Building Quality into Decision-Making Processes in Medicines' Development, Regulatory Review and Health Technology Assessment

Transparency • Predictability • Consistency

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R&D BRIEFING 61

CIRS Centre for Innovation in Regulatory Science

Background to quality decision making

"*An organisation that seeks to improve its productivity should also routinely measure the quality of its decision making*" (From Thinking Fast and Slow, Kahneman, 2011)

The various decisions made by pharmaceutical companies, regulatory authorities and health technology assessment (HTA) agencies throughout the life cycle of medicines are critical for ensuring that appropriately safe and effective medicines become available in a timely and efficient manner. Despite this, there is a paucity of research into the quality aspect of decision making in medicines' research and development.

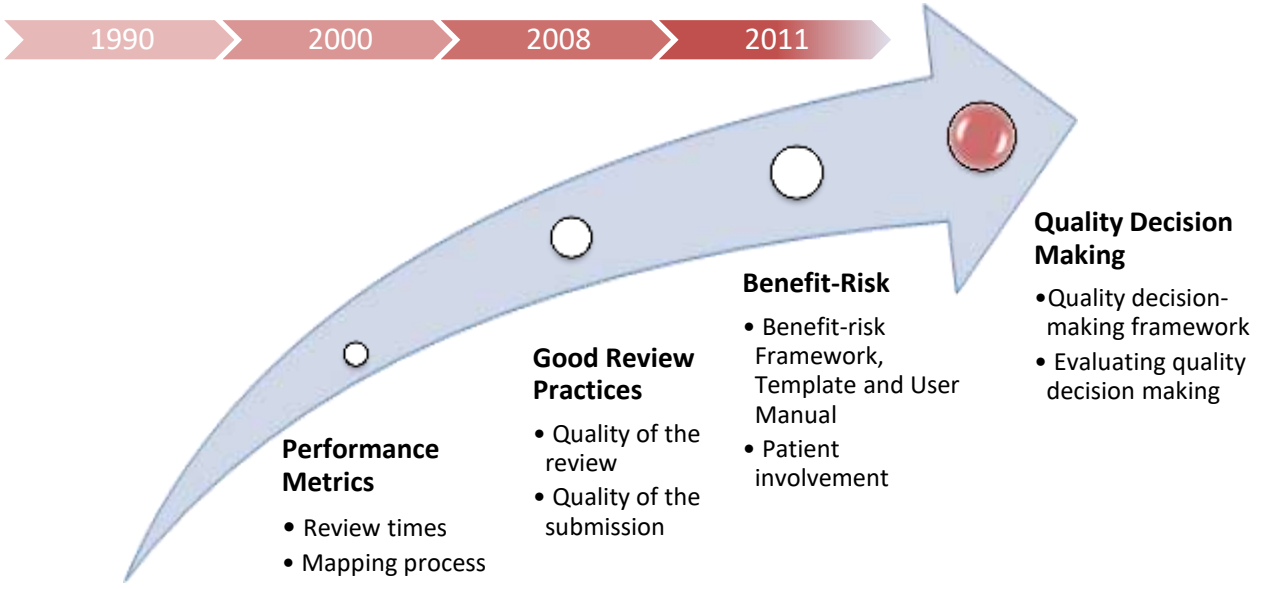
At a Centre for Innovation in Regulatory Science (CIRS) Workshop in 2004, Professor Larry Phillips, a Professor of Decision Analysis at the London School of Economics, discussed the "science of decision making" saying that ". . . In an uncertain world, it is perfectly possible to make a good decision that has poor consequences and, equally, to make a bad decision and come up with a good outcome. On balance, however, the long-running use of good systems for making decisions will generally give better outcomes."

In addition, recent CIRS Workshop participants have recommended that the quality of the decision-making processes for these functions be considered separately from the decisions themselves.

"Delinking the regulatory review process from the process of making decisions should be explored. Although the quality of decision making is of equal importance to the quality of review process and procedure, methods for enhancing and measuring that quality have yet to be outlined." (Recommendation from CIRS Emerging Markets Workshop December 2011)

"Explicitly explore quality in decision making separately from the quality of submissions and reviews and develop or identify an instrument to be used to assess the robustness of deliberative processes within HTA agencies" (Recommendation from CIRS HTA Workshop December 2013)

