



June 10, 2019
Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, Massachusetts 02109

Re: Call for Public Input on ICER Value Framework

To Whom It May Concern:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to respond to the Institute for Clinical and Economic Review's (ICER) open call for stakeholder feedback on how it can improve its value assessment framework. PhRMA is a voluntary, non-profit organization representing the nation's leading research-based pharmaceutical and biotechnology companies which are devoted to inventing medicines that allow patients to lead longer, healthier, and more productive lives.

PhRMA is also a long-standing supporter of evidence to support health care decision-making, including value assessment frameworks. Advancing better evidence and tools to support sound health care decision-making, including support for advancing the science and use of value assessment frameworks, is a core principle adopted by our members and is central to our policy agenda.^{1,2}

We appreciate ICER taking steps to open its value framework to public comment. Over the past several years, ICER has taken several steps to improve its value framework that align closely with past input PhRMA has provided. For example, we appreciate ICER taking steps towards improved transparency of its models for manufacturers.

However, we believe that ICER can further improve its methods, its process, and the structure of its framework by addressing the full range of recommendations provided by PhRMA and other stakeholders. ICER has received feedback on individual assessments expressing significant concern in several areas, including, but not limited to the premature timing of ICER's analyses, shortcomings of cost-per-quality adjusted life year (QALY) based cost effectiveness analysis (CEA), and the lack of disease-specific clinical expertise on ICER's voting panel.

Because of these and other flaws, ICER's framework continues to pose a significant risk of being misused in ways that have unintended negative consequences for patients and does not provide a sound basis for supporting health care decision making or driving forward a value-based health care system.

We urge ICER to continue to improve its framework, including exploring entirely novel methods of value assessment. As outlined below, it is clear that traditional, QALY-based CEA is fundamentally misaligned with the United States' competitive, complex and pluralistic system, and when used in isolation cannot meet the needs of today's stakeholders or 21st century science. While QALY estimates

¹ PhRMA. "Policy Solutions: Delivering Innovative Treatments to Patients." Available at: <http://phrma-docs.phrma.org/sites/default/files/policy-solutions.pdf>

² PhRMA Value Collaborative. More information available at: <http://www.phrma.org/advocacy/the-value-collaborative>

may provide useful insight to a limited subset of decision makers, they should not set the rule for single pricing or policy decisions, which has the invariable effect of obscuring the important issues identified above.

In addition to moving beyond traditional, QALY-based value assessment, there are several key steps that PhRMA believes ICER must take to establish a methodologically rigorous, patient-centered value framework that can effectively support decision-making by stakeholders:

- I. Actively promote alternative approaches to value assessment, such as multi-criteria decision analysis (MCDA), and reject traditional, QALY-based CEA.
- II. Expand assessments and results to reflect all relevant patient-centered outcomes and relevant patient subgroups based on clinical needs and preferences.
- III. Remove the arbitrary and subjective budget threshold.
- IV. Take a holistic perspective on value that reflects the full range of health care services and interventions and allocate a proportionate share of reviews to other health care services.
- V. Meaningfully integrate clinicians and stakeholders with disease-specific expertise into the value assessment process.

We appreciate ICER's consideration of our recommendations. PhRMA believes that, if these recommendations are adopted and ICER's revised framework is fully validated, it could play a positive role in the movement towards better value in health care. We provide more detail below as to specific concerns, as well as steps that ICER can and should take to address them.

I. Actively promote alternative approaches to value assessment, such as multi-criteria decision analysis, and reject traditional, QALY-based CEA.

It is now recognized by many stakeholders and researchers that traditional methods of QALY-based value assessment are controversial and outmoded. From thought leaders in the field of health economics, to leaders of industry, to patient advocates, many have commented on the shortcomings of QALY-based cost effectiveness in general, and the inappropriateness of their application in the U.S. health care system in particular. ICER itself has acknowledged the concerns expressed by stakeholders and the flaws in QALYs³ and yet persists in generating value-based prices based on QALYs, and similarly flawed metrics.

