert Sauermann, Head, Department of Pharmaceutical Affairs, Austrian Federation of Social Insurances

Austria has a population of nine million people, 99.9% of whom are covered by the Austrian healthcare system and three statutory health insurances. The insurance bodies have political links as they are governed by employers' and employees' representatives, such as labour unions. The Federation of Social Insurances is an independent umbrella organisation that conducts centralised HTA as well as price negotiation and reimbursement decisions of out-patient pharmaceuticals through its Department of Pharmaceutical Affairs.

Information exchange

Payers come together to exchange information on economics and pricing. The Pharmaceutical Pricing and Reimbursement Information (PPRI) network facilitates exchange between public officials of European social insurances and promotes a common understanding of pharmaceutical policy issues. The European Integrated Price Information Database (EURIPID) is a voluntary non-profit collaboration of 28 national pricing and reimbursement authorities in Europe. Its members have committed to provide national data, such as pricing, reimbursement and usage data, and to foster information and data exchange between EU countries.

The Medicine Evaluation Committee (MEDEV) is a network of 22 European pharmaceutical pricing and reimbursement authorities and HTA agencies that provides an informal platform for information exchange and sharing of expertise. MEDEV also works closely with other organisations and networks, such as the EMA, European Social Insurance Platform, the European Commission and European Parliament, helping to assess how EU-level activities may impact on national assessment, pricing and reimbursement.

Horizon scanning

Payers are collaborating on horizon scanning through the International Horizon Scanning Initiative (IHSI) Database, which has several benefits including access to comprehensive, independent information; facilitation of healthcare system preparedness and budgetary precautions; cost savings and efficient use of resources; and strengthening of international cooperation. The IHSI is a spin-off of the Beneluxa Initiative, which brings together payer and HTA organisations in Belgium, the Netherlands, Luxembourg, Austria and Ireland to share information and conduct joint HTAs and joint pricing and reimbursement negotiations.

Summary

Payer-payer collaboration across jurisdictions can take various forms, such as through information sharing, horizon scanning and joint negotiations. It is important to consider how a collaboration will operate, for example, whether it is voluntary, which may require more company engagement to promote uptake, as well as its size, which can affect the ability for partners to build trust. Common challenges that European payers can tackle together include communication of public needs, such as sustainability and affordability of medicines; pharmaceutical policy developments, such as the upcoming HTA Regulation and General Pharma Legislation; joint negotiation or purchase; and advancing the European Health Data Space so the use of RWD in payer decision making can be improved.

Payer - payer collaboration - how?

- Bottom up – Top down?
- Pilot projects - new frameworks?
- Voluntary - Mandatory (by legislation, contract, setting standards)

Payers' challenges to focus on together?

- National (!) „cross-jurisdictional" cooperation
- Communication of public needs (sustainability, affordability, evidence, health data, …)
- Balanced EU Pharma legislation
- Joint negotiation / purchase? Effect by EU-HTA-Regulation?
- European health data space for research + Darwin EU: payers have the health data, question of quality to analyse and improve use, compliance, epidemilogy, re-negatioate MEAs