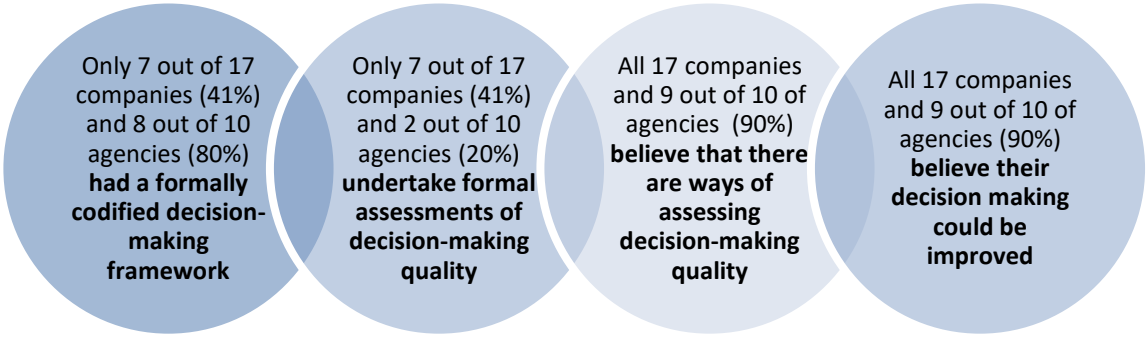
As a consequence, CIRS initiated a programme that aims to address the research gap in quality decision making in the area of medicines' development, review and HTA assessment. This programme represents a natural evolution of CIRS work in performance metrics, good review practices and benefit-risk assessment. The overall aim is to develop a quality decision framework and evaluate quality decision-making practices in order to identify markers that build quality into decision making throughout medicines' development, regulatory review and reimbursement.



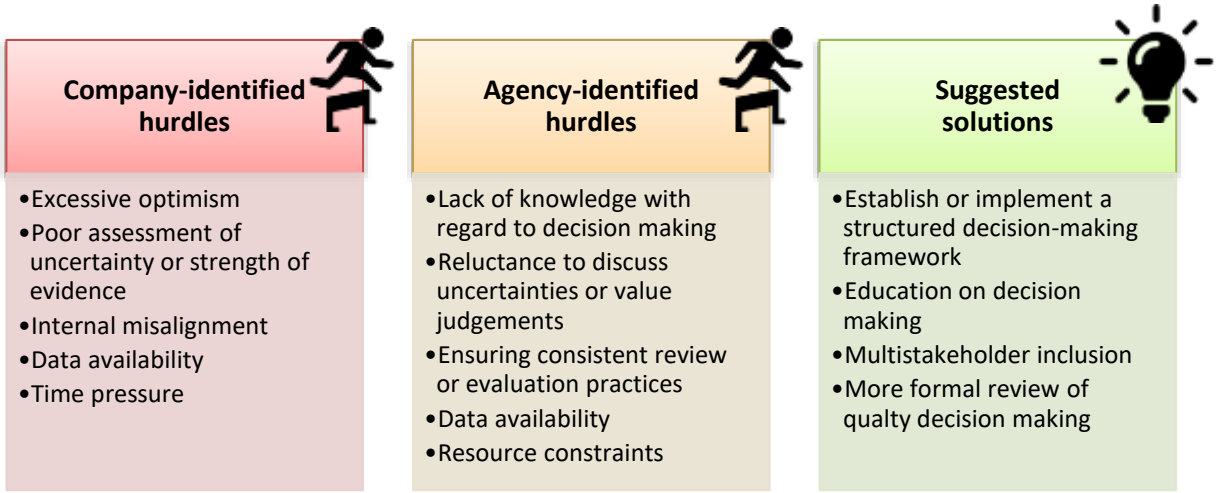
Background to quality decision making

As part of its programme in quality decision making, *in 2015, CIRS conducted a study among 17 pharmaceutical companies and 10 regulatory agencies* to identify current decision-making practices used by companies' in their decision to submit and by agencies' in their decision to approve a new drug application. It also looked to ascertain how they measure the quality of the decision-making process and the challenges and solutions[1].

Key results from the questionnaire indicated that:



Moreover, the majority of company and agency participants identified instances of decision-making biases within their organisation. *Other hurdles by companies and agencies to quality decision quality decision making, as well as suggested solutions are listed below:*



The study results demonstrated that the quality of decision making is influenced by the processes and procedures within companies and agencies. Organisations believe their decision making could be improved and the first step to achieve this, which CIRS has already initiated, would be to assess current practices and evaluate the quality of decision making within regulatory and HTA agencies as well as pharmaceutical companies. In addition, CIRS will be conducting a similar questionnaire to the above, but amongst HTA agencies and pharmaceutical companies to explore quality decision making in the area of medicines' reimbursement.

[1] Bujar M, McAuslane N, Salek S, Walker S. Quality of regulatory decision-making practices: issues facing companies and agencies. *Ther Inn Reg Sci.* 2016;DOI: 10.1177/2168479016628573.

Development of the 10 Quality Decision-Making Practices

In order to investigate and identify the important issues that influence quality decision making, semi-structured interviews were carried out with 29 key opinion leaders from regulatory agencies and pharmaceutical companies[2]. The study participants were invited to discuss and review their perception of decision making within their organisation, its role in drug development and regulatory review, their awareness and use of decision-making techniques and the impact and monitoring of decisions. The analyses resulted in the identification of a number of overarching themes in quality decision making, which are exemplified below with quotations from interviewees.

