WORKSHOP SYNOPSIS

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

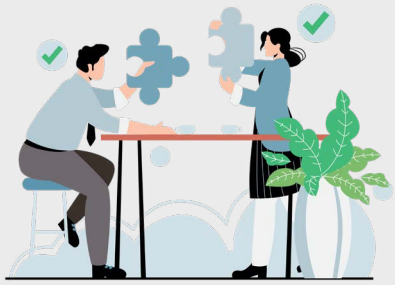
INFOGRAPHIC SUMMARY

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

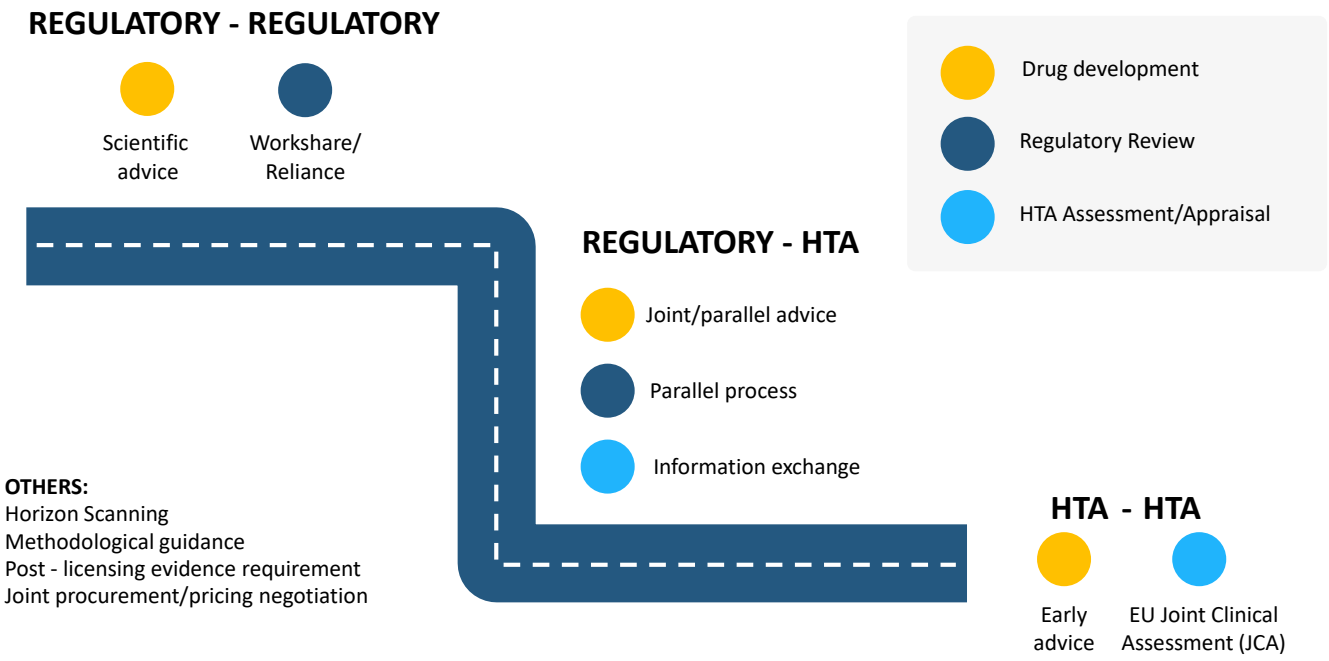
Explore a new forum for stakeholders to discuss unmet need and national health priorities.

Background

This workshop was part of a CIRS series exploring new ways of working within and across regulatory and health technology assessment (HTA) agencies, providing 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, 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



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.

Workshop sessions

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 breakout groups were asked to discuss and develop recommendations on three topics:

1. **HTA collaborative models** – What are the key considerations or frameworks that enable the construction and delivery of an efficient and effective model?
2. **Changing mindsets** – How can this best be achieved within companies and agencies to enable work-sharing collaborative models?
3. **Good collaborative practices for companies and agencies** – What needs to be in place to move from principle to implementation?

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 (see below for Access), 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.