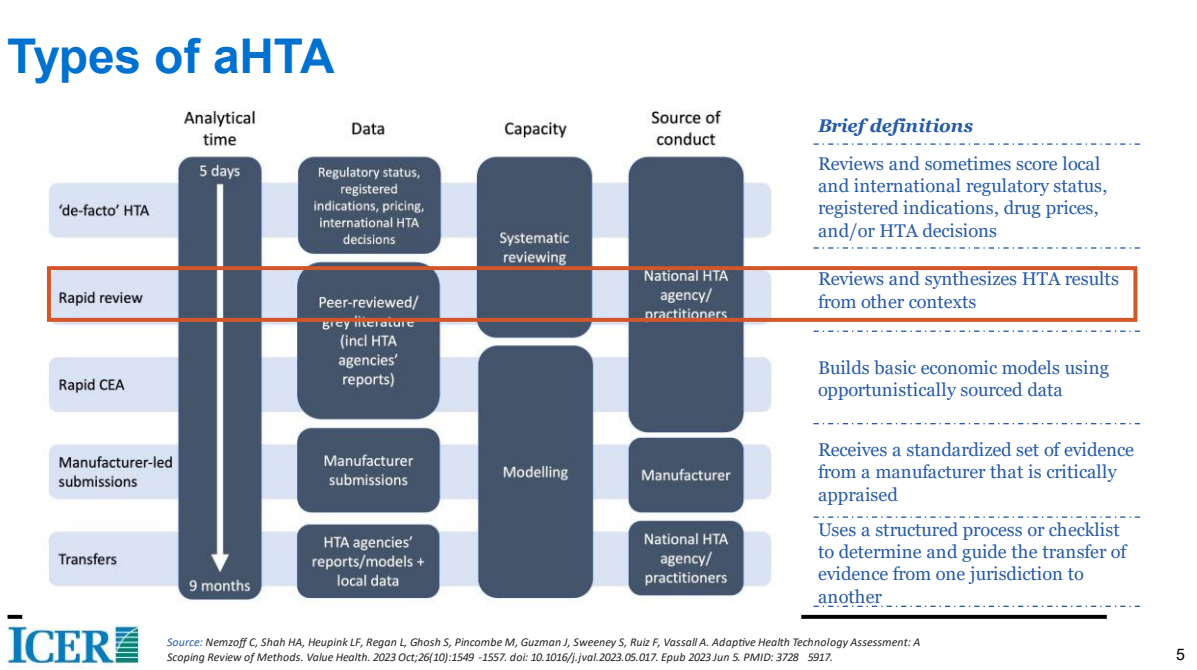
Session 6: Evolution of collaboration and workshare in the review and HTA assessment of new medicines

Adaptive HTA – A novel method for efficient application of HTA methods and principles

Dr Daniel Ollendorf, Chief Scientific Officer and Director of Methods and Engagement, Institute for Clinical and Economic Review (ICER), USA

Adaptive HTA

Adaptive HTA is an umbrella term for a variety of HTA methods to combine evidence synthesised elsewhere with local adaptation and context. It recognises the benefits of HTA as well as limitations on available personnel, resources and funding. Adaptive HTA is often applied in settings with limited HTA capacity, such as in low and middle-income countries (LMICs), or when many decisions must be made in a limited timeframe e.g. benefit package refinement. There are several types of adaptive HTA (see below).



Rapid review

Rapid review imports and contextualises HTA reports done in other jurisdictions. The International Decision Support Initiative has recently published guidance on rapid review, which provides a structured method with seven core modules (from topic selection through to recommendation) as well as four optional modules (including transferability checklists). Importantly, there is a decision point on whether adaptive HTA is the right approach to take, or whether there is rationale for doing a full traditional HTA e.g. uncertain evidence, need for local data, longer timeframe to make the decision, high priority/impact technology.

The PICO approach is used to match the scope of interest to the scope that was used in the other HTA reports and published cost-effectiveness studies. When summarising evidence, new extraction of clinical and economic data should be limited (given that this information has already been evaluated in the transferred HTA reports, and key

uncertainties highlighted. Recommended supporting analyses include price benchmarking between countries, treatment cost calculation and budget impact estimation.

Understanding the local context is critical in rapid review, as uncertainty is increased and accuracy potentially reduced when transferring data between settings. Important questions to consider are:

- Is implementation of the intervention feasible?
- Will population coverage be adequate?
- Is the intervention socially acceptable?
- Is the evidence generalisable to the local population?
- Will patient support services be available?
- How will implementation affect current care pathways?
- How might drivers of cost-effectiveness findings differ locally?

Pilot study in India

A study published in *BMJ Evidence-Based Medicine* has demonstrated the feasibility of using adaptive HTA to assess the cost-effectiveness of emicizumab prophylaxis for haemophilia A with inhibitors in the Indian context. Only two foreign HTA reports were found to be suitable evidence sources for the study, which was due to two reasons: (1) differences in clinical practice in India compared to more established HTA settings, and (2) frequent redaction of the economics section of HTA reports.

