CIRS CONTEMPORARY INSIGHTS WORKSHOP

EXPLORING APPROACHES TO DECISION MAKING

11-12 JUNE 2015

WASHINGTON, DC, US

A BRIEF SUMMARY*

***A FULL REPORT TO FOLLOW**

CIRS CENTRE FOR INNOVATION IN REGULATORY SCIENCE

Synopsis authors

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

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BACKGROUND

The overarching elements of a framework for benefit-risk assessment have been well articulated over the last five years, resulting in a commonality in the steps taken by both agencies and companies to assess a medicine's benefit-risk profile. As companies and agencies embed this framework into their decision-making process as a key tool to inform the benefit-risk assessment, a number of key questions arise:

- *How can we ensure that the framework is actively used as part of the decision process?*
- *What is the process for its incorporation within current decision-making procedures?*
- *How can the framework help improve the quality of the decision to progress or submit a new medicine?*

Beyond the implementation of a benefit-risk framework, these questions also represent a formal approach to quality decision making within an organisation.

The science of decision making is well established, although in reality, the process incorporates a mixture of science and art and decision making within companies and agencies is, in large part, influenced by organisational processes and procedures. A number of common characteristics identify a good-quality decision including creative implementable options; meaningful, reliable information upon which to base a decision; clearly identified values and tradeoffs for each supportive element; logically correct reasoning and a commitment to action.[1] Indeed, these characteristics map well to the steps articulated in the CIRS Universal Methodology for Benefit-Risk Assessment (UMBRA) Framework.[2]

One way to determine whether quality decisions are being made is to assess the outcome of the decision. However, this is not often practical and consequences can be extremely difficult to measure; in fact, a good, well-made decision may have poor consequences and a bad decision may have good outcomes. Currently, research and insight into decision-making approaches for individuals and organisations involved in medicines research and development is lacking. An enhanced understanding of how to identify and apply quality decision-making practices may facilitate decision-making approaches and subsequently may enable improved practices and consistency in good-quality decision making by individuals and organisations.

CIRS has undertaken a project to identify the important issues that influence quality decision making from the perspective of the individual and organisations. As a result of this background research, a draft framework for good decision making in the development and review of medicines has been developed. This Workshop focused on identifying the other factors and influences that companies and agencies need to consider to ensure they are building quality into their decision-making processes.

WORKSHOP OBJECTIVES

- **Discuss the potential influences** on good decision making within companies and agencies and whether a framework can improve the process
- **Identify considerations for both companies and agencies** when applying decision frameworks to their decision-making processes
- **Recommend** methods to ensure the building of quality into decision-making processes

WORKSHOP CHAIRS

Dr Sandra Kweder, Deputy Director, Office of New Drugs, Food and Drug Administration, USA

Professor Sir Alasdair Breckenridge, Former Chair, Medicines and Healthcare Products Regulatory Agency, UK

Prof Robert Peterson, Executive Director, Drug Safety Effectiveness Network, Canadian Institute of Health Research

References

1. CIRS. Workshop report: Building Quality into Regulatory Submissions and the Review Process: Knowing and meeting customer expectations, Cobham, Surrey, UK, December 2004.
2. Leong J, McAuslane N, Walker S, Salek S. Is there a need for a universal benefit-risk assessment framework for medicines? Regulatory and industry perspectives. *Pharmacoepidemiol Drug Saf*. 2013 Sep:22:1004-1012.

WORKSHOP PROGRAMME

SESSION: UTILISING DECISION FRAMEWORKS: HOW ARE COMPANIES AND AGENCIES USING THE BENEFIT-RISK FRAMEWORK TO BUILD QUALITY INTO THEIR DECISION-MAKING PROCESS?

Chair's welcome and introduction	**Dr Sandra Kweder**, *Deputy Director, Office of New Drugs, Food and Drug Administration, USA*
From benefit-risk frameworks to quality decision making	**Prof Stuart Walker,** *Founder, CIRS*
Improving the quality of regulatory decision making	
FDA viewpoint	**Dr Richard Moscicki**, *Deputy Center Director for Science Operation, US Food and Drug Administration, DIA*
EMA viewpoint	**Prof Hans-Georg Eichler,** *Senior Medical Officer, EMA*
Health Canada viewpoint	**Barbara Sabourin,** *Director General, Therapeutics Products Directorate, Health Canada*
Improving the quality of company decision making	
Project team decisions – Submission decision for new drug applications	**Dr Richard Hermann,** *Safety Scientist, AstraZeneca, USA* **Sharon Olmstead,** *Global Head, Development and Regulatory Policy Novartis, USA*
Beyond benefit-risk - Building quality into decision making	
Company viewpoint	**Dr Bennett Levitan,** *Director, Janssen, USA*
Agency viewpoint	**Prof John Skerritt,** *National Manager, Therapeutic Goods Administration, Australia*
Chair's introduction	**Professor Sir Alasdair Breckenridge**
Building quality into the decision-making process: What frameworks are companies and agencies using?	
CIRS survey on current processes and practices within companies and regulatory and HTA agencies	**Dr Neil McAuslane**, *Scientific Director, CIRS*
Challenges and opportunities within current practices and processes	
Company viewpoint	**Dr Joseph Scheeren,** *Head, Global Regulatory Affairs Pharma and Consumer Care, Bayer Consumer Care, Switzerland*
Regulatory viewpoint	**Prof Dr Hans Hillege**, *Alternate CHMP Member, Medicines Evaluation Board, The Netherlands*
HTA viewpoint	**Dr Chander Sehgal,** *Director, Common Drug Review (CDR) and Optimal Use, Canadian Agency for Drugs and Technologies in Health*
Which models have been used based on decision theory and how can these be applied to health issues?	**Dr Lawrence Phillips,** *Emeritus Professor of Decision Sciences, London School of Economics and Political Science, UK*