Theme 1

*"There is a difference between the **organisational decision-making process and that of the individual.** We have a good understanding of how a committee makes a decision, but we do not necessarily understand how individuals on that committee have made their own decision"* Regulatory agency

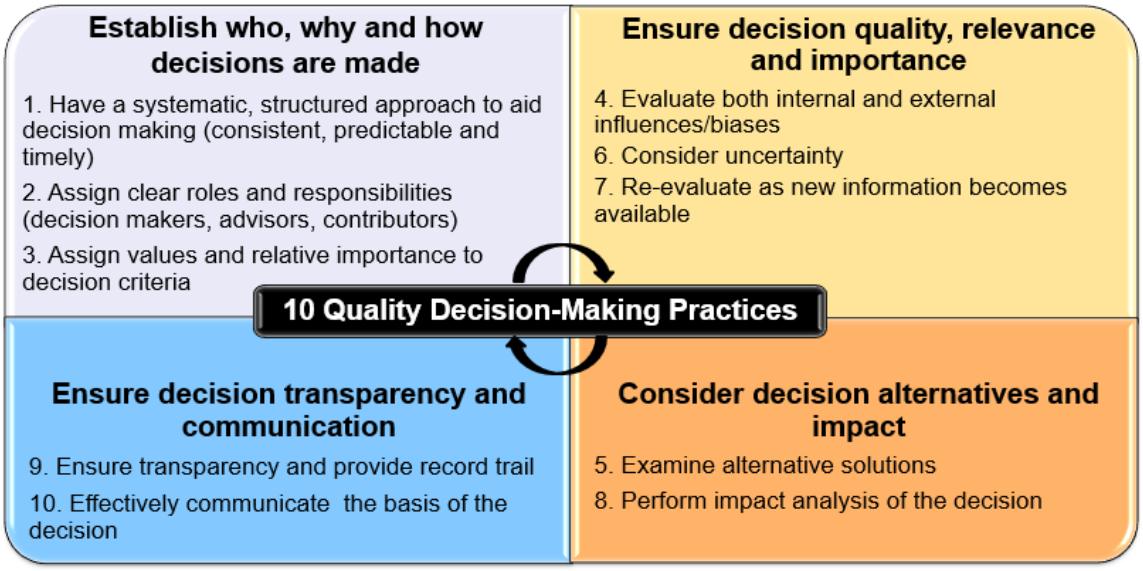
Theme 2

*"Transparency, the justification for decisions, and **understanding why a decision has been made need to be documented**, it is good practice"* Regulatory agency

Theme 3

*"**It is important that we are trained in decision making.** We also need an understanding and practical application of the tools which can assist our decision making"* Pharmaceutical company

A major outcome of this study has also been the identification of the *10 Quality Decision-Making Practices (QDMPs)* that underpin a quality process and that were considered as relevant by both pharmaceutical companies and regulatory agencies. This set of holistic practices can be mapped against the key frameworks used during medicines' development, particularly in the area of benefit-risk assessment as well as the science of decision making. The 10 QDMPs are organized into four areas, namely, 'Establish who, why and how decisions are made', ' Ensure decision quality, relevance and importance', 'Consider decision alternatives and impact' and 'Ensure decision transparency and communication'.



[2] Donelan R, Walker S, Salek S. Factors influencing quality decision-making: regulatory and pharmaceutical industry perspectives. *Pharmacoepidemiol Drug Saf*. 2015;24: 319-328.

Development of the 10 Quality Decision-Making Practices

As a result of the discussion from CIRS Workshops in June 2015 and February 2016[3], the following Guidance Notes were produced to describe the 10 QDMPs in more detail.

QDMP 1. Have a systematic, structured approach to aid decision making (consistent, predictable and timely)

- *Establish the decision context, objectives and assumptions made.*
- *Employ frameworks, guidelines and tools for structuring the decision-making process.*
- *Such an approach should ensure that the process is systematic, which in turn would enable better consistency compared with similar past decisions, as well as predictability and timeliness.*

QDMP 2. Assign clear roles and responsibilities (decision makers, advisors, information providers)

- *The roles and responsibilities should be clearly defined in terms of individuals who provide information (including external input), compared with those who advise on the decision or make the final decision.*
- *The roles and responsibilities of each stakeholder (regulatory authorities, HTA agencies and companies) should be transparent and well communicated, which should help manage expectations.*

QDMP 3. Assign values and relative importance to decision criteria

- *The relevant criteria for the decision must be determined to ensure that these are in line with the decision context and overall objective. The criteria should be weighted, for example, by ranking or rating their relative importance.*

QDMP 4. Evaluate both internal and external influences/biases

- *Stakeholders need to be aware of personal considerations, subjective influences and biases, acknowledge them and minimise where possible. Potential biases that need to be considered[4]:*
  - *Action-oriented bias: excessive optimism, overconfidence in own judgement and gut-feeling*
  - *Interest-oriented bias: inappropriate attachments and misaligned incentives*
  - *Pattern recognition: generalising based on recent events and seeking out information that supports a favoured decision, which could lead to perpetuating previous mistakes*
  - *Stability bias: preference for status quo and tendency for inertia in the presence of uncertainty*

