Public Policy Statement: Principles for Health Technology Assessment (HTA) and Comparative Effectiveness Research (CER)

Around the globe, medical, administrative, and political decision-makers increasingly rely on scientific evidence of the benefits and risks of medical interventions to make judgments on commercial and medical use of alternative treatments. These judgments can variously inform individual medical decision making, improve the impact of health care interventions on individual and population health, and help allocate limited health care resources where they can most benefit society.

No one term or set of principles covers this entire landscape. In addition, the similarity and overlap of activities along the continuum contributes to confusion about the distinctions between different activities, the definitions of terms, and the public policy directed at these activities. There are a variety of analytic methods that draw conclusions from medical evidence, including methods that compare the relative effectiveness of alternative interventions ("comparative effectiveness research"), and methods that assess the total medical, economic and societal impact of a treatment option compared to alternatives ("health technology assessment").

As a general rule, Merck supports efforts to base medical and societal decision making more completely on medical evidence and to improve the quality of evidence and the quality of decision making in order to improve overall health outcomes and health status around the world. Merck believes that the effectiveness of medicines produced, their appropriate use, and their contribution to better health outcomes depend on strengthening the science behind medicines that reach the market and better aligning patient, provider and payer decisions with that science. The incentives to continue biopharmaceutical innovation depend on the accurate measurement of the value of innovative medicines and compensation to innovators that is commensurate with that value.

To achieve these objectives, Merck believes that all approaches to analysis of evidence to support healthcare decisions should adhere to a set of basic principles. These principles apply in general to the creation of evidence and its application to decisions1, even though individual countries and regions will vary in their structures and processes for:

- Comparative effectiveness research (CER) – conducting and synthesizing research comparing risks and benefits in real world settings of alternative interventions to prevent, diagnose, treat, or monitor health conditions;
- Health technology assessments (HTAs) – appraising the comparative value of alternative interventions in the context of their medical risks and benefit, and their economic, social, and ethical implications; and
- Treatment and payment decisions – using these appraisals to render decisions on appropriate treatment, reimbursement, and allocation of health care resources,

Despite these differences, the general process of collecting and analyzing data and applying the conclusions from these analyses in reimbursement decisions is similar from country to country . What varies significantly is the types of entities that perform these different activities (e.g. government agencies, independent organizations, individual health plans); and the degree to which the conclusions and decisions are centralized in a single national entity or diffused among a variety of competing entities.

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The US is developing a strong central role in evidence generation and synthesis of comparative feffectiveness data (comparative effectiveness research) through a government agencies (AHRQ and NIH) and a new independent organization (Patient Centered Outcomes Research Institute (PCORI)), while the assessment of value and decisions on reimbursement are left to a large number of individual private or public health plans. By contrast, the EU centralizes the value appraisal process through national HTA agencies, which work closely with the national health plan(s) on centralized reimbursement decisions.

Merck supports CER and HTA conducted using sound scientific methods and appropriately applied for the purpose of improving health outcomes for patients and efficiencies in the health care system overall. Better health care results come from clinical decisions that respond appropriately to individual patient needs and circumstances by incorporating practitioner judgment and experience and patient preferences. Merck believes that CER and HTA entities and processes can play a valuable role in advancing new medical and scientific information that can help improve the quality of care on an ongoing basis.

To meet these goals, CER and HTA programs should adhere to the following principles:

Structure of CER and HTA Programs

- **Independence of Analysis**: In order to avoid the potential for bias in the analysis or conclusions from evidence, research that draws conclusions on comparative effectiveness or value should be overseen and conducted by entities that are independent from entities that will make clinical, coverage/reimbursement, or resource allocation recommendations or decisions. Conclusions from the studies, limited to answering the questions posed in the study, should be publicly available to permit an independent assessment of their application to clinical or resource-related decisions. In instances in which a payer commissions or conducts a comparative effectiveness assessment or technology appraisal, it is essential that the process be transparent and the payer disclose the methodology, limitations, and sources of bias in order to establish credibility for the analysis and conclusions.

- **Focus on Priority Health Care Issues**: Comparative effectiveness research or health technology assessments should be focused initially on topics for which there are evidence gaps and which are of the greatest immediate consequence for society, based on a priority-setting process that has broad stakeholder input. Priorities should be set based on the burden to the society of the disease, the potential for effective treatment, the presence and consequence of variability in practice, and the potential for influencing treatment and resource allocation decisions -- using analytical methods (value of information analysis) to help guide prioritization)

- **Evaluation of Reviews**: Agencies responsible for overseeing and conducting systematic comparative effectiveness research or HTAs in the public domain should provide for a periodic evaluation of their reviews to assess methods used, conclusions reached, and the clinical and financial impact of the reviews. The processes and methods of the agencies should be improved in response to these findings.