SYNDICATE SESSIONS

Topic A: Good decision practices for submission/review/recommendation by companies and agencies (Regulatory and HTA): What should be the characteristics/ attributes of a good decision framework?	**Chair: Prof Sir Alasdair Breckenridge** **Rapporteur: Mary Jo Pritza,** *Senior Director, Regulatory Affairs, Astellas Pharma Global Development, USA*
Topic B: Good decision practices for submission/review/recommendation by companies and agencies (Regulatory and HTA): How should good quality decision-making practices be measured?	**Chair: Barbara Sabourin**, *Director General, Therapeutics Products Directorate, Health Canada* **Rapporteur**: **Adrian Griffin**, *Vice President, Global HTA and Reimbursement Strategies, Johnson & Johnson, UK*
Topic C: Good decision practices for submission/review/recommendation by companies and agencies (Regulatory and HTA): What are the main challenges to good decision practices and what are the possible solutions?	**Chair**: **Prof John Skerritt**, Deputy Secretary for Regulatory Services, Department of Health, Canberra, Australia **Rapporteur: Dr James Leong,** *Centre of Regulatory Excellence, Duke-NUS Graduate Medical School Singapore*

SESSION: SYNDICATE FEEDBACK AND PERSPECTIVES

Chair introduction	**Prof Robert Peterson,** *Executive Director, Drug Safety Effectiveness Network, Canadian Institute of Health Research*

Feedback of syndicate discussion and participants viewpoint following each syndicate discussion

Stakeholder perspectives - Improving the quality of decision-making processes and practices

Patient perspectives	**Patricia Furlong**, *Founding President and CEO, Parent Project Muscular Dystrophy, USA*
Payer perspective	**Dr C Bernie Good,** *Professor of Medicine, and Pharmacy, Chief, Section of General Internal Medicine at the VA Pittsburgh Healthcare System (VAPHS)*
PCORI perspective	**Jean Slutsky,** *Chief Engagement and Dissemination Officer and Program Director for Communication and Dissemination Research, Patient-Centered Outcomes Research Institute (PCORI)**, USA*

Future perspectives: How should the quality of decision-making processes be measured?

Company perspective	**Karen Hauda,** *Senior. Director, Regulatory Policy, Novo Nordisk Inc, USA*
Policy and academic perspective- Singapore	**Professor John Lim,** *Deputy Director of Medical Services, Ministry of Health, Singapore and Executive Director, Centre of Regulatory Excellence, Duke-NUS Graduate Medical School, Singapore*
HTA agency perspective	**Dr Alan MacDonald,** *Vice-Chair of SMC and Chair of the SMC New Drugs Committee, Scottish Medicines Consortium*
Way forward – CIRS three-year plan	**Lawrence Liberti,** *Executive Director, CIRS*

SYNDICATE SESSION RECOMMENDATIONS

Topic A: What should the characteristics or attributes of a good decision framework be?

Chair: Prof Sir Alasdair Breckenridge **Rapporteur: Mary Jo Pritza,** Senior Director, Regulatory Affairs, Astellas Pharma Global Development, USA

Recommendations

A decision framework should employ the decision-making steps developed through the CIRS Quality of Decision Making Orientation Scheme (QoDOS).

- **Frame the process:** reach agreement on the decision context; describe roles clearly and assign responsibilities; understand the constraints including legal framework, financial and time
- **Identify and validate inputs:** employ scientific rigor especially in the examination of the integrity of information for validation and confidence in the decision; apply knowledge as it becomes available; and experience; Assign values and relative importance to weights; use an objective approach and maintain awareness of your biases and preferences; consider uncertainty throughout; examine alternative decision options
- **Commit to action:** consider consequences of decision to stakeholders; effectively communicate the basis of the decision; ensure transparency and audit trail

Topic B: How should good-quality decision-making practices be measured?

Chair: Barbara Sabourin, *Director General, Therapeutics Products Directorate, Health Canada* **Rapporteur**: **Adrian Griffin**, Vice President, Global HTA and Reimbursement Strategies, Johnson & Johnson, UK

Recommendations

- Companies and agencies should use established key performance indicators such as number of first-cycle approvals, achievement of pricing and reimbursement objectives, adherence to timelines
- Agencies should solicit qualitative feedback on understanding of decision from end users
- Companies and agencies should adhere to established quality management personnel practices such as training, maintained SOPs and knowledge management and recognise geographic cultural and functional diversity while minimising risk of bias and maximising ability to resolve differences
- Agencies should ensure that decisions, especially precedent-setting decisions can be transparently linked to evidence

Topic C: What are the main challenges to good decision practices and what are the possible solutions?