QDMP 5. Examine alternative solutions

- *Decision makers should actively explore possible options during the decision-making process.*
- *The alternatives need to be assessed, for example using a SWOT analysis, against the relevant decision criteria in order to determine the best outcome.*

QDMP 6. Consider uncertainty

- *The extent and limitations of available information need to be judged for each decision criterion in relation to the alternative options.*
- *Stakeholders must be explicit regarding acceptability of benefits and harms and how this affects their approach.*

QDMP 7. Re-evaluate as new information becomes available

- *This should be actively carried out at all stages during the lifecycle of medicines' development.*
- *This may be a safeguard against plunging in or procrastination and/or perpetuating previous mistakes as well as identifying cultural/organisational/hierarchical influences (e.g. individual vs. organisational, group successes and group failures).*

QDMP 8. Perform impact analysis of the decision

- *The impact of the decision needs to be considered on both internal and external stakeholders.*
- *The analysis must relate to present situation, but also to the future and should take into account elements of quality/validity of data, political/financial/competitor influences and procedures for similar decisions.*

QDMP 9. Ensure transparency and provide a record trail

- *It must be clear how the decision was made and details must be consistently documented in a manner that can be easily followed or audited by appropriate stakeholders.*

QDMP 10. Effectively communicate the basis of the decision

- *The basis of the decision needs to be appropriately communicated to the relevant stakeholders, both internally and externally.*

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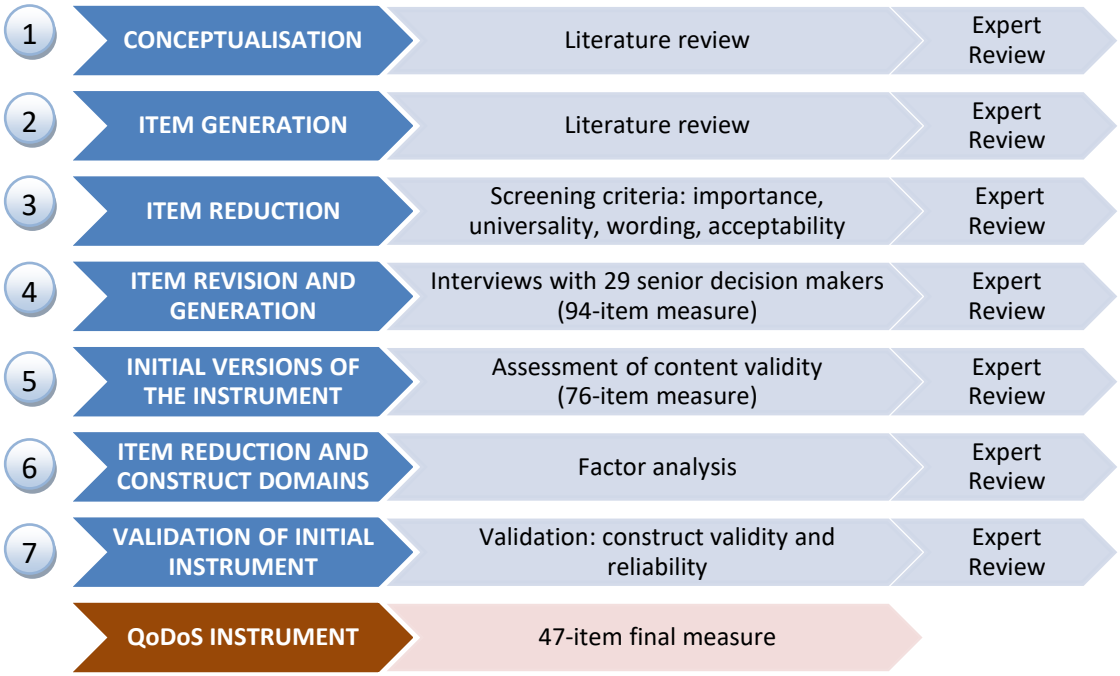
[3] The Centre for Innovation in Regulatory Science. *Publications*. Available at: http://www.cirsci.org/past-workshops-and-publications/

[4] Lovallo D, Sibony O. *The case of behavioral strategy*. McKinsey Quarterly. Available at: http://www.mckinsey.com/insights/ strategy/ the_case_for_behavioral_strategy.

Development of the Quality of Decision-Making Orientations Scheme

Recognising the importance of quality of decision making as well as the paucity of information and available instruments, CIRS in collaboration with Cardiff University, initiated a study to develop and validate an instrument for evaluating quality of decision making[5]. This collaboration is now being continued with the University of Hertfordshire. The instrument, named the Quality of Decision-Making Orientation Scheme (QoDoS) was developed and validated using a standardised approach and qualitative as well as quantitative techniques. A flowchart representing the stages in the development of the QoDoS is shown below.