Analytic Methods

- **Science-Based**: Analysis and conclusions derived from evidence should remain as true to the science as possible. The analysis or study should adhere to the fundamental rules of the scientific method: it should fully disclose the study methodology and limitations of its execution; it should fully disclose any potential sources of bias; its execution should adhere rigorously to the methodology; and its methods and results should be replicable. The study should only draw conclusions that are fully supported by the evidence.

- **Methods "Fit for Purpose"**: Merck believes different types of evidence are necessary to support different types of analyses and answer different types of questions. For any type of analysis, the method applied in developing the evidence for that analysis should be "fit for purpose." Questions of efficacy – the potential for a particular intervention to modify a condition – require tightly-controlled studies (such as a randomized clinical trials (RCTs)) that are hypothesis testing and can answer questions of causation. Questions of effectiveness – the effect an intervention actually has in a real-world setting with a diverse population – may require a mix of controlled studies (e.g., pragmatic or large scale RCTs) and observational studies (e.g.,registries, electronic medical record and/or insurance claims data bases). Questions of value – the resources and trade-offs required to achieve a particular effect – require acceptance of a broader range of evidence that can help assess the clinical, economic, and social consequences of the use of particular interventions, including the value seen by patients themselves.

- **Explicit and Relevant Goal and Topic**: Projects to complete a comparative effectiveness assessment or an HTA should begin with a topic selection document that clearly specifies the purpose and research questions for the study. The topic selection document should be developed with broad stakeholder input and should be available for public review and comment prior to initiation of the study.

- **All Relevant Technologies Includ**ed: Synthesis of research for assessments of comparative effectiveness or appraisals of health technology should include studies on a full range of alternative therapies that target a specific medical condition, including devices, procedures, diagnostics, drugs and biologicals, treatment strategies, care management, and healthcare delivery systems.

- **Value Defined Broadly**: In conducting an HTA, the value of a specific new technology should be defined broadly to include benefits, risks, and costs that are clinical (e.g., morbidity and mortality effects), economic (e.g., productivity gain, government budget impact, cost effectiveness) and social (e.g., quality of life, preference, satisfaction); and should measure both direct and indirect effects for patients, families, caregivers, employers, and society as a whole.

Conduct of Assessments

Transparency of Processes: The processes used to analyze and draw conclusions from evidence, and the basis for making decisions should be accessible and transparent for stakeholders.

Broad Stakeholder Engagement: To enhance the credibility of evidence-based reviews and the broad acceptability and application of their conclusions, a full range of stakeholders (patients, providers, payers, employers and industry) should be involved in all parts of the process. Entities overseeing and conducting research should be governed by and seek advice from boards and committees that reflect a full spectrum of health care stakeholders. Stakeholders should able to engage in topic selection activity and framing questions; proposing and critiquing methodology; providing published and proprietary study results that are relevant to the questions; reviewing and commenting on draft reports; and providing input in appeals processes. Stakeholders should also help inform evaluation and revision of the process itself.

Sensitivity to Individual Variation: While much of the available data on medical interventions is necessarily collected on the basis of large, diverse populations, when practical, studies used to inform comparative effectiveness or value determinations should be sufficiently powered to describe individual variation and the diversity of individual patient response.

Periodic Updating: To maintain relevance, analysis and conclusions from evidence analyses should be periodically reviewed and updated to reflect new studies and new methodologies.

Disclosure of Sources of Bias and Uncertainty: The review process and reports should acknowledge methodological limitations; address the generalizability and transferability of findings beyond the study populations; and disclose sources of potential bias and uncertainty in the estimates.

Responsiveness to New Data and Methods: Findings should be reviewed periodically and should be updated as new well-validated methodologies are introduced that may affect the conclusions or new data is generated that affect the findings in reports the reviewing entity has previously published.

Application in Decision Making

Timely Findings: The results of studies and dissemination of those results should be timely in relation to key clinical or system-wide decisions that need to be made. Comparative assessments and technology appraisals should not become a source of delay in approval of new treatments.

Effectively Communicated to Decision Makers: Results of comparative studies should be effectively communicated to key constituencies that will make treatment, reimbursement and budget allocation decisions.

Decisions Congruent with Findings: Once available, the findings from assessments and appraisals that have broad credibility should guide evidence-based decision making. Clinical guidelines, coverage and reimbursement decisions, and other systems for influencing treatment decisions should be congruent with findings from comparative effectiveness and value determinations. The link between the decision and the findings that support that decision should be transparent and clearly defined. Stakeholders should be able to review and appeal economic decisions.

Reward for innovation: Treatment, reimbursement and budget decisions need to ensure appropriate use and provide adequate compensation commensurate with the effectiveness and value that new products contribute to patient outcomes and health care budgets. Congruence between demonstrated value and commensurate compensation will continue to encourage and reward investments of financial and other resources in the discovery and development of new technologies.

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