Summary

Adaptive HTA is an umbrella term for a variety of methods used to combine evidence synthesised elsewhere with local adaptation and content. However, the trade-off for greater speed and efficiency is some sacrifice of accuracy or increase in uncertainty, so caution is required in adjusting and adapting transferred HTA data to the local context. Transparency is essential if HTA reports are to be considered a 'social good' through adaptive HTA.

HTA strengthening and capacity building – New initiative in Taiwan

Dr Li Ying (Grace) Huang, Senior Director, Division of HTA, Center for Drug Evaluation (CDE), Taiwan

Taiwan began conducting HTAs in 2007 to support the National Health Insurance Administration (NHIA) in its drug reimbursement decisions. The Division of HTA operates under the Center for Drug Evaluation (CDE), which was established in 2008. Initially, the focus was on HTA evaluations for drugs, and in 2011, this expanded to include medical devices, patient involvement (2015), horizon scanning (2019), and medical technology reassessment (2021). The HTA process drew references from agencies in Australia, Canada, and the UK.

Capacity building

The HTA workload of CDE has greatly increased over the last decade, prompting several capacity building efforts. These not only aim to enhance the expertise of HTA organisations and researchers in Taiwan but also to raise awareness about HTA among various stakeholders and to encourage students to consider pursuing careers in the HTA field. For example, in 2022, CDE and the Taiwan Society for Pharmacoeconomics and Outcome Research jointly held a 'challenge camp' for bachelor's, master's and doctoral students, which was very well received. A series of training programmes and workshops have also been established to equip stakeholders with essential HTA methodologies, fostering a culture of evidence-based decision making in healthcare.

Taiwan's capacity building initiatives include partnerships with international HTA organisations, facilitating knowledge exchange and best practices to strengthen local capabilities and improve assessment outcomes. Taiwan has recently hosted the HTA International Asia Policy Forum (2023), an APEC workshop on "Advancing HTA for sustainable universal health coverage" (2024) and the workshops related to the Taiwan-UK Collaboration Agreement (2023, 2024).