Chair: **Prof John Skerritt**, *TGA, Australia* **Rapporteur: Dr James Leong,** *Centre of Regulatory Excellence, Duke-NUS Graduate Medical School Singapore*

Recommendations

- To meet the challenge of strong decision makers who may be against new practices and cultural risk aversion: industry should bring in staff from other departments, assign cross functional responsibilities, agree on the use of a common framework and processes, collecting and addressing divisive opinions and conducting training, use external advisors and advisory committees.
- To meet the challenge of a lack of official guidelines for acceptable outcomes and standards and consistent robust practices and understanding by other key stakeholders: health technology assessment agencies should employ common terminology, offer flexibility of non-binary decisions, clearly indicate data used and uncertainties identified in decisions and employ education as needed.
- To meet the challenge of incorporating patient perspectives: regulatory agencies should encourage public forums to articulate the rationale for decisions; allow public and sponsors to comment during meetings; collate and share disease-level information among all stakeholders and define the involvement of patients within regulatory processes

PRESENTATION HIGHLIGHTS

BUILDING QUALITY INTO THE DECISION PROCESS: WHAT FRAMEWORKS ARE COMPANIES AND AGENCIES USING?

To provide a framework for discussions at this Workshop, CIRS undertook a focussed survey on current processes and practices within companies and regulatory agencies.

Scientific Director, CIRS, **Dr Neil McAuslane** reported the results of the survey which revealed companies' and agencies ' current decision-making processes and procedures, challenges and views regarding decision-making frameworks and methods for measuring the quality of the decision-making process.

Hurdles for making a good quality decision?

Company	Agency
• Excessive optimism: Overconfidence	• Lack of knowledge with regard to decision making concepts
• Poor assessment of uncertainty/strength of evidence	• Reluctance to discuss uncertainties/value judgments
• Internal misalignment: Competing interests	• Ensuring review or evaluation practices are consistent
• Previous experience biases	• Internal and external biases:
• Data /Information availability	• Data /Information availability
• Time pressure	• Resource Constraints: Time pressure

Some suggested solutions to the hurdles

- **Establish or implement a structured DM framework/** method that requires values/preferences/uncertainty to be made explicit
- **Education** on decision-making concepts/theory
- **Create an environment** that encourage dissenting opinions and challenging ideas
- **Ensure transparency** and information access
- **Have a robust system** which focuses on evidence and facts
- **Multistakeholder inclusion** - including patients
- **More formal review of decisions** (both positive and negative) and process

Responses received from 19 individuals in 17 companies and from 11 individuals from 9 agencies indicated that

- Companies and agencies were mixed as to whether their organisation's decision making was qualitative or quantitative and whether decisions were made by consensus or individuals.
- Formal decision-making frameworks are used at 65% of responding companies and 78% of agencies; formal benefit-risk frameworks are used at 59% of companies and 89% of agencies.

Action-oriented biases drive us to take action less thoughtfully than we should. *Interest biases* arise in the presence of conflicting and even purely emotional incentives. *Pattern-recognition biases* lead us to recognize patterns even where there are none. All respondents recognised action, interest or pattern decision-making biases within their organisation; however, only 41% of companies and 11% of agencies undertake formal assessments of decision-making quality.

Virtually all (100% company, 90% agency) participants agreed that the quality of decision making can be measured and 95% of company and 91% of agency participants felt that there was room for improvement for their organisation's decision-making processes.

From a free-text survey response:

". . . the value of quality decision making is not only just for the decision (and its implications), but to the effectiveness of teams, the productivity between teams and leadership, and to enforce a level of trust across the broader organisation"

FROM BENEFIT-RISK TO QUALITY DECISION MAKING: IMPROVING AGENCY AND COMPANY DECISION MAKING

The use of structured benefit-risk frameworks has resulted in improved decision-making processes at regulatory agencies such as the US FDA, Health Canada and EMA and at companies such as AstraZeneca and Novartis.

The FDA Center for Drug Evaluation and Research (CDER) identified the need for a more structured benefit-risk assessment in the review process to better communicate the reasoning behind CDER decisions; that is, which benefits and risks or other factors were considered, how the evidence was interpreted and how the benefits and risks were weighed and to ensure that the "big picture" is kept in mind during a complex, detailed review. Accordingly, as detailed by **Dr Richard Moscicki,** *Deputy Center Director for Science Operation, US Food and Drug Administration,* the CDER framework has been implemented in the review of new molecular entities for new drug and biologic license applications (NDAs; BLAs) and feedback from review teams has been favourable and moving forward, CDER will Implement the framework in new indications and other NDAs and BLAs.

At Health Canada, **Barbara Sabourin,** *Director General, Therapeutics Products Directorate*, reported that although the use of a more structured approach to assessing benefit risk and uncertainty has led to improvements in decision-making processes, these processes also include other elements such as good review practices, performance metrics, workflow systems and appropriate delegation.

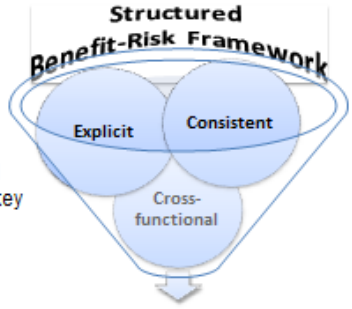
Structured frameworks that process incoming signals and information such as data, values, uncertainty and attitude toward risk will likely add transparency and predictability to evaluations; make value judgements explicit and are likely to ensure quality of a decision. **Prof Hans-Georg Eichler,** *Senior Medical Officer, EMA* explained that to obtain all the necessary information to make decisions, the EMA is facilitating the participation of patients and consumers in benefit-risk evaluation through such tactics as a recent feasibility study conducted among two patient groups and select EMA staff using decision conferencing and a questionnaire.