The QoDoS items were generated from 29 face-to-face semi-structured interviews with key opinion leaders from the pharmaceutical industry (n=10), contract research organisations (n=10) and regulatory agencies (n=9). The thematic analysis yielded a 94-item initial version of the QoDoS with a five-point Likert frequency scale response option.

Content validity was established using an expert panel to confirm that the emphasis and the focus of the QoDoS is fit-for-purpose. The experts rated the language clarity, completeness, relevance and scaling of each item on a four-point scale (Strongly agree, agree, disagree and strongly disagree) and the agreement among the panel members was high with an intra-class correlation coefficient value of 0.89 (95% confidence interval = 0.056, 0.99).

Factor analysis was performed on the resulting 76-item instrument and produced a *47-item measure (QoDoS)* organised into four sections namely, organisational decision-making approaches, organisational decision-making culture, individual decision making competencies and individual decision-making style.

The 47-item QoDoS showed high internal consistency (n = 120, Cronbach's alpha = 0.89), high reproducibility (n = 20, intra-class correlation = 0.77) and a mean completion time of 10 minutes. This suggests that the QoDoS is a practical instrument possessing strong psychometric properties of validity and reliability. Moreover, the QoDoS items can be mapped according to the 10 Quality Decision Making-Practices (page 4) and consequently, the degree of incorporation of these 10 QDMPs into agency and company processes can be evaluated. The full instrument is shown on pages 7 and 8.

[5] Donelan R, Walker S, Salek S. The development and validation of a generic instrument, QoDoS, for assessing the quality of decision making. *Frontiers Pharmaceutical Medicine and Outcome Research*. 2016; 7: 180.

The QoDoS instrument for evaluating quality decision making

The Quality of Decision-Making Orientation Scheme (QoDoS) ©

The statements in the questionnaire relate to your views on your personal and your organisation's *decision-making processes for major strategic choices within your organisation.*

Please mark clearly one box for each statement. Assume that Not at all = 0% of time; Sometimes = 25% of time; Frequently = 50% of time; Often = 75% of time; Always = 100% of time. If not sure, please tick the box that you feel is the most appropriate.

No data that will identify an individual or an organisation will be reported, or details made to a third party.

Background questions

Gender: ☐ Male ☐ Female ☐ Other

Job title: _____

How many years of professional experience have you to date? _____

Organisation: ☐ Regulatory Agency ☐ Pharmaceutical Industry ☐ HTA ☐ Academia ☐ Other

Part I: Organisational-level influences

	Not at all	Sometimes	Frequently	Often	Always	Not applicable
A. Decision-Making Approach						
1. My organisation evaluates the impact of the decisions it makes						
2. My organisation's decision making is transparent						
3. My organisation's decision making is consistent						
4. My organisation uses a structured approach in its decision making						
5. My organisation's decision making is influenced by external stakeholder's demands						
6. My organisation assigns qualitative values to its decision-making criteria						
7. My organisation assigns quantitative values to its decision-making criteria						
8. My organisation is open to using better alternatives in its decision making						
9. My organisation encourages innovative decision making						
10. My organisation considers uncertainties in relation to its decision making						
11. My organisation provides training in the science of decision making						
12. My organisation re-examines its decision making as new information becomes available						
B. Decision-making culture						
13. My organisation has suffered a negative outcome due to slow decision making						
14. My organisation's culture has resulted in its inability to make a decision						
15. My organisation's decision making is influenced by organisational politics						
16. My organisation's decision making results in making the same mistake as in the past						
17. My organisation's decision making is influenced by the vested interest of individuals (e.g. conflict of interest)						
18. My organisation underestimates problems which adversely impact its own decisions						
19. My organisation continues with projects/products which should be terminated at an earlier stage						
20. My organisation's decision making is influenced by similar organisations or competitors						
21. My organisation's decision making is influenced by incentives or penalty payments						
22. My organisation effectively communicates the decisions it makes						
23. My organisation provides clear and unambiguous instructions for decision making						