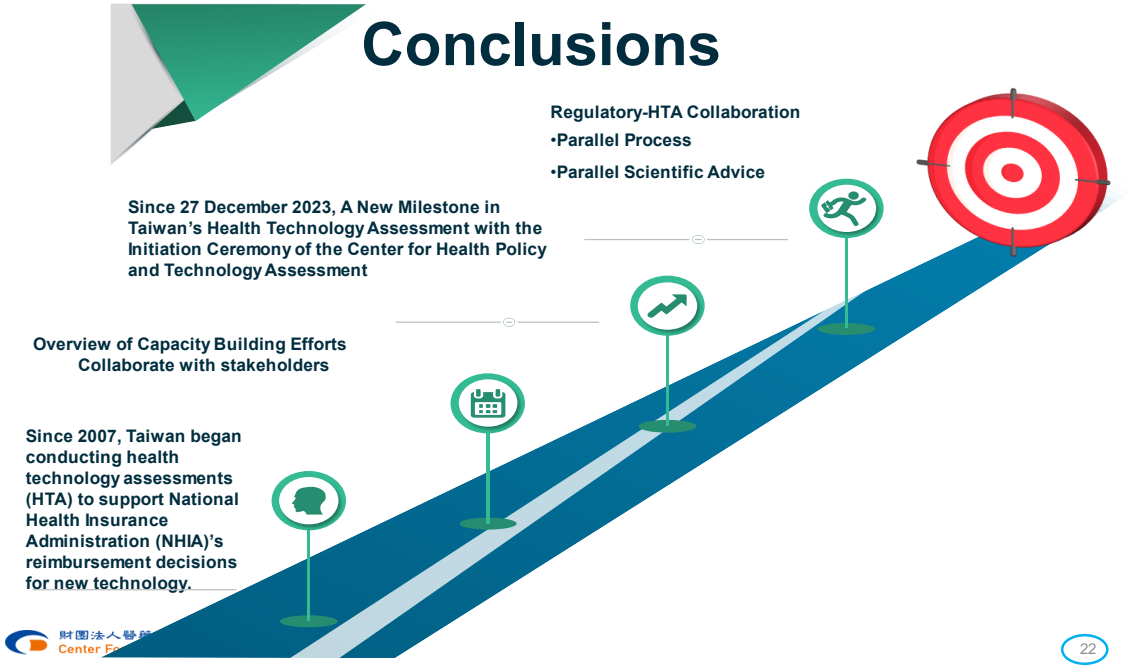
Future vision

In January 2024, the Center for Health Policy and Technology Assessment (CHPTA) preparatory office began operating, marking a new milestone for HTA in Taiwan. The preparatory office is primarily composed of the CDE HTA team in collaboration with the National Health Insurance Administration (NHIA). The CHPTA will continue to develop HTA methodologies and capacity to improve patient access schemes based on value and cost-effectiveness, thereby providing robust support for the NHI programme. In addition, CHPTA has implemented a parallel review mechanism, which eligible applicants may apply for after submitting a registration application with the Taiwan Food and Drug Administration (TFDA). Drugs eligible for parallel submission are as follows:

1. Drugs recognised by TFDA for priority review, accelerated approval, paediatric or rare severe disease treatment, or breakthrough therapy designation.
2. Drugs that have not yet been marketed internationally at the time of application for evaluation and registration in Taiwan.
3. Internationally marketed drugs that have been approved for manufacturing in Taiwan within two years of application for evaluation and registration in Taiwan.
4. Drugs that have been marketed in the top ten medically advanced countries for five years or more at the time of application, evaluation, or registration in Taiwan but have been newly developed with new ingredients in Taiwan.
5. Drugs based on new technology with better efficacy and lower costs than those currently included in the NHI programme.

Summary

Since 2007, the HTA process in Taiwan has evolved to promote cooperation with different stakeholders and capacity building efforts. International collaborations are key to facilitating knowledge exchange and best practices to strengthen local capabilities. It is hoped that regulatory-HTA collaboration in Taiwan will become closer with the implementation of parallel review and in the future, parallel scientific advice.



Next generation of collaborative, work-sharing and reliance models – Next steps and key considerations