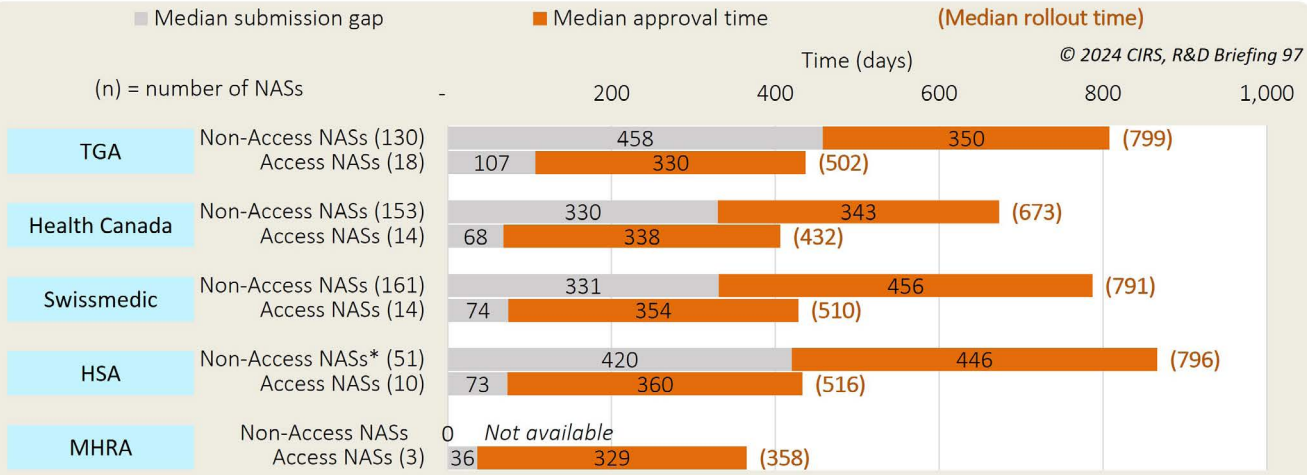
From an industry perspective, extending Project Orbis to include additional regulators and other therapeutic areas could make it even more impactful.

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.

Comparison of median submission gap, approval time, and rollout time for NASs approved via Access Consortium vs. Non-Access NASs (2019-2023)



NAS: New active substance; TGA: Australian Therapeutic Goods Administration; HAS: Singapore Health Sciences Authority; MHRA: UK Medicines and Healthcare products Regulatory Agency.

Submission gap is calculated as the time from the date of submission at the first regulatory agency (out of the European Medicines Agency, US Food and Drug Administration, Japan Pharmaceuticals and Medical Devices Agency, Health Canada, Swissmedic and TGA) to the date of regulatory submission to the target agency. Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. Rollout time is calculated from the date of submission at the first regulatory agency to the date of regulatory approval at the target agency.

**The timelines for other NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme.*

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 HTA Regulation (HTAR)** has created a mandatory form of HTA-HTA collaboration; HTA agencies are working together through the EU HTA Coordination Group 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.






Workshop programme

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

Chair: Niklas Hedberg, Chief Pharmacist, TLV, Sweden

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

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

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

Dr Eveline Trachsel, Head of Authorisation, Swissmedic, Switzerland

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

Meindert Boysen, Chair, HTAi Global Policy Forum

Niklas Hedberg, Chief Pharmacist, TLV, Sweden

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

Dr Farah Husein, Director, Science and Methods, Canada's Drug Agency

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

Chair: Dr Michael Berntgen, Head of Scientific Evidence Generation Department, European Medicines Agency (EMA)

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

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

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

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

Josephine Mosset, Policy Officer, Cancer Patients Europe, Belgium

Karen Reynolds, Director General, Pharmaceutical Drugs Directorate, Health Canada

Dr Anja Schiel, Senior Assessor/Statistician, Norwegian Medicines Agency (NoMA)

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

Sessions 3/4: Breakout Sessions

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

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

Adrian Griffin, Vice President for HTA Policy, Janssen, UK

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

Session 5: Focus on HTA-Payer and Payer-Payer collaborations

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

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

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

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

Chair: Dr Brian O'Rourke, Chair, CIRS HTA Steering Committee

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

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

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

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

Dr Yot Teerawattananon, Secretary General, HITAP, Ministry of Public Health, Thailand

Dr Supriya Sharma, Chief Medical Advisor, Health Canada

Dr Michael Berntgen, Head of Scientific Evidence Generation Department, EMA

Prof Hans-Georg Eichler, Consulting Physician, Association of Austrian Social Insurance Institution, Austria

About CIRS

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

Synopsis prepared by:

Dr Jenny Sharpe, Communications Manager, CIRS

v2 Published December 2024

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