The QoDoS instrument for evaluating quality decision making

Part II: Individual-level influences

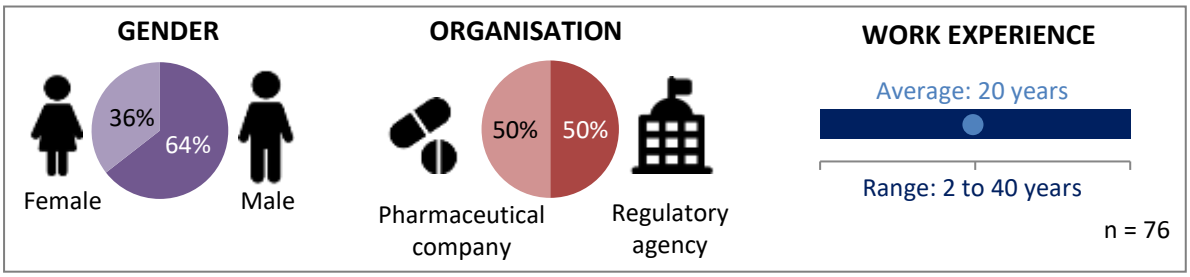
	Not at all	Sometimes	Frequently	Often	Always	Not applicable
A. Decision-making competence						
24. My decision making is knowledge based						
25. My decision making is consistent						
26. I consider uncertainty and unknowns in my decision-making approach						
27. I generate a Strengths-Weaknesses-Opportunities-Threats (SWOT) analysis in my decision making						
28. I present contingencies or achievable options as part of my decision making						
29. My decision making is transparent						
30. I understand the context of the decision I am being asked to make						
31. I understand the importance of the decisions I make						
32. I use a structured approach in my decision making						
33. I assign qualitative values to its decision-making criteria						
34. I assign quantitative values to its decision-making criteria						
35. I receive training in the science of decision making						
36. I use intuition or “gut-feeling” in my decision making						
37. My professional experience is important when having to make challenging decisions						
B. Decision-making style						
38. Emotion is part of my decision making						
39. I have experienced “paralysis by analysis” caused by my slow decision making						
40. I have experienced a negative outcome by a decision not being made						
41. In my decision making, I make the same mistakes as in the past						
42. Recent or dramatic events greatly impact my decision making						
43. My procrastination has resulted in a negative outcome						
44. My decision making could be improved by assigning relative importance to decision criteria						
45. I underestimate problems which adversely impact my decision making						
46. I continue with projects/products which should be terminated at an early stage						
47. I feel that I could make better quality decisions						

Confidentiality

If an organisation was to use this survey, it should be noted that all information collected from individual agencies and companies will be kept strictly confidential. No data that will identify an individual agency or company will be reported, or detail made to a third party. External reports or presentation of the data will include only anonymous figures and any appropriate analytical interpretation. Agency or company data will only be provided to the relevant organisations concerned.

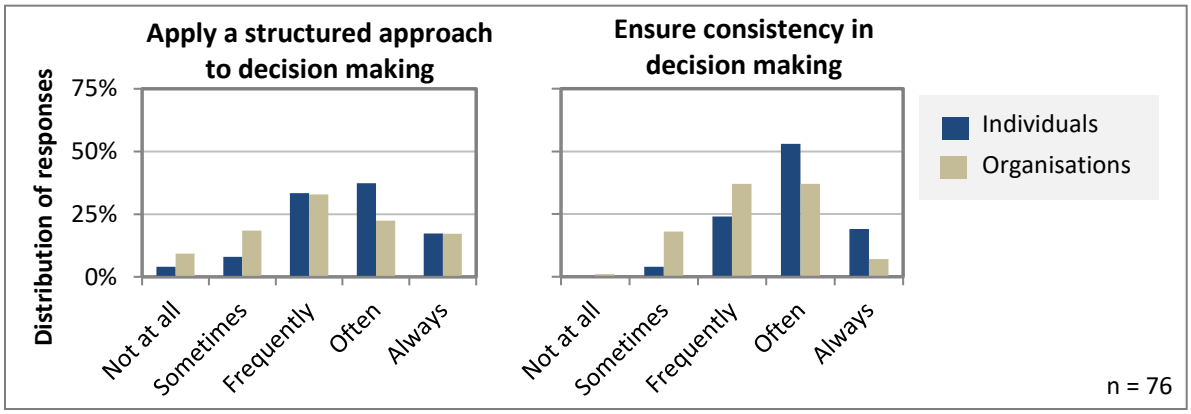
Practical application of the QoDoS instrument

One of the objectives of the CIRS programme is to utilise the QoDoS to assess the quality of decision-making process and evaluate the level of incorporation of the 10 Quality Decision-Making Practices within companies, regulatory and HTA agencies. In order to demonstrate the practicality and applicability of the QoDoS for evaluating quality decision making, a study was initiated with 76 participants from 12 regulatory agencies and 23 international pharmaceutical companies, who were asked to complete the tool[6]. The demographics were as follows:



Study results: Organisational and individual decision making

The QoDoS enables an evaluation of decision making across both individuals and the perspective of individuals on the organisation as eleven of the QoDoS items are analogous for the organisational and individual parts of the instrument. The results for two common QoDoS items, 'Apply a structured approach' and 'Ensure consistency in decision making' indicate that both were incorporated more at the individual level rather than organisational level of decision making.



Although in practice the two scores should be similar as people make up an institution, individuals tend to score themselves more highly and be more critical of an organisation. While this could be a potential sign of bias, areas of disparity between the two could also indicate areas for improvement for the individuals, which should translate into better practices within the organisation.