Academic perspective

Prof Lotte Steuten, Deputy Chief Executive, Office of Health Economics (OHE), UK

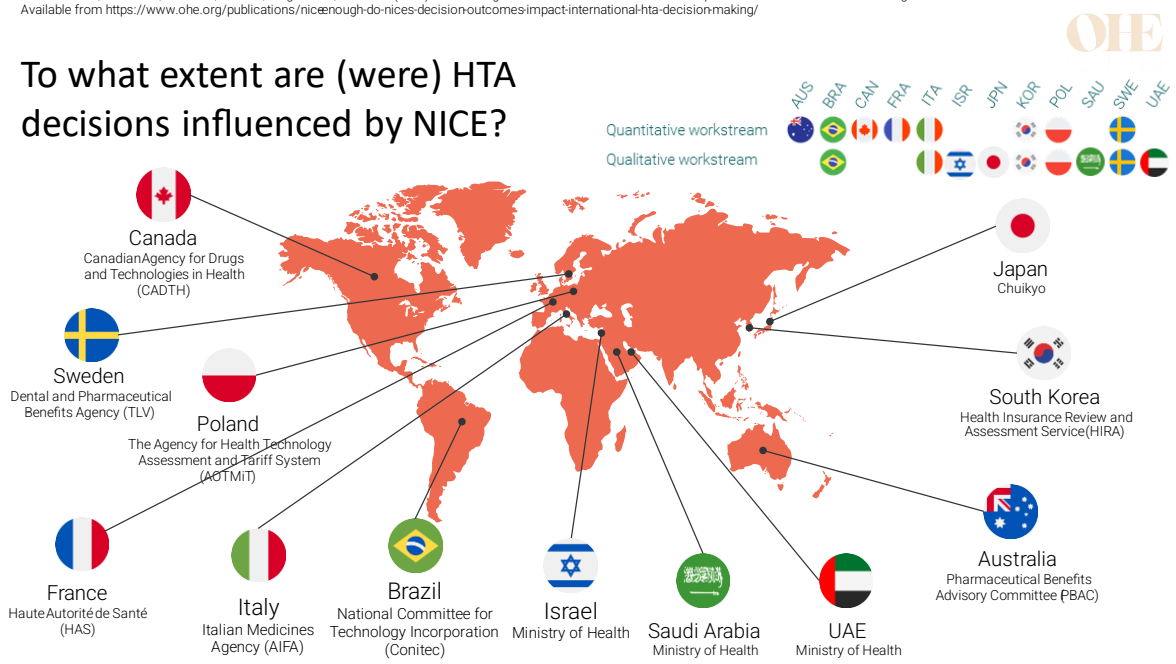
Patient outcomes are key

Having a clear vision and end goal for a collaboration is essential. Stakeholders may wish to work towards less variation in patient access, fewer inefficiencies, more sustainable and future proof regulatory and HTA processes and methods etc, while tacking common challenges. While opinions can vary on the success of collaborations, patient outcomes should always be the focal point.

Influence of HTA decisions made elsewhere

In 2023, OHE conducted a study assessing the influence of NICE decisions in international HTA decision making. Decision outcomes from HTA reports from 12 countries were analysed and qualitative interviews with key stakeholders conducted (see below). The study demonstrated that NICE decisions have some influence in other countries; positive NICE decisions correlated with positive outcomes elsewhere, while negative NICE decisions were often associated with no HTA appraisal in other countries. This highlights the impact that HTA agencies' reports can have on decision making in other countries, alongside evidence on the local context.

Henderson N., Brassel S., O'Neill P., Allen R., Largeron N., Garau M. (2023) NICE enough? Do NICE's Decision Outcomes Impact International HTA Decision-making?. OHE Contract Research. Available from https://www.ohe.org/publications/nice-enough-do-nices-decision-outcomes-impact-international-hta-decision-making/



Summary

Collaborations must be principled, pragmatic and patient-focused. Defining what a good collaboration looks like e.g. better, faster, cheaper, and then measuring this systematically, is key to learning and adapting collaborative models. Findings ways to make the process of producing and adapting HTA information more intentional, systematic and consistent could be beneficial to the global HTA community.

Patient perspective

François Houÿez, Director of Treatment Information and Access, EURORDIS – Rare Diseases Europe

Importance of communication

The objectives of collaborations need to be clearly communicated to patient communities and the public. For example, during the COVID-19 pandemic, some patient advocates believed that the World Health Organisation and mature regulators such as FDA and EMA were working together to ensure that only selected vaccines from Western countries were rolled out globally. Better communication from the regulators and WHO may have helped to prevent some of these negative perceptions.

Exchange of HTA information

International exchange of HTA information and reports can help single or very small numbers of patients with certain rare diseases to access treatments that are not available in their country. For example, EURORDIS was contacted by the family of a child with hypophosphatasia who needed enzyme therapy, but this was not covered in Georgia where they lived. Although there were only thought to be 3-5 hypophosphatasia patients in Georgia, the Ministry of Health needed evidence that there was no choice but to treat these patients, as it was concerned that other patient groups would make similar requests. EURORDIS identified and extracted key information from HTA reports and shared this with the Georgian Ministry of Health, who then assessed the information in the local context and finally agreed to cover the treatment costs.

Summary

Clear communication on the objectives and benefits of collaboration to patients and the public is important to ensure their support. Working with patients and patient organisations could help to identify key information in HTA reports that can then be exchanged internationally to support local decision making. However, this can be challenging if there are mixed opinions on the product among the patient community. To avoid duplication and facilitate information exchange, there needs to be an international repository of all regulatory and HTA evaluations (positive and negative), including English translations.

Next generation of collaborative, workshare or reliance models: Next steps and key considerations

Panel discussion

Each participant was asked to provide their reflections on the next generation of different types of collaborative models.