ICER's reliance on QALYs is highly problematic because they simply do not reflect the reality of treating patients in today's health care system. While the QALY, which provides a single number summarizing the "value" of a treatment, is a commonly used metric for quantifying health benefits, patients do not receive treatments in isolation; the provision of health care is a complicated, multifaceted process with patients receiving care along an entire continuum – from diagnostic testing, clinician consultation, disease management and monitoring, to medication therapy and occasionally hospitalization. The impact, value, and outcomes of each of these services may rely on steps taken before or after, as well as circumstances unique to each patient – including factors such as existence of

³ ICER. The QALY: Rewarding the Care That Most Improves Patients' Lives. December 2018. Available at: https://icer-review.org/wp-content/uploads/2018/12/QALY_evLYG_FINAL.pdf

preferences, comorbid conditions and care seeking behavior.⁴ As noted in a recent paper, it is extraordinarily difficult to translate QALY-based assessments into real-world decision-making in clinically appropriate, patient-centered ways.⁵

In the call for input on its value framework, ICER also sought feedback on the cost effectiveness thresholds used to establish its value-based prices. This question itself, and attempts to objectively answer it, illustrates the inherent flaw of the cost per QALY threshold. If inquiring as to how high or low the thresholds should be set, ICER is simply asking the wrong question. Just as the QALY cannot adequately capture the many aspects of value and wide heterogeneity of patient preferences, a cost effectiveness threshold is not reflective of the intricate reality of the U.S. health care system. And while we acknowledge that our health care system is complex, and involves many perspectives and stakeholders, at its nexus is the patient and provider, who are, and should continue to be ultimately responsible for treatment decisions. Insurers can play a role in guiding treatment options based on formulary coverage and placement, but coverage decisions vary by payer due to differences in enrollee population and willingness to pay. Fundamentally, an approach that relies on a single or several thresholds is incompatible with a system built on patient-centered, individualized treatment decision-making and which comprises hundreds of individual payers with diverse needs and attributes.

The evLYG is not an acceptable supplement or replacement for the QALY.

ICER, clearly aware of the controversy surrounding QALYs, announced a new metric for quantifying value, the equal-value life year gained (evLYG). While we appreciate ICER's acknowledgement that the QALY is inherently discriminatory and problematic, the evLYG does not serve as an appropriate supplement or replacement for the QALY. While attempting to address one issue with the QALY, the discrimination due to discounting utilities for individuals with disabilities, ICER has created several more.

The limitations of the evLYG are clear. For example, when using the evLYG, medicines for conditions that do not reduce life expectancy, like a treatment for eczema or a cure for blindness, would have no value to the health care system. Additionally, the evLYG would value two medicines, one that reduces side effects and one that does not, as equal value. Neither the QALY nor the evLYG properly capture the value of a medicine to patients and people with disabilities. Americans should not be forced to choose between discrimination and capturing quality of life in value assessments. Such a conflict simply highlights the fact that traditional cost-effectiveness assessments cannot possibly serve as an appropriate tool for guiding health care decisions and resource allocation.

⁴ Valderas JM, Starfield B, Sibbald B, et al. "Defining Comorbidity: Implications for Understanding Health and Health Services," *Ann Fam Med*, vol. 7, no. 4, pp. 357-363, 2009.

⁵ Sawhney TG, Pyenson B, Buzby E. "The utility of ICER reports for private payer drug coverage decision-making: Cost-effectiveness assessments." Milliman. September 19, 2018. Available at: <http://www.milliman.com/insight/2018/The-utility-of-ICER-reports-for-private-payer-drug-coverage-decision-making-Cost-effectiveness-assessments/>

ICER should explore new methods of value assessment, such as multi criteria decision analysis.

In their report on value assessment, the ISPOR Special Task Force on U.S. Value Assessment Frameworks strongly recommended that stakeholders explore novel methods of value assessment.⁶ Since then, numerous thought-leaders and organizations have invested resources into the development of transformative, patient-centered forms of value assessment. This includes the PhRMA Foundation, which recently issued a challenge to stakeholders to develop transformative, non-QALY methods of value assessment.⁷ The Foundation received more than 20 responses and plans to publish several of the papers later this year.

