ISPOR
The professional society for health economics and outcomes research

Improving healthcare decisions

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Dear the European Commission:

ISPOR – the professional society for health economics and outcomes research - is pleased to respond on behalf of its membership to your consultation entitled "**Health technology assessment – procedural rules for assessing and managing conflicts of interest**." We appreciate the opportunity to comment on these draft guidelines.

ISPOR is a scientific and educational society with many of its members engaged in evaluating health technologies, including pharmaceuticals, medical devices, and other interventions. We have a large membership living and working in 100 countries globally; nearly 20% (1 in 5) of our membership resides within the European Union. Members across our organization come from a range of disciplines, including health economics, epidemiology, public health, pharmaceutical administration, psychology, statistics, medicine, and more, from a variety of stakeholder perspectives, such as the life sciences industry, academia, research organizations, payers, patient groups, government, and health technology assessment bodies. The research and educational offerings presented at our conferences and in our journals are relevant to many of the issues and questions raised in this request for information.

The response to this consultation was led by the ISPOR Patient Council. We solicited comments from our most senior advisory body, the Health Science Policy Council, Institutional Council, and several of our special interest groups. The attached document provides a summary based on their comments. We hope they prove useful.

ISPOR would be happy to answer any questions about our response, to serve as a partner, or to participate in any follow-up consultations on the relevant program items mentioned within the report.

Sincerely,

Robert Abbott
CEO & Executive Director
ISPOR

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Health technology assessment – procedural rules for assessing and managing conflicts of interest

We are pleased to present our collective comments on the assessing and managing of conflict of interest (COI) in the context of health technology assessments in the European Union (EU). This submission is made on behalf of representation from the ISPOR Rare Disease Special Interest Group and Patient Centered Special Interest Group, as well as various patient organizations and individual expert patients with lived experience that participate in ISPOR Patient Representatives Roundtable discussions. As a multistakeholder organization, ISPOR serves a diverse range of groups, including patient organizations, healthcare professionals, researchers, and industry representatives. We understand that patients often face financial and organizational resource constraints that limit their ability to contribute completely & comprehensively without taking extensive time away from personal and work priorities to ensure the best representation of their community needs for patient-focused innovative medicines. They may rely on funding from health technology developers, grants, and other sources. We acknowledge that these financial dependencies can create perceived or actual COI, potentially excluding these vital stakeholders with experiential knowledge from participating in assessments and decision making. Our comments aim to highlight the challenges faced by patient organizations and individual expert patients with lived experience in navigating these COI concerns while advocating for their essential role in the health technology assessment decision-making process. We believe that a balanced approach is necessary to ensure that what matters most to patients is heard and considered throughout the evaluation and decision-making process, whilst maintaining the highest quality assessments which are fair, impartial and transparent. Please consider co-creation of additional guidance to clarify the procedural and methodological details regarding COI within the EU Health Technology Assessment Regulation which is like the constructive mitigating process of EMA procedural guidance on inclusion of declared interests.

The document is well-written, comprehensive, understandable, and utilizes standard language. The document is written for experts who will be formally engaged in the JCA work by participating on a committee or group, and it is primarily directed at self-declaration by the experts. The guidance document covers different forms of COI (actual, potential, appearance/perception), addresses financial remuneration and stock holdings, includes family members, and suggests transparency of the declarations for all, not just for patients.

The public needs to trust the decision-making process to be high quality, independent, impartial and transparent. Importantly, expertise is based on real-world knowledge and experience, which should lead to a well-informed opinion. Finding genuine subject matter experts (SMEs) without any COI as currently defined may be difficult. Therefore, we propose adding guidance that outlines the process for identifying authentic experts if a suitable person cannot be found free from interests. Instead of excluding experts with potential conflicts, we suggest additional guidance that clarifies the exception process and implements a timely, transparent (publicly available/posted) decision-making process which explains a constructive rationale for balancing measures of the need for expert input with effective COI management and transparency, such as: 1) educating and encouraging SMEs to fully disclose their actual potential conflicts of interest, as outlined in the document, and maintaining transparent communication about the nature and extent of these conflicts to help stakeholders understand the context and assess the associated risks and requirement to recuse oneself from discussions where their conflict applies; 2) Including SMEs with and without potential conflicts of interest ensures that while expert opinions are considered, ultimate decisions are not unduly influenced; and 3) Establishing an ethics committee to review and approve the involvement of SMEs with conflicts of interest.

While there was previously flexibility regarding COI and European Medicines Agency (EMA) guidances, this new Implementing Act requires similar additional guidance for clarifying and implementing a more constructive approach at mitigating risks, ensuring a balance between impartiality, and availability of the best

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expertise. The three-year timeframe and expansion of the definition of COI beyond only financial support need to be clearly explained. Future confidentiality agreements may be structured based on this guidance. If the confidentiality agreements are not flexible, especially for rare disease patients, this may be used as a reason for not involving patient experts which would raise concerns regarding the credibility/legitimacy of the value assessment and decision making.

There is a high risk that those less familiar with the disease, technology, and potential outcomes could be informing a very complex decision-making process. This could lead to incorrect assessment and understanding of information, creating more uncertainty in an area where HTA already struggles with uncertainty. The limited consideration given to rare diseases in clinical trials and the exclusion of clinical experts and individuals with lived experience from the decision-making process are significant concerns. The impact of this guidance on the representation of rare disease perspectives will be significant. Given the potential impact on patient access, care and engagement, there must be a 3-year grace period until a clear understanding of these points may be provided in additional comprehensive guidance for patient experts.

Additional concerns have been raised regarding transparency, representation, communication, and equity:

- **Transparency**: How will conflicts of interest be managed? We suggest the rationale for these decisions be made publicly available, yet we appreciate and respect the decision to refrain from publishing the patient's details. We suggest this algorithm/process for balancing independent expertise, impartiality, COI and robust expertise be made publicly available. How will conflicts of interest beyond financial support be evaluated? We suggest that the procedural guidance on inclusion for EMA COI are considered and additional guidance provided for this Implementing Act. What is the oversight process for ensuring content completion, validity, and decision-making?
- **Representation**: What level of representation will be given to each representative in the decision-making process? How will stakeholders be assured that their views and experiences will be considered as part of the collective representation?
- **Communication**: How can we be assured that clear and effective, timely communication and rationale are provided for decision-making?
- **Equity**: How can we be assured that all viewpoints will be considered equally?

Further rephrasing considerations are listed below:

- Annex I, Page 1: The term "patient expert" can be misunderstood as experts who study patients. It is recommended that this term be replaced with "expert patients" to avoid confusion.
- Annex I, Page 2: Employment: there is a note regarding 'unpaid' employment. Please provide clarification on this matter. Should employed be "under contract" instead, since it notes 'unpaid'?

We acknowledge ISPOR members, Angie Botto-van Bemden, Derick Mitchell, Nan Qiao, Birgitta Termander and Sheela Upadhyaya, for their assistance in assembling these comments, as well as ISPOR staff Laura Pizzi, Clarissa Cooblall, Kelly Lenahan, and Sahar Alam.