HTA-HTA collaborations – Dr Yot Teerawattananon, Secretary General, Health Intervention and Technology Assessment Program (HITAP), Thailand

- HTA to HTA collaboration is urgently needed in low- and middle-income countries (LMICs), as often health priority setting is insufficiently developed, and there are misconceptions about HTA e.g. cost cutting, as well as feasibility issues e.g. no local data and capacity.
- Regional networks like HTAsiaLink can serve as an example of initiatives that facilitate knowledge exchange, share best practices to strengthen local capabilities and find solutions to common issues.
- The next generation of HTA-HTA collaboration should focus on building capacity and providing support to emerging countries that lack HTA capabilities; it is important to consider what 'public goods' are generated from collaboration, and how they can be shared with the wider community.
- Unlike in high-income countries, where HTA agencies make coverage decisions, in most LMICs, HTA primarily provides advice to payers on coverage decisions. Therefore, it is essential to involve payers in HTA collaborations, particularly in LMICs, to ensure alignment in policy and address concerns where payers may be hesitant to pursue faster access due to limited resources.

Regulatory-regulatory collaborations – Dr Supriya Sharma, Chief Medical Adviser, Health Canada

- Regulators must be clear about the goals of collaborating and use technology as an enabler for collaboration.
- It is important to consider the sustainability of collaborations; they cannot just rely on relationships between individuals.
- With regards to reliance, internal change management should not be underestimated; it is important to start small and make incremental steps to demonstrate success and allay potential concerns.
- While collaboration has facilitated various achievements in the regulatory field, there needs to be more focus on underserved sub-populations, increased patient involvement, combatting misinformation and disinformation and working towards mitigating drug shortages.

Regulatory-HTA collaborations – Dr Michael Berntgen, Head of Scientific Evidence Generation Department, EMA

- EMA is committed to facilitating access to medicines in the EU through collaboration with HTA agencies, as outlined in its draft Network Strategy to 2028.
- Key considerations for regulatory-HTA collaboration:
    - Need for clear communication and terminology. For example, in the context of the HTA Regulation, 'joint' means joint working between HTA agencies; EMA is only involved in the 'parallel' steps e.g. parallel joint scientific consultation, parallel assessment.
    - Sharing of confidential information between decision makers e.g. between EMA and the HTA Secretariat and Coordination Group.
    - Sharing experiences and best practices globally to inform each other.
- Next steps for regulatory-HTA collaboration:
    - Increased collaboration on post-licensing evidence generation to address uncertainties.
    - Joint methodological work e.g. technical guidance.
    - Establish a common understanding on the definition of value of a health technology.

Payer collaborations – Prof Hans-Georg Eichler, Consulting Physician, Association of Austrian Social Insurance Institutions

- HTA agencies and payers must collaborate otherwise HTA becomes redundant.
- There can be different levels of payer-payer collaboration, with varying impact and feasibility:
    - Monopsony – where all payers globally come together to negotiate as one buyer.
    - Collaboration on pricing e.g. equity-based tier pricing, international differential pricing.
    - Collaboration on reimbursement e.g. could payers agree on a common framework for performance-based managed entry agreements? Or agree (or at least discuss) the treatment population to be covered?
    - Exchanging information and sharing experiences e.g. successes and failures in restricting prescribing practices.
- Payers should start with the most feasible collaborations and grow these with experience.

List of attendees

Affiliations are stated as they were at the time of the meeting.