For example, the University of Colorado, which already has a strong working relationship with ICER, has established the Pharmaceutical Value initiative (pValue), to test and apply novel methods for value assessment that encourage stakeholder engagement and promote value-based decision making, beginning with MCDA. As they note, “MCDA is particularly helpful in an area like coverage and reimbursement decision-making, where the available alternatives are characterized by multiple, sometimes conflicting, criteria, some of which are judged objectively, some subjectively, and by multiple decision-makers, each with his or her own views on a particular criterion’s relative importance.”⁸ Applying MCDA would allow individual users of ICER’s reports to assign weight to different elements of value, and arrive at their own estimate of a treatment’s worth, which is not currently the case in ICER’s value assessments. It has the potential to make value assessment customizable, transparent and comprehensive, while incorporating other elements of value that patients care about. We recognize that ICER explored use of multi-criteria decision analysis in the past and strongly encourage them to revisit the idea, while simultaneously abandoning traditional CEA.

II. Expand assessments and results to reflect all relevant patient-centered outcomes and relevant patient subgroups based on clinical needs and preferences.

Regardless of the approach ICER takes to value assessment, whether it is QALY-based cost effectiveness analysis, or MCDA, it is imperative that ICER takes a comprehensive, patient-centered perspective on value. ICER should follow the recommendations of thought leaders in the field by expanding their value elements to incorporate other elements of value that matter to both patients and society. It should also ensure that the significant heterogeneity in clinical characteristics and preferences in patients is captured. Our health care system is becoming increasingly patient-driven and personalized, and ICER should strive to capture those characteristics.

Historically, ICER has frequently responded to such critiques by conducting scenario or subgroup analysis that are not reflected in ICER’s results or press releases. This is unacceptable. The vast majority

⁶ ISPOR Special Task Force on U.S. Value Assessment Frameworks. “A Health Economics Approach to US Value Assessment Frameworks—Summary and Recommendations of the ISPOR Special Task Force Report.” Value in Health. February 2018. Available at: [https://www.valueinhealthjournal.com/article/S1098-3015\(17\)33894-9/fulltext](https://www.valueinhealthjournal.com/article/S1098-3015(17)33894-9/fulltext)

⁷ PhRMA Foundation. PhRMA Foundation Issues a Call for Papers to Improve Health Care.” January 31, 2019. Available at: <http://www.phrmafoundation.org/wp-content/uploads/2019/02/News-Release-VA-Challenge-Awards-2019-5.pdf>

⁸ The University of Colorado Pharmaceutical Value. “Complimenting Coverage and Reimbursement Decisions With Multi-Criteria Decision Analysis.” AJMC. May 27, 2019. Available at: <https://www.ajmc.com/contributor/the-university-of-colorado-pharmaceutical-value/2019/05/complimenting-coverage-and-reimbursement-decisions-with-multicriteria-decision-analysis>

of stakeholders do not have time to read the entirety of ICER's reports. Publishing a limited subset of results conveys a sense of certainty and homogeneity that is simply false.

ICER should strive to incorporate all relevant outcomes into its final value-based prices.

The ISPOR Special Task Force also recommends the inclusion of a “a more comprehensive economic evaluation that could include novel elements of value.”⁹ Studies have long shown that patients place significant emphasis on outcomes other than prolonged survival or cost, and that these preferences vary considerably depending on factors such as type and severity of disease and individual life circumstances. Payers, the end-user of ICER's reports, have diverse needs and preferences as well. Many individuals and organizations, such as the Innovation and Value Initiative, are developing methods to incorporate these value elements, such as insurance value and option value, quantitatively into health technology assessment, and ICER should leverage their work.

Accounting for all relevant value elements not only further aligns ICER with the needs of patients, but best practices in the field. The First Panel on Cost Effectiveness in Health and Medicine recommended using a societal reference case; this recommendation is now 20 years old, and ICER has still not adopted it. In recognition that most CEAs did not include a true societal perspective, the recent update recommended two base cases, which allowed for the inclusion of the narrower health systems perspective but re-emphasized the importance of the societal perspective.¹⁰

ICER continues to root its value-based prices solely in the payer perspective, which is problematic and diverges from the stated principle of putting patients first, and at the center of the discussion. ICER should consider not only using two base cases for its value assessments but releasing value-based prices based on both perspectives.

ICER often ignores important differences among patient subgroups.