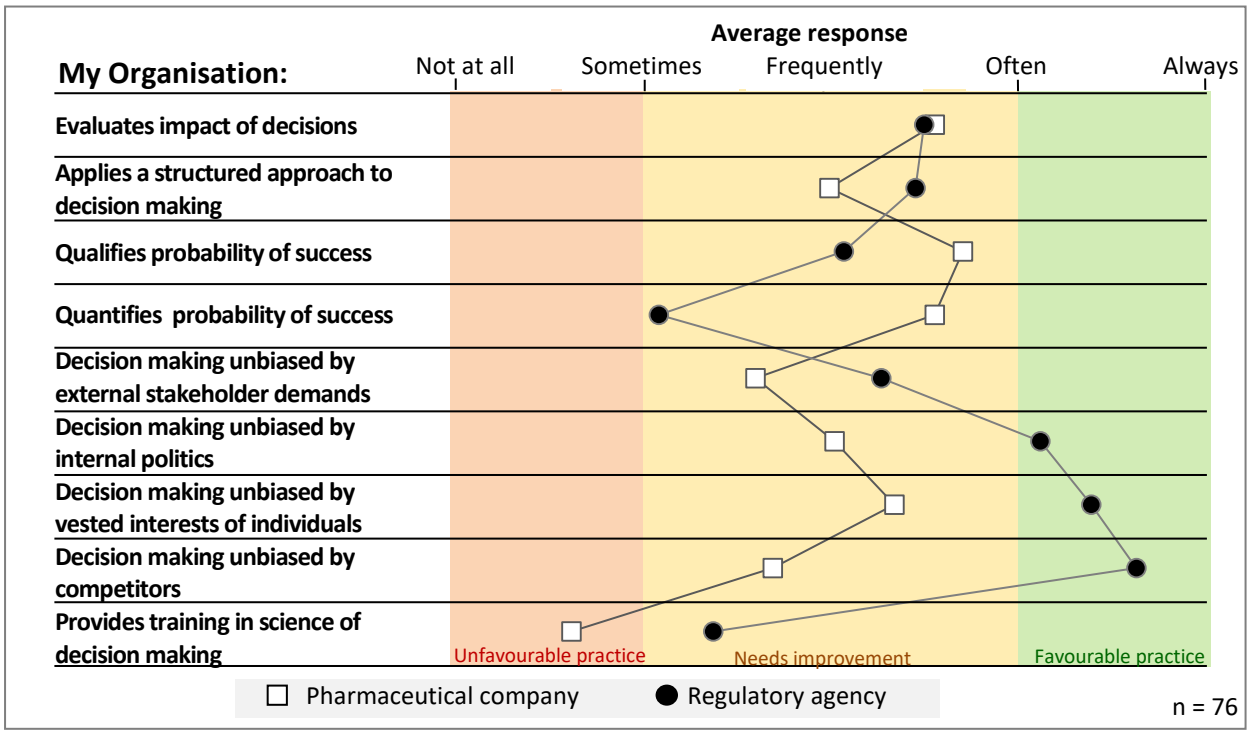
Study results: Pharmaceutical company and regulatory agency organisational decision making

An assessment of regulatory agency and pharmaceutical company organisational-level responses identified differences between the two stakeholders. Both considered evaluating the impact of the decisions as important, with agencies using a structured, systematic approach to decision making more frequently than companies. Conversely, there was a general tendency for biases due to politics, competitors or incentives to have more impact on company decision making compared with agencies.

[6] Bujar M, Donelan R, McAuslane N, Salek S, Walker S. Assessing quality of decision making in medicines' development and the regulatory review: Identifying biases and best practices. *Ther Inn Reg Sci*. 2016; doi:10.1177/2168479016662681