Regulatory agencies		
Dr Michael Berntgen	Head of Scientific Evidence Generation Department	**European Medicines Agency (EMA)**
Prof Ton de Boer	Chair	**Medicines Evaluation Board (MEB), The Netherlands**
Louise Knowles	Deputy Director Innovation Accelerator and Regulatory Science	**Medicines and Healthcare Products Regulatory Agency (MHRA), UK**
Karen Reynolds	Director General, Pharmaceutical Products Directorate	**Health Canada**
Dr Supriya Sharma	Chief Medical Adviser	**Health Canada**
Shannon Thor	Deputy Director, Europe Office	**Food and Drug Administration (FDA), USA**
Dr Eveline Trachsel	Head of Medicinal Product Authorisation and Vigilance	**Swissmedic, Switzerland**
HTA and payer organisations		
Meindert Boysen	Chair	**Health Technology Assessment International (HTAi) Global Policy Forum**
Dr Nick Crabb	Chief Scientific Officer	**National Institute for Health and Care Excellence (NICE), UK**
Prof Hans-Georg Eichler	Consulting Physician	**Association of Austrian Social Insurance Institutions**
Roy Foot	Principal Pharmacist	**Scottish Medicines Consortium (SMC), UK**
Niklas Hedberg	Chief Pharmacist	**TLV, Sweden**
Dr Li Ying (Grace) Huang	Senior Director, Division of Health Technology Assessment	**Center for Drug Evaluation (CDE), Taiwan**
Dr Farah Husein	Director, Science and Methods	**Canada's Drug Agency**
Jeanette Kussel	Director, NICE Advice	**National Institute for Health and Care Excellence (NICE), UK**
Dr Dan Ollendorf	Chief Scientific Officer and Director of HTA Methods and Engagement	**Institute for Clinical and Economic Review (ICER), USA**
Dr Detlev Parow	Former Head, Department of Medicines, Medical Remedies and Selective Contracts	**DAK – Gesundheit, Germany**
Dr Robert Sauermann	Head, Department of Pharmaceutical Affairs	**Austrian Federation of Social Insurances**
Dr Anja Schiel	Senior Adviser, Lead Methodologist in Regulatory and Pharmacoeconomic Statistics	**Norwegian Medicines Agency (NOMA), Norway**
Dr Yot Teerawattananon	Secretary General	**HITAP, Thailand's Ministry of Public Health**
Dr Marc Van de Casteele	Coordinator, Pharmaceutical Expertise, Department of Pharmaceutical Reimbursement	**Belgian Health Care Institute RIZIV-INAMI, Belgium**

Kun Zhao	Professor, Department of HTA	**National Centre for Medicine and Technology Assessment, China**
Pharmaceutical companies and consultancies		
Nadia Assenova	Vice President, Regulatory Affairs, International	**Moderna, Switzerland**
Sunera Awan	Head of Regulatory Affairs UKI	**Bayer, UK**
Dr Indranil Bagchi	Global Head, Pricing and Market Access	**GlaxoSmithKline, USA**
Abbie Ba-Mancini	Head of Global Value and Access, Hematologic Malignancies	**Takeda, USA**
Bart Barefoot	Senior Director and Head, Europe Regulatory Policy	**GlaxoSmithKline, UK**
Carolyn Bodnar	Executive Director Value & Access	**Eisai, UK**
Lucia D'Apote	Executive Director, GRR&D Policy	**Amgen, Switzerland**
Marie Eckart	Europe Joint HTA Lead	**Takeda, Switzerland**
Jeffery Francer	Vice President, Head of Global Regulatory Policy and Strategy	**Eli Lilly, USA**
Sandra Gavart	HTA Leader, Early Portfolio and Operations	**Eli Lilly, Belgium**
Dr Alicia Granados	Global Head, Scientific Advocacy and Insights	**Sanofi, Spain**
Adrian Griffin	Vice President, HTA and Market Access Policy	**Janssen, UK**
Dr Michael Happich	Senior Director, HTA	**Eli Lilly, Germany**
Dr Adam Heathfield	Access Innovation	**Pfizer, UK**
Dr Esteban Herrero-Martinez	Director, Regulatory Intelligence and Policy	**AbbVie, UK**
Vanessa Horne	Associate Director, EMEA Regulatory Affairs	**Ultragenyx, UK**
Ana–Belen Irigaray	Senior Director, Regulatory Affairs	**Beigene, Switzerland**
Mohit Jain	Vice President, Global Value Access & Strategic Pricing – Global Head	**Biomarin, UK**
Dr David Jefferys	Senior Regulatory and Product Development Consultant	**Jefferys Consulting Ltd, UK**
Dr Nicole Kubitz	Senior Director, HTA & Decision Science	**Johnson & Johnson Innovative Medicine, Germany**
Dr Marisca Marian	Global Access Lead	**Bayer, Switzerland**
Laetitia Mariani	Director, HTA Collaborations, International Market Access & Pricing	**AbbVie, Switzerland**
Dr Mark Mayer	Vice President, Global Regulatory Policy and Strategy	**Eli Lilly, USA**
Katarzyna Migalska	Lead RA Regulatory Intelligence	**Astellas, UK**
Karolina Minda	Senior Director, Global (ex-China) Early Pipeline	**Beigene, Norway**
Dr Antonia Morga	Senior Director, Global HEOR and HTA Strategy Lead	**Astellas, UK**
Charlie Nicholls	Head of Global HEVA (HEOR) – General Medicines	**Sanofi, UK**