Individual patient differences occur due to many factors, such as genetic variation, differences in comorbidities, and quality-of-life preferences. The Second Panel on Cost-Effectiveness in Health and Medicine agreed and was clear in calling for heterogeneity to be considered through the presentation of subgroup-specific cost-effectiveness ratios. Yet ICER has been slow to recognize heterogeneity, and often fails to release value-based prices for all relevant subgroups, even when it conducts subgroup analyses as part of its assessment. By drawing attention to the average effectiveness of a treatment for an entire patient population, ICER ignores, and encourages payers to ignore, important differences in the clinical needs and preferences of patients. It also puts ICER out of step with the movement towards more personalized health care.

In some circumstances these summarized results are being applied by a decision maker without their full understanding of the modeling, the assumptions, and levels of uncertainty. ICER should consider providing confidence intervals to the reports to reflect the level of uncertainty. In addition, summaries require a more detailed listing/outline of the limitations associated with their derived point estimates.

⁹ Lackdawalla DN, Doshi JA, et al. “Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report.” *Value in Health*. February 2018. Available at: [https://www.valueinhealthjournal.com/article/S1098-3015\(17\)33892-5/abstract](https://www.valueinhealthjournal.com/article/S1098-3015(17)33892-5/abstract)

¹⁰ Neumann PJ, Sanders GD, Russell LB, et al. *Cost-Effectiveness in Health and Medicine*. Oxford University Press. 2017.

III. Value frameworks should focus on value. ICER should remove the arbitrary and subjective short-term budget threshold from its framework.

ICER's short-term affordability analysis sets a threshold for spending on all new medicines following launch, regardless of the patient population, or health system burden of the condition. ICER's reliance on short-term affordability thresholds runs counter to efforts to achieve truly value-based care. While we appreciate that ICER has taken steps to improve the short-term affordability component of its framework, we continue to believe that ICER should cease estimating short term affordability to avoid serious, unintended consequences for future patients and innovation.

ICER's short-term affordability threshold punishes innovation and could have significant consequences for patient outcomes.

By creating an inverse relationship between the number of FDA approvals per year and the budget impact threshold, ICER is effectively recommending an approach that would punish the biopharmaceutical for developing too many new products. Not only would such a policy disincentivize innovation, it would incentivize and reward low sector output. As Former Assistant Secretary for Planning and Evaluation at Health and Human Services (HHS), Robert Rubin, observed, "If the [ICER] arbitrary budget cap were to be implemented, then new drugs for common diseases like diabetes or congestive heart failure or atherosclerotic cardiovascular disease may be left on the drawing board."¹¹

ICER further penalized innovation by applying their short-term affordability cap only to newly-launched treatments, making no effort to analyze existing spending on health care. This siloed view ignores the fact that better use of medicines impacts other aspects of the health care system, often reducing costs on other services. In fact, the Congressional Budget Office scores policies that increase use of medicines as achieving a 0.2 percent saving on non-drug health costs for each 1 percent increase in the use of drugs. Applying a short-term budget threshold completely disregards this important relationship, a limitation that reinforces silo-based thinking about health care.

The impact on innovation could have serious consequences for patient outcomes – a recent analysis assessed the hypothetical impact of applying ICER's short-term budget impact threshold to Lipitor (atorvastatin) at its launch. If used to limit access to Lipitor, the budget threshold could have resulted in just 28 percent of the 2.9 million people who actually received the treatment having access to atorvastatin in the five years following launch.¹² This limited access in the first five years on the market could have resulted in an estimated 72 thousand additional major vascular events and nearly 19 thousand additional deaths.¹³

ICER argues that spending on treatments and interventions beyond the short-term budget threshold "could displace equally or more valuable care." However, by focusing only on the value of medicines

¹¹ "Value Pricing For Drugs: Whose Value, What Price?" *Health Affairs*. March 28, 2016

¹² Ortendahl JD, Broder MS, Harmon AL. "Modeling the Mortality Impact of Budget Thresholds." Partnership for Health Analytic Research. ISPOR Poster Presentation. May 2019. Available at: <https://www.ispor.org/heor-resources/presentations-database/presentation/intl2019-1479/89987>

¹³ Ortendahl JD, Broder MS, Harmon AL. "Modeling the Mortality Impact of Budget Thresholds." Partnership for Health Analytic Research. ISPOR Poster Presentation. May 2019. Available at: <https://www.ispor.org/heor-resources/presentations-database/presentation/intl2019-1479/89987>

and disregarding the remaining 86 percent of health care, ICER risks facilitating the exact behavior they state they are attempting to avoid. ICER's dismissal of these concerns, stating the threshold serves as an alert to payers to allow for future planning, does nothing to diminish its potential impact on patient access and outcomes.