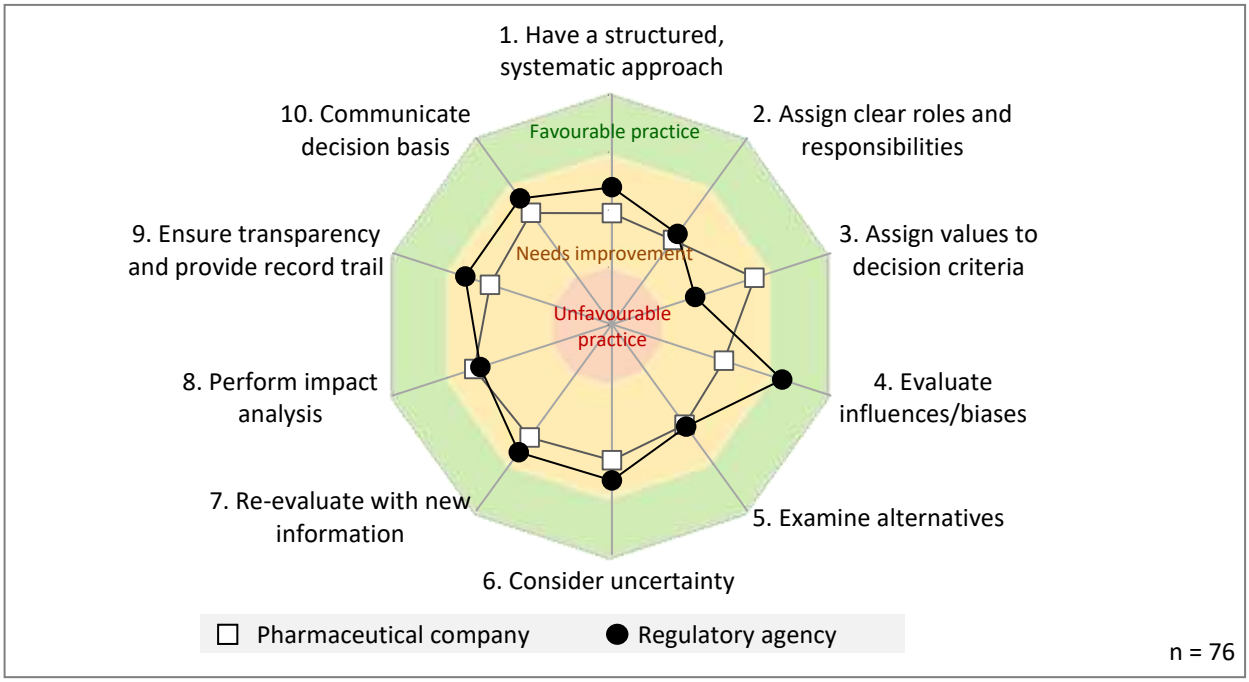
Practical application of the QoDoS instrument

Whilst it was recognised that the science of decision making is important, training in this area was rarely provided. All responders from agencies and 92% from companies felt that they could improve the quality of their decision making. Nine selected organisational-level QoDoS items are shown below:



Evaluating the 10 Quality Decision-Making Practices

Finally, the organisational level agency and company responses were mapped against the 10 QDMPs, demonstrating key differences between company and agency practices and confirming the need for improvement and training in decision making for both stakeholders.



The potential impact of evaluating decision making with the QoDoS

The applicability of the QoDoS for evaluating decision making

The findings of the study with pharmaceutical companies and regulatory agencies demonstrate that the QoDoS has the ability to identify differences in decision making between individuals and their organisation as well as differences between companies and agencies.

The potential impact for evaluating quality decision making with the QoDoS in association with the 10 Quality Decision Making Practices

Individual knowledge: Simply completing the instrument can increase an individual's awareness of the issues in decision making, different biases and influences that need to be considered when making decisions, as well as best practices that should be incorporated into an organisation's decision-making framework.

Internal Monitoring: The QoDoS can be used by organisations to internally monitor and visualise decision making within and across different teams and divisions to identify strengths and weaknesses. This should facilitate raising sensitive issues by individuals relating to decision making, help with relationship building and ultimately increase trust within the organisation. The QoDoS could also provide the ability to measure change over time in order to determine the impact of training and other improvement initiatives in order to ultimately improve effectiveness across teams, increase productivity in R&D decision making, reduce uncertainty and result in more consistent outcomes for organisations.

External Benchmarking: The QoDoS can be utilised to externally benchmark an organisation's decision-making practices and performance compared with other organisations. This in turn could provide a basis for discussion of the issues in the quality of the decision-making processes, thereby encouraging a level of trust and partnership and helping to identify areas for improvement and collaboration. Ultimately, the QoDoS should enable organisations to build quality, transparency and consistency into the critical decisions that are undertaken during the lifecycle of medicines.

Routine assessments with the QoDoS may offer a number of benefits to organisations and individuals.

Conclusions

In 2015, CIRS initiated a programme in Quality Decision Making with the following aims and activities:

ACTIVITIES	AIMS
Surveys and other research projects *QoDoS studies* *International Workshops*	• Evaluate the current decision-frameworks and understand the characteristics of different decision-making processes • Assess the quality of decision-making processes and practices that need to be considered when making a decision, as well as influences and biases that may impact the process • Develop the principles of a quality decision framework and identify markers and practices that build quality into decision making

Medicines' Development → Regulatory Review → Health Technology Assessment

An enhanced understanding of how to identify and apply quality decision-making practices may facilitate decision-making approaches and subsequently will enable improved practices for both the individual and the organisation. Ultimately, this will enable improved transparency, predictability and consistency in critical decisions in medicines' development, review and health technology assessment.

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About CIRS

CIRS – The Centre for Innovation in Regulatory Science Limited – is a neutral, independently managed UK-based subsidiary company, forming part of Clarivate Analytics (UK) Limited. CIRS' mission 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 and to facilitate access to medical products through these activities. This is CIRS' purpose. CIRS is operated solely for the promotion of its purpose. The organisation has its own dedicated management and advisory boards, and its funding is derived from membership dues, related activities, special projects and grants. (www.cirsci.org)Website: www.cirsci.org

If your organisation would be interested in participating in a QoDoS study, please contact one of the authors listed above.