Exposure to the CIRS PhRMA Benefit-Risk Action Team (BRAT) framework has resulted in improved cross-functional decision making and the ability to deliver a structured safety assessment at AstraZeneca. **Dr Richard Hermann,** *Safety Scientist* said that early-project teams have voluntarily investigated how decision frameworks might help them in designing next-phase studies, Late-project teams are hoping to incorporate more structure into how they perform their public benefit-risk evaluation reports (PBERs).

Sharon Olmstead, *Global Head, Development and Regulatory Policy Novartis, USA* reported that cross-functional alignment has also been enhanced through use of a structured framework at Novartis, which also uses a form of the BRAT framework. This structured benefit-risk approach is currently used from submission to PSUR/PBRER for all new major products The company anticipates future opportunities in earlier development phases to apply a structured benefit-risk approach ahead of submission.

A structured benefit-risk framework enables good decision making

- Built on well-established decision analysis principles, promoting consistency, traceability, transparency and predictability by making value judgements explicit
- Provides a decision-making platform throughout the medicine life cycle including which benefit and risk outcome measures were considered and why and the magnitude of benefit and risk effects
- Helps with cross-functional alignment and decision making, enabling agreement on key messages and early management endorsement and promoting a consistent message internally and externally
- Acts as a communication tool for internal decision making and sponsor – health authority alignment, providing more transparent documentation of how efficacy ranks in comparison to risks



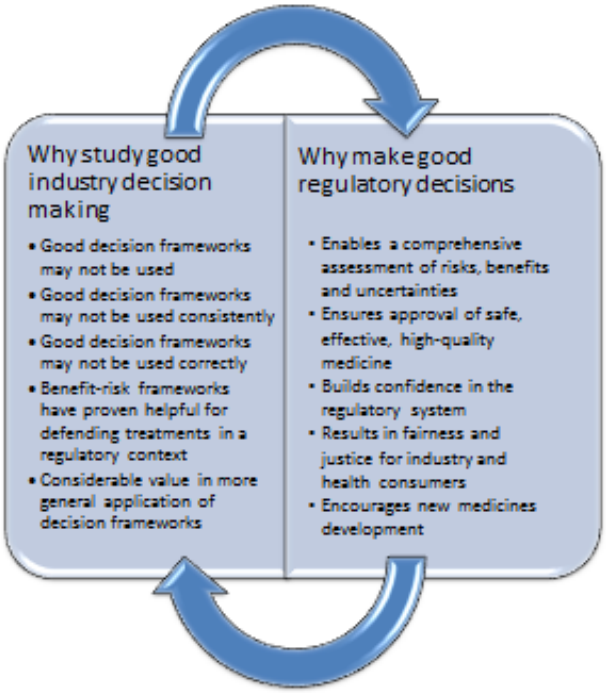
Good decision making

BEYOND BENEFIT-RISK FRAMEWORKS: BUILDING QUALITY INTO DECISION MAKING

Decision analysis frameworks are already being used in healthcare decision making. In recognition of the importance of quality decision making, companies and agencies are now advancing its study and practice to accommodate different types of structured frameworks.

Within industry, there is considerable motivation for studying organisational decision making because good decision-making approaches may not be used at all or may not be used consistently or correctly. **Dr Bennett Levitan,** Director, Janssen Research and Development, USA noted that benefit-risk frameworks have proven helpful for defending the rationale for treatments in a regulatory context and there is considerable value in the more general application of decision frameworks for industry decision making, but it must be determined, if a framework is required for all types of decisions. In one example of the application of a framework, Johnson and Johnson used a multi-criteria decision framework to justify consideration of a top-ranked indication for a new compound that had not been previously seriously considered.

Quality in regulatory decision making ensures that safe, effective and high-quality medicines are approved for the market and **Dr John Skerritt**, *Deputy Secretary for Regulatory Services, Department of Health, Canberra, Australia* reported that the Australian TGA uses multiple processes to ensure quality decision making such as separation of dossier evaluator from the decision maker, predictability in the process/ milestones, critical evaluation of clinical trial studies for quality in design; clear statements of regulatory rationale, use of guidance documents; peer review of component evaluations, training of evaluators, communities of practice and examination of conclusions. The Australian regulatory system relies on the decision of an individual and although there is significant input from stakeholders, formal consultations and internal and national review, different clinical backgrounds and perspectives by the decision makers, and varying emphasis on population versus individual patient benefits could influence consistency and quality of decisions.



Dr Lawrence Phillips, Emeritus Professor of Decision Sciences, London School of Economics and Political Science, UK presented sample applications of decision analysis frameworks in healthcare decision making.

- A Bayesian belief network was used to challenge the accepted maximum PH value that rules out lung intubation in the placement of nasogastric tubes in adults. Bayesian belief network values include that it translates data into knowledge, captures uncertainty about cause-effect relationships and uncertainty in the data and includes interactions among events.
- Decision tree analysis was used to decide whether to approve a vaccine with inadequate safety data in the 2009 European H1N1 influenza virus pandemic. Decision tree values include that it enables alternative assumptions about future events and reactions to them to be tested and focuses thinking on only those events that are important to the consequences.
- Multi-criteria decision analysis was used to rank 20 psychoactive substances according to harms to users and harms to others through facilitated workshop. MCDA values include that it provides a common unit for expressing the value of data, incorporates judged trade-off weights equalling preference values across the criteria and clearly distinguishes data from judgements about the data.