The calculation used to determine the annual threshold is arbitrary, highly variable, and dependent on inputs unrelated to value.

ICER relies on a budget impact threshold that is highly dependent on the individual inputs comprising its calculation. Such volatility raises the question of whether it is fit for purpose. For example, in a recent whitepaper on ICER's budget impact threshold, actuaries outlined several technical and conceptual issues that limit its usefulness to private payers, one of which was the arbitrary nature of the calculation, which resulted in dramatic variation year over year.¹⁴ They found that "GDP growth plus 1 percent is not consistent with either historical experience or expected future pharmacy cost growth."¹⁵ Tethering the threshold to highly variable inputs such as GDP growth and the number of FDA approvals results in unpredictable thresholds driven by variables unrelated to the value of a medicine. One study found that applying ICER's methodology to the 1992 to 2012 period resulted in annual thresholds varying from \$1.36 billion in 2004 to *negative* \$607 million in 2009.¹⁶

Each individual input has a dramatic impact on the threshold from year to year. In a recent analysis, Avalere replicated ICER's budget impact threshold analysis, substituting the number of FDA approvals while holding all other variables constant, to quantify the impact of changing a single variable in the calculation. When using the lowest, average, and highest number of FDA approvals over the past 20 years, the recalculation resulted in thresholds of \$1.81 billion, \$1.18 billion, and \$684 million, respectively.¹⁷ Avalere's analysis concluded that as the number of FDA approvals per year increased, the short-term budget threshold, and percentage of patients that could be treated before crossing the threshold, decreased.

IV. Take a holistic perspective on value that reflects the full range of health care services and interventions and allocate a proportionate share of reviews to other health care services.

Medicines are distinct from nearly any other health care service available to patients today. Investment in research and development provides value across the globe in ways that investment in other health care sectors, like building new hospitals and training additional physicians, are unable to achieve. The innovation lifecycle facilitates this global benefit through the use of generics and biosimilars that

¹⁴ Sawhney TG, Pyenson BS, Buzby E. "The utility of ICER reports for private payer budgeting: Budget impact analyses." Milliman. January 2019. Available at: <http://www.milliman.com/insight/2019/The-utility-of-ICER-reports-for-private-payer-budgeting-Budget-impact-analyses/>

¹⁵ Sawhney TG, Pyenson BS, Buzby E. "The utility of ICER reports for private payer budgeting: Budget impact analyses." Milliman. January 2019. Available at: <http://www.milliman.com/insight/2019/The-utility-of-ICER-reports-for-private-payer-budgeting-Budget-impact-analyses/>

¹⁶ Ortendahl JD, Broder MS, Harmon AL. "Modeling the Mortality Impact of Budget Thresholds." Partnership for Health Analytic Research. ISPOR Poster Presentation. May 2019. Available at: <https://www.ispor.org/heor-resources/presentations-database/presentation/intl2019-1479/89987>

¹⁷ Leinwand B, Shah A. "ICER's Use of FDA Approval Volume to Calculate Budget Impact Thresholds: A Scenario Analysis." Avalere. July 2018. Available at: <https://avalere.com/insights/icers-use-of-fda-approval-volume-to-calculate-budget-impact-thresholds-a-scenario-analysis>

prevent unrestricted monopolies while ensuring biopharmaceutical companies can recoup their research and development costs while investing in future innovations.

Due to this lifecycle, over the next 5 years, savings due to the entrants of lower cost competitors following loss of exclusivity for brand medicines will more than offset spending on newly-launched brand medicines over the same period.¹⁸ Despite these unique characteristics of the sector, and the fact that spending on prescription medicine accounts for just 14 percent of total health care costs in the U.S. – half of which (7 percent of total health care) is on brand medicines – ICER’s assessments focus primarily on new brand medicines.^{19, 20}

Because ICER fails to examine all relevant aspects of clinical care and patient management, their assessments cannot effectively guide health care resource allocation decisions.