Marie-Pierre Petitjean	European Regulatory Experts Head	**Sanofi, France**
Katrin Rupalla	Head of Global Regulatory Affairs	**Johnson & Johnson, USA**
James Ryan	Director, HTA Policy, HTA and Modelling Science	**AstraZeneca, UK**
Dr Vanessa Schaub	Head, Global & EU HTA Strategy	**F. Hoffmann La Roche, Switzerland**
Dr Steven Slater	Portfolio Team Regulatory Strategy Lead	**F. Hoffmann La Roche, UK**
Dr Natalie Steck	Director, HTA Strategy and Policy	**Merck Sharp & Dohme (MSD), Switzerland**
Ana Tenreiro da Cruz	Regulatory Affairs Manager	**Bayer, UK**
Amanda Tombs	Regulatory Affairs Director – Global Policy	**AstraZeneca, UK**
Academic and non-profit organisations		
François Houÿez	Director of Treatment Information and Access	**EURORDIS – Rare Diseases Europe, France**
Prof Finn Børlum Kristensen	Professor of HTA	**University of Southern Denmark, Danish Centre for Health Economics**
Prof Andrew Mitchell	Honorary Professor, Department of Health Economics Wellbeing and Society	**The Australian National University, Australia**
Josephine Mosset	Policy Officer	**Cancer Patients Europe, Belgium**
Prof Sam Salek	Professor of Pharmacoepidemiology	**University of Hertfordshire, UK**
Prof John Skerritt	Enterprise Professor for Health Research Impact	**University of Melbourne, Australia**
Prof Lotte Steuten	Deputy Chief Executive	**Office of Health Economics (OHE), UK**
Dr Sean Tunis	Senior Fellow	**Tufts Center for the Evaluation of Value and Risk in Health, USA**
Centre for Innovation in Regulatory Science (CIRS)		
Penelope Cervelo	Research Analyst	**CIRS**
Gill Hepton	Administrator	**CIRS**
Adem Kermad	Senior Research Analyst	**CIRS**
Dr Neil McAuslane	Scientific Director	**CIRS**
Dr Brian O'Rourke	Chair of HTA Steering Committee	**CIRS**
Dr Jenny Sharpe	Communications Manager	**CIRS**
Dr Belen Sola	Research Analyst	**CIRS**
Anna Somuyiwa	Head	**CIRS**
Prof Stuart Walker	Founder and Senior Adviser	**CIRS**
Dr Tina Wang	Associate Director, HTA Programme and Strategic Partnerships	**CIRS**

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The Centre for Innovation in Regulatory Science (CIRS) is a neutral, independent UK-based subsidiary of Clarivate plc. Its mission is to identify and apply scientific principles for the purpose of advancing regulatory and health technology assessment (HTA) policies and processes in developing and facilitating access to pharmaceutical products. CIRS provides an international forum for industry, regulators, HTA bodies and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy. It is governed and operated by Clarivate 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.

Workshop organised by:

Dr Neil McAuslane, Scientific Director, CIRS

Dr Tina Wang, Associate Director, HTA Programme and Strategic Partnerships, CIRS

Dr Magda Bujar, Associate Director, Regulatory Programme and Strategic Partnerships, CIRS

Anna Somuyiwa, Head, CIRS

Report prepared by:

Dr Jenny Sharpe, Communications Manager, CIRS

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Keep in touch

Centre for Innovation in Regulatory Science (CIRS)
70 St Mary Axe, London EC3A 8BE, UK
Email: cirs@cirsci.org
Website: www.cirsci.org
www.linkedin.com/company/centre-for-innovation-in-regulatory-science-ltd