CHALLENGES AND OPPORTUNITIES WITHIN CURRENT PRACTICES AND PROCESSES

Companies and agencies currently employ multiple processes and procedures for quality decision making; the success of the outcomes of those decisions may depend on stakeholder perspective.

As outlined by **Dr Joseph Scheeren,** Head, Global Regulatory Affairs Pharma and Consumer Care, Bayer Consumer Care, Switzerland, decision making at Bayer is accomplished through use of a wide variety of stakeholder perspectives. The Global Product Development Committee, the decision-making body for all project and portfolio decisions comprises representatives from strategic, marketing and R&D departments. In addition, continuous patient involvement facilitates an environment for developing better drugs, improving therapeutic compliance, and ensuring the most efficient use of development resources and a medical and regulatory governance framework ensures the right medical and regulatory decisions are made by the right persons according to the right standard. Finally, benefit-risk profiles are developed for all development products to facilitate decision making

Prof Dr Hans Hillege, Alternate Member, Committee for Medicinal Products for Human Use (CHMP), Medicines Evaluation Board, the Netherlands discussed The European Medicines Agency (EMA) initiative to develop a standardised framework for benefit-risk assessment, which began in 2009. The EMA integrated the results from research and field tests in this area to develop a methodology that can accommodate the needs of the various National Competent Authorities and the CHMP. The two main decision-making tools to emerge from this research are the qualitative Effects Table, which is currently being generally implemented in EMA templates and the quantitative multi-criteria decision analysis, which may be used as required while taking into consideration the complexity of this process. Developing quantitative methods that are both theoretically sound and easy to use by decision makers; however, has proven to be far from straightforward and the ultimate aim will be to arrive at methodologies that allow regulators to simultaneously explore imprecision in the preference statements and uncertainty in effect size estimates and long-term clinical consequence.

The Canadian Agency for Drugs and Technologies in Health (CADTH) employs multiple processes and procedures to ensure the quality of its decision making including publicly available procedure documents; consistency across different types of reviews; engagement with customers and stakeholders; timeliness; a clear critical path and the provision of sufficient time for each step of decision making. **Dr Chander Sehgal,** Director, Common Drug Review (CDR) and Optimal Use, CADTH reported that the CADTH advisory body, the Canadian Drug Expert Committee (CDEC) employs a detailed deliberative framework to aid in their decision processes. CDEC deliberations include: patient group input, clinical studies demonstrating safety and efficacy compared with alternatives. therapeutic advantages and disadvantages relative to current therapy. and cost and cost-effectiveness relative to current accepted therapy. The CDEC public member focuses on patient input to provide context for deliberating the clinical and economic evidence and the other two discussants present reports on the clinical and pharmacoeconomic evidence. After deliberation and clinical input as required, CDEC votes on a recommendation to CADTH and provides a rationale for that recommendation.

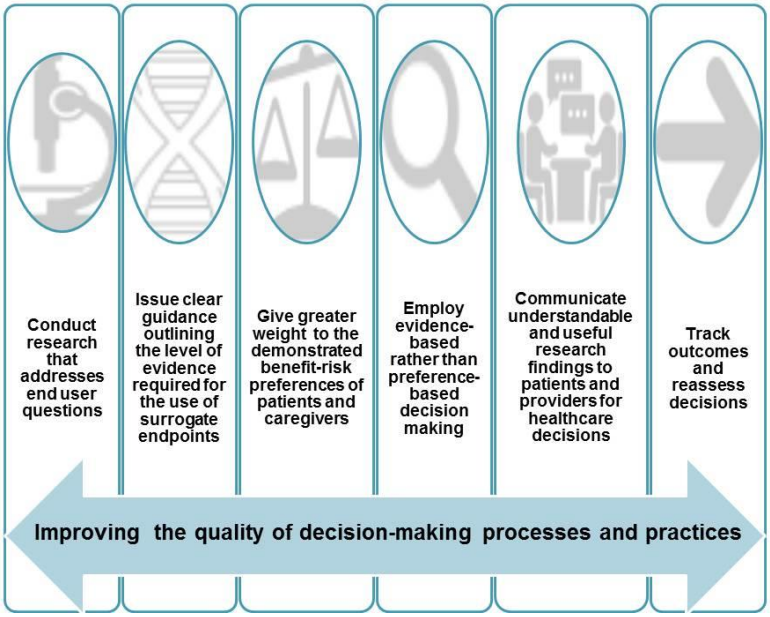
Decision-making characteristics from individual industry, regulatory and HTA perspectives

Characteristic	Industry: Bayer	Regulatory: EMA	HTA: CADTH
Transparency	Publicly available process	Publicly available process; publish EPARS; voting process private	Publicly available process; voting process private
Tools	Medical regulatory governance framework; benefit-risk workshops, templates, follow benefit-risk guidance	PROACT- URL Framework; Effects Table; MCDA (future)	CDEC deliberative framework
Stakeholder engagement	Milestones decided at the Global Product Development Committee includes representatives from business, research and development; Involve patients continuously from the early stages of drug development	Patient engagement programme; scientific advice programme including pilot for joint HTA scientific advice	Opportunity for industry and patient input; fee for service scientific advice

STAKEHOLDER PERSPECTIVES - IMPROVING THE QUALITY OF DECISION MAKING PROCESSES AND PRACTICES

Patients, payers, clinicians and their advocates have assumed an active role in the development of processes and guidelines for the evaluation of new medicines.