ICER’s myopic view on medicines is not only unfounded, but undermines their stated mission of driving a “more effective, efficient, and just health care system.”²¹ If ICER was truly dedicated to improving health care and guiding evidence-based resource allocation, assessments would take a holistic view of the health care system, not focus on a sector that accounts for such a small share of total health spending.

Dwarfing the amount spent on medicines, health care inefficiency and waste is estimated to account for more than a quarter of health care spending.²² A multi-stakeholder analysis spearheaded by the American Board of Internal Medicine and AcademyHealth categorized more than 400 common procedures and health care interventions as “low value,” or providing no or minimal benefit to patients. Among the interventions identified, more than 75 percent were non-drug related.²³ Low-value care is a major driver of inefficiency in health care and an untapped opportunity to increase quality and reduce spending.

As ICER’s value framework explains, “waste and inefficiency pose major problems.”²⁴ However ICER’s assessments primarily focus on new medicines, in contrast to their stated intention of not targeting a single group,²⁵ while making no attempt to assess and recommend prices for health care services well known to be of low value.

Dismissing this glaring inconsistency by citing lack of evidence on other health care services comparable to the quality of evidence available for drugs reinforces the disconnect between ICER’s stated mission of ensuring “the United States evolve toward a health care system that provides sustainable access to high-value care for all patients” and their actions.²⁶ Notably, limited evidence for a

¹⁸ IQVIA. “2018 Medicine Use and Spending.” Published May 2019.

¹⁹ Centers for Medicare & Medicaid Services. National Health Expenditures Data.

²⁰ Berkeley Research Group, “The Pharmaceutical Supply Chain: Gross Drug Expenditures Realized by Stakeholders,” January 2017. Available at: <http://www.thinkbrg.com/newsroom-publications-vandervelde-blalock-phrma.html>

²¹ ICER. “About.” Available at: <https://icer-review.org/about/>

²² Institute of Medicines. “Best Care at Lower Cost: The Path to Continuously Learning Health Care in America.” 2012. Available at: <http://www.nationalacademies.org/hmd/Reports/2012/Best-Care-at-Lower-Cost-The-Path-to-Continuously-Learning-Health-Care-in-America.aspx>

²³ American Board of Internal Medicine Foundation. Choosing Wisely. April 2014. Available at: <http://www.choosingwisely.org/>

²⁴ ICER. “Final Value Assessment Framework for 2017-2019.” Available at: <https://icer-review.org/final-vaf-2017-2019/#overview>

²⁵ ICER. “Final Value Assessment Framework for 2017-2019.” Available at: <https://icer-review.org/final-vaf-2017-2019/#overview>

²⁶ ICER. “Final Value Assessment Framework for 2017-2019.” Available at: <https://icer-review.org/final-vaf-2017-2019/#overview>

specific medicine does not hinder ICER's ability to carry out assessments and assign value-based prices in those cases.

ICER's singular focus on medicines is the proverbial man looking for his keys under the lamp post. The newest innovations with the most robust evidence supporting their efficacy are often the easiest for payers to target and restrict access. However, if the goal is to improve efficiency, affordability, and health system sustainability, while ensuring patients have access to the most innovative treatments, a holistic perspective is critical.

V. Meaningfully integrate clinicians and other stakeholders with disease-specific expertise into the value assessment process.

PhRMA appreciates ICER's recent efforts to further engage with stakeholders. That said, we remain concerned that ICER is not fully integrating patients and other critical stakeholders into the value assessment process. ICER must ensure that individuals participating in the value assessment process, particularly clinical experts, have disease-specific experience and expertise. ICER should publish the process and necessary qualifications for participation in the appraisal committees, as well as other committees and boards that govern and advise ICER. Once ICER selects individuals to participate in committees, those individuals' qualifications and experience should be made public. At a minimum, clinical experts should have specific clinical expertise within the relevant disease area, and have experience interacting with patients who suffer from the illness or condition.

PhRMA and ICER have a mutual interest in the development of sound, patient-centered decision support tools. We appreciate ICER's engagement with our industry in the revision of its value framework, and hope that you consider incorporating our feedback as the framework evolves.

Sincerely,



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