Patricia Furlong, Founding President and CEO, Parent Project Muscular Dystrophy (PPMD), USA provided two examples of PPMD efforts to change industry and regulatory decision-making processes and decisions. 1) To promote patient-centered drug development in the area of Duchenne Muscular Dystrophy (DMD), PPMD conducted a national survey caregivers of a child with DMD utilising best-worst scaling to quantify treatment preferences. The plan for next steps in this project include a treatment preference study in teens and adults with DMD, and clinicians treating DMD; extending studies to European populations; an increased focus on defining meaningful benefits; understanding tolerance for uncertainty in benefits and presenting risks as probabilities and using these studies as a model for community engagement and informing regulators of preferences. 2) As part of planned FDA engagement to demonstrate the PPMD approach as a model for advocacy-academia partnerships in promoting patient-centered drug development, PPMD developed draft FDA guidance for DMD to industry using a Steering Committee, working groups and an Advisory Committee and a professional writer. The guidance was submitted to the FDA and elements of this document were incorporated into draft guidance released by the FDA 9 June 2015.



The US Veterans Administration (VA) like all large healthcare systems, must often make decisions based on less than ideal evidence base. **Dr C Bernie Good,** Professor of Medicine, and Pharmacy, Chief, Section of General Internal Medicine at the VA Pittsburgh Healthcare System explained, however that in the absence of better comparative effectiveness data, the VA seeks to perform its own internal comparative effectiveness research to evaluate its decisions, and make adjustments when indicated. Once a decision is made, it is key for the agency to leverage its electronic medical records to track outcome and assess decisions and perform other assessments, such as national Medication Use Evaluations. The VA calls for more collaboration of large healthcare organisations to collect outcomes data, perform comparative effectiveness research.

The Patient-Centered Outcomes Research Institute (PCORI) is an independent research institute authorised by the US Congress in 2010 and governed by a 21-member Board of Governors representing the entire healthcare community. **Jean Slutsky,** Chief Engagement and Dissemination Officer and Program Director for Communication and Dissemination Research, PCORI USA said that PCORI funds comparative clinical effectiveness research that engages patients and other stakeholders throughout the research process and seeks answers to real-world questions about what works best for patients based on their circumstances and concerns. PCORI has a mandate to conduct a peer review of primary research and make its findings available to clinicians, patients and the general public in a comprehensible and useful format, thus enabling healthcare decisions.

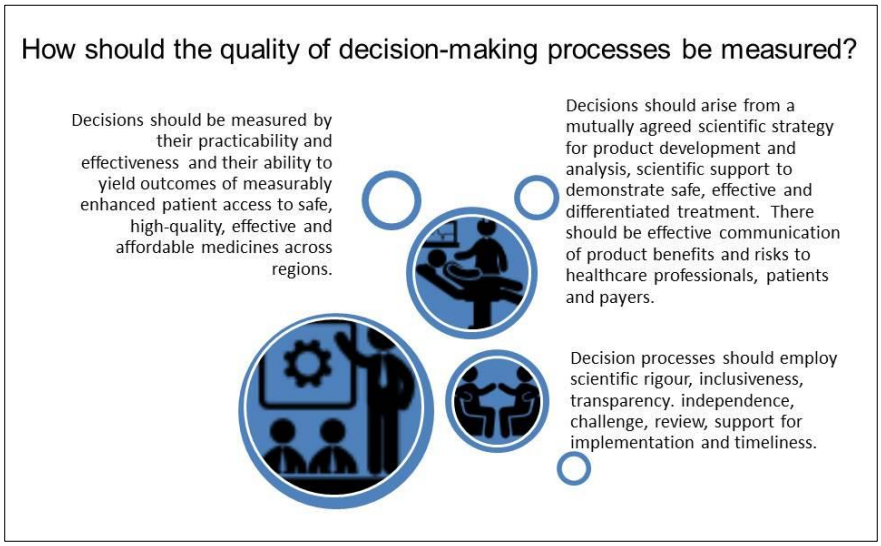
FUTURE PERSPECTIVES: HOW SHOULD THE QUALITY OF DECISION-MAKING PROCESSES BE MEASURED?

Decision-making at companies, academic institutions and health technology assessment agencies can be judged based on adherence to mutually agreed scientific strategies and supported through robust scientific evidence and is required to be consistent, practical, effective, transparent, independent, inclusive and timely and have support for implementation.

At Novo Nordisk, it is believed that a benefit-risk profile should be constructed by relevant divisions within the organisation and facilitated by process experts in Industry and agencies. Importantly, however, this profile should also be built through the development of patient-reported outcomes with help from caregivers and society to improve the value of the product for patients. **Karen Hauda,** Senior. Director, Regulatory Policy, Novo Nordisk Inc, USA said that early benefit-risk evaluation for company-developed products allows for critical evaluation of endpoints to tailor clinical trials and decision making regarding optimal product labelling. The success of effective decision making for new medicines can be determined through critical factors including a mutually agreed scientific strategy for product development and analysis, scientific support to demonstrate safe, effective and differentiated treatment and effective communication of product benefits and risks to healthcare professionals, patients and payers.

Professor John Lim, Executive Director, Centre of Regulatory Excellence, Duke-NUS; Deputy Director of Medical Services, Ministry of Health, Singapore posited that the quality of decision making from a systems perspective should be measured not only by consistency and scientific robustness of decisions, but also by practicability and effectiveness. Decisions should yield outcomes of measurably enhanced patient access to safe, high-quality, effective and affordable medicines across regions. However, the quality of decisions depends on available tools, frameworks and standards. Currently, existing problems and gaps in the regulatory system include divergence and fragmentation of regulatory processes within and across regions and silos poor communication amongst various stakeholders. Neutral academic platforms such as the Centre for Regulatory Excellence (CORS) at Duke-NUS Graduate School, Singapore could convene key stakeholders to candidly discuss and propose realistic, robust systems and policy solutions. CORE champions convergence and collaboration across Asia, promoting regulatory innovation and research and providing training to build regulatory competencies and develop regulatory leadership.

At the Scottish Medicines Consortium, quality is measured by the procedural principles of the National Institute for Health and Care Excellence (NICE). **Dr Alan MacDonald,** Vice-Chair of SMC and Chair of the SMC New Drugs Committee, Scottish Medicines Consortium reports that at SMC, binary decision making is practiced in which comparative clinical and cost effectiveness are considered rather than benefit-risk. Recent SMC changes include the implementation of the Patient and Clinician Engagement (PACE) initiative, the aim of which is to describe the added benefits of the medicine, from both patient and clinician perspectives, which may not be fully captured within the conventional clinical and economic consideration. Multiple challenges to quality decision making remain ongoing; however, including a political context in which quality of process may be measured against "desired" outcomes, questions of true transparency surround public meetings and the need for increased flexibility in decision making may stand in opposition to the need for greater structure in the weighting of subjective criteria.



FROM BENEFIT-RISK FRAMEWORKS TO QUALITY DECISION MAKING: THE CIRS 3-YEAR PLAN

As the discussion of benefit-risk evaluation has evolved among all healthcare stakeholders, the Centre for Innovation in Regulatory Science has developed a long-term strategy to encompass quality decision making

CIRS founder, **Professor Stuart Walker** detailed some of the currently available methodologies for the benefit-risk evaluation of medicines include the CIRS Universal Methodology for Benefit-Risk Assessment, an eight-step framework accompanied by a documentation system, which has been found to be fit for purpose by over a dozen international regulatory agencies.

In response to stakeholder recommendations, CIRS is currently broadening its programme of benefit-risk evaluation to include the assessment of quality decision making and CIRS Workshop participants have already suggested attributes of a good decision framework.

The 3-year CIRS strategy for its work in quality decision making has already been initiated including the identification of current practices through tactics such as the conduct of a stakeholder survey and Workshop and the development of the Quality of Decision Making Scheme (QoDOS) draft framework for good decision making and will continue with the validation of QoDOS and the implementation of a programme of advocacy for best practices.

CIRS Executive Director, Lawrence Liberti confirmed that in the implementation of this programme, CIRS is acting on the advice of its Scientific Advisory Council and employing its organisational strengths of experience, neutrality, advocacy and international presence as well as its extensive data repository to embark on a three-year programme for quality decision making.

The aims of the programme are to develop the general principles of a good decision framework, identify processes and practices that build quality into decision making within drug development, the regulatory review and health technology assessment. It is envisioned that the programme will help companies and agencies develop an understanding of how alongside the establishment of decision frameworks such as benefit-risk, other considerations may impede or enable good decision making within their respective organisations. The identification of the principles of a good decision-making framework will enable companies and agencies to embed these into their decision-making processes; develop a structured, systematic approach and documentation system and categorise markers or measures of the process that can be assessed.

The programme represents an evolution of the work of CIRS Workshops, research and publications in benefit-risk, patient involvement in decision making, the Balanced Quality Scorecard system for agencies and companies, good review practice in APEC jurisdictions and participation in the drafting of good review practices by the World Health Organization. It will also continue the work of Dr Ronan Donelan through doctoral research validating the Quality of Decision Making Orientation Scheme (QoDOS).

Attributes of a good decision framework

Potential Attributes	Benefits
Structure , Clarity, Consistency	Allows comparison between decision in comparable situations/products and review/challenge of the decision by others
Clear Roles and Responsibilities	Clear decision makers and advisors/contributors, encompasses debate, a range of perspectives
Efficiency and Effectiveness	Timely, provides benefit to those in receipt of decision
Constraints, Biases and Context	Identifies uncertainties, biases, limitations, subjectivity/ objectivity context and rationale of the decision or question being asked Human factor in decision making
Transparent	Allowing confidence with the decision and trust of the decision maker
Considers impact	Consider impact to a range of stakeholders, is forward looking and acknowledges the potential need to revisit decisions over the life cycle continuum
Helps range of stakeholders	Other reviewers, other agencies, sponsors, competitors, payers, physicians, patients, public citizens

From Syndicate recommendations CIRS Workshop, Beijing, 2013

WORKSHOP ATTENDEES

Regulatory agencies

Prof Sir Alasdair Breckenridge	Former Chairman	Medicines and Healthcare Products Regulatory Agency, UK
Dr Sara Eggers	Operations Research Analyst	Food and Drug Administration, USA
Prof Hans-Georg Eichler	Senior Medical Officer	European Medicines Agency
Soujanya Giambone	Operations Research Analyst, Office of Program and Strategic Analysis, CDER	Food and Drug Administration, USA
Prof Dr Hans Hillege	Alternate CHMP Member	Medicines Evaluation Board, The Netherlands
Dr Sandra Kweder	Deputy Director, Office of New Drugs, CDER	Food and Drug Administration, USA
Dr Richard Moscicki	Deputy Center Director of Science Operations, CDER	Food and Drug Administration, USA
Barbara Sabourin	Director General	Therapeutic Products Directorate, Health Canada
Dr Helen Sile	Medical Officer, Guidance and Policy Team – OND-IO, CDER	Food and Drug Administration, USA
Prof John Skerritt	National Manager	Therapeutic Goods Administration, Australia
Graham Thompson	Operations Research Analyst	Food and Drug Administration, USA
Hong Yang	Biologist	Food and Drug Administration, USA

Patient-centred organisations

Patricia Furlong	President	Parent Project Muscular Dystrophy, USA
Jean Slutsky	Chief Engagement and Dissemination Officer and Program Director for Communication and Dissemination Research	Patient-Centered Outcomes Research Institute (PCORI), USA
Durhane Wong-Rieger	President and CEO	Canadian Organization for Rare Disorders

Academic institutions

Dr Mamoru Narukawa	Associate Professor	Kitasato University Graduate School of Pharmaceutical Sciences, Japan
Dr James Leong	Head of Education	Centre of Regulatory Excellence, Duke-NUS Graduate Medical School Singapore
Prof John Lim	Deputy Director of Medical Services and Executive Director, Centre of Regulatory Excellence	Ministry of Health, Singapore and Duke-NUS Graduate Medical School, Singapore
Prof Larry Phillips	Emeritus Professor of Decision Sciences	London School of Economics and Political Science, UK

Health technology assessment and reimbursement agencies

Dr Alan MacDonald	Vice Chairman	Scottish Medicines Consortium, UK
Prof Robert Peterson	Executive Director, Drug Safety Effectiveness Network	Canadian Institute of Health Research
Dr Chester "Bernie" Good	Chairperson, Medical Advisory Panel for Pharmacy Benefits Management	Department of Veterans Affairs, VA Pittsburgh, USA
Dr Chander Sehgal	Director, CDR and Optimal Use of Drugs	Canadian Agency for Drugs and Technologies in Health

Pharmaceutical companies

Stephane Andre	Head of EU/International Regulatory Affairs / Product Development Regulatory	F.Hoffmann-La Roche, Switzerland
Randal Batenhorst	Vice President, Global Regulatory Affairs Therapeutic Groups / Labelling	GlaxoSmithKline, USA
Gary Bloomgren	Vice President, SABR	Biogen, USA
Sjaak Bot	Head of EMEA Regulatory Affairs	Janssen Biologics B.V., The Netherlands
Linda Bowen	Head of US Regulatory Policy and Intelligence	Sanofi, USA
Dr George Butler	President	Regaff Inc, USA
Carlos Garner	Senior Director, Global Regulatory Affairs	Eli Lilly and Company, USA
Adrian Griffin	**Vice President, Global HTA and Reimbursement Strategies**	**Johnson & Johnson, UK**
Dr David Guez	R&D Special Projects Director	Institut de Recherches Internationales Servier, France
Benjamin Gutierrez	Senior Director, Value Evidence and Outcomes	GlaxoSmithKline, USA
Thomas Harris	Senior Vice President, Global Regulatory Affairs	Takeda Pharmaceuticals, USA
Karen Hauda	Senior Director, Regulatory Policy	Novo Nordisk Inc, USA
Dr Richard Hermann	Safety Science Physician	AstraZeneca, USA
Dr David Jefferys	Senior Vice President, Global Regulatory, Government Relations, Public Affairs and European Product Safety	Eisai Europe Ltd, UK
Eva Katz	Associate Director	Janssen Research and Development, USA
Dr Margaret Kreider	Senior Director, Global Regulatory Affairs	GlaxoSmithKline, USA
Dr Bennett Levitan	Senior Director, Epidemiology	Janssen Research & Development, USA
Dr Steven Miller	Vice President	Janssen Research and Development, USA
Howard Moy	Director, Market Access	Sanofi, USA
Allison Nance	Executive Director, Global Regulatory Affairs	Celgene Corporation, USA
Sharon Olmstead	Global Head, Development and Regulatory Policy	Novartis Pharmaceuticals Corp, USA
Dr Roopal Thakkar	Vice President, Regulatory Affairs	AbbVie, USA
Alan Poirier	Director, Regulatory Policy and Global Intelligence	Pfizer, USA
Mary Jo Pritza	Senior Director, Regulatory Affairs	Astellas Pharma Global Development, USA
Ronald Robison	Vice President, Regulatory Affairs, Quality and Patient Safety	AbbVie, USA
Dr Joseph Scheeren	Head, Global Regulatory Affairs Pharma and Consumer Care	Bayer Healthcare AG, Switzerland
Brian Schlag	Senior Director, Group Leader, Global Regulatory Affairs	Actelion, USA
Wan Tsong	Director – Market Access Product Lead	Eisai Inc, USA
Karen Weiss	Vice President	Janssen Pharmaceuticals, USA
Gergana Zlateva	Payer Insights & Access, North America Cluster Lead	Pfizer Inc, USA

Centre for Innovation in Regulatory Science

Madga Bujar	Research Analyst
Patricia Connelly	Manager, Communications
Lawrence Liberti	Executive Director
Dr Neil McAuslane	Director
Prisha Patel	Manager, Global Development Programme
Professor Stuart Walker	Founder
Tina Wang	Portfolio Manager, HTA Programme