

October 26, 2015

Steven D. Pearson, MD, MSc, FRCP
President
Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, Massachusetts 02109

Re: Value Assessment Framework

Dear Dr. Pearson,

I am pleased to write on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA) to convey our feedback regarding the value framework released by the Institute for Clinical and Economic Review (ICER) on September 8, 2015. 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 and our member companies are also committed to the development of sound evidence to demonstrate the clinical and economic value of new medicines in an evolving health care market. In addition to the extensive, high-quality research conducted by manufacturers, both in pre-market clinical trials and ongoing post-market research, this commitment is reflected through our principles in support of evidence-based medicine and leadership in independent research organizations and consortia such as the Patient-Centered Outcomes Research Institute (PCORI).

PhRMA appreciates ICER's work to develop and encourage use of assessments of new medicines and other interventions to support sound, evidence-based decision-making at all levels of health care. The framework developed by ICER is one of many tools that are designed to assess the value of health care interventions based on available evidence. As you know, others include the technology assessments conducted by federally-supported agencies and organizations such as the Agency for Healthcare Research and Quality (AHRQ) and PCORI, as well as third-party assessments conducted by groups including the Cochrane Collaboration¹ and the ECRI Institute². More recently, several oncology specialty organizations have developed tools that seek to evaluate and communicate information on the value of treatments to providers and patients. The diversity of these tools and frameworks for evidence-based decision-making reflects the complexity, clinical nuance, and rapid change that is intrinsic to value assessment, particularly in an area like biopharmaceuticals where the role of treatments, relevant comparators, clinical evidence base, and cost information can all change rapidly after introduction of a new treatment.

¹ Cochrane Collaboration. <http://www.cochrane.org/>

² ECRI Institute. <https://www.ecri.org/about/>

In light of these issues, as well as the extent to which more subjective assumptions and interpretations of research results are an element of value assessments such as ICER's, we recommend against including a national "target" price for new tests and treatments, as these recommendations will be based on a flawed model and inaccurate assessments of "provisional value," and will fail to reflect the dynamic and variable nature of value as it is achieved in the private sector.

We urge ICER to address the remaining flaws in its framework as discussed below, particularly as it attempts to link its assessments to pricing or policy recommendations. PhRMA appreciates the steps ICER has taken to engage the biopharmaceutical research sector in the development of its value assessment model, and the steps it has taken to consider and respond to input on product-specific assessments it has conducted using the model. We hope that ICER will consider the additional steps we outline below to further improve the openness and transparency of the model and the assessments ICER develops based on it.

PhRMA is concerned that the approach ICER takes in its value framework could confuse decision-makers about the value of new tests and treatments, and makes assumptions that create inherent bias against innovation. We are concerned that because the value framework does not adequately consider the patient perspective or the heterogeneity of patient populations, its use could result in barriers to high-value, individualized treatment decision-making and patient access to appropriate medical treatments.

Inherent Biases Against Innovation

PhRMA is concerned that ICER's model purports to identify "provisional" and "achieved" value, but uses methods that in the health system value phase of the analysis that are rooted in budget impact thresholds rather than broader value metrics. This could lead to confusion and result in the erroneous conclusion that policy is being set based on a value assessment when in fact it is based on a cost containment objective. ICER should rename the "health system value" phase of the analysis to "budget impact" or modify its methodology to avoid potential confusion.

In addition, PhRMA is concerned that the ICER model contains inherent biases against innovative technology that have the potential to improve the lives of millions of patients and improve the efficiency of the health care system. Additionally, ICER's value framework focuses narrowly on new drugs and devices rather than looking at a broader range of medical items and services. Further, it establishes budget impact thresholds based on the number of drugs and devices recently approved by the Food and Drug Administration (FDA), which have the effect of penalizing most heavily those sectors that are most innovative, and discouraging high-risk investments in therapeutic areas of high unmet need such as Alzheimer's disease.

- *Static budgetary allocations ignore opportunities for health system efficiency via reallocation achieved via innovation.* PhRMA recommends that ICER adjust its methodology to account for the potential efficiencies created by medical innovation. ICER's current methodology assumes that the allocation of spending in the health care

system does not change, and that less efficient medicines or treatment strategies continue, even as more efficient and innovative therapies are introduced. By ignoring the long-term benefits, medical cost offsets, and improvements in total cost of care of a new therapy, access could be denied or limited to drugs yielding substantial benefits simply because of their up-front impact on spending. Because the budgetary thresholds are based on increases relative to current spending, implementation of the ICER methods favors the status quo, regardless of the value or effectiveness of existing treatment coverage and/or other medical interventions. A new drug could be far more cost effective than any number of medical or surgical services that are provided in current practice, yet access could be denied on the basis of total projected spending on the new innovation. ICER's current methods have the potential to constrain progress and suggest that society does not prefer to allocate more resources to productive and valuable goods and services and fewer resources to others in the future.

- *Evaluation of medical technology only at the time of launch.* ICER should consider revising its approach to valuing medical technology to account for the evolving nature of a medicine's role and full clinical value over time. The apparent value of a new medicine can evolve not only due to changes to a therapy's place in a line of treatment, but also changes in the evidence base. A recent report by Boston Healthcare Associates underscores this point, showing how ongoing research revealed greater clinical value than that demonstrated in initial clinical trials of new treatments for lung cancer, renal cell carcinoma, chronic lymphocytic leukemia, and multiple myeloma.³
- *Creation of disincentives to develop innovative treatments for large populations.* PhRMA is concerned that ICER's approach to assessing the budgetary impact of new medicines is biased against innovations that treat large patient populations. All factors equal, a drug that will benefit more people is also more likely to violate ICER's spending threshold. Under ICER's approach, new medicines that increase total costs by more than the threshold amount could be denied coverage in the second stage of the value framework, even if the new medicines or care options were found to have significant "care value" in the first stage. PhRMA is concerned that if ICER's methods were accepted by payers and policy-makers, it would disincentivize the biopharmaceutical industry from producing new drugs that benefit larger fractions of the population. If an ICER-type standard had been in place, then the significant progress we have made against serious diseases and conditions with high public health burden, like HIV/AIDS and cardiovascular disease (CVD), likely would not have occurred.

³ Nicole Sweeney and Thomas F. Goss, PharmD. The Value of Innovation in Oncology: Recognizing Emerging Benefits Over Time. May 2015.

- *Exclusion of existing technologies.* ICER should also apply the value framework to existing treatments and services, rather than focusing exclusively on new treatments. By focusing solely on new treatments and technologies, ICER is disregarding potential inefficiencies within current standards of care, which could be eliminated in favor of newer, more efficient treatments that will result in better outcomes and savings for the health care system.
- *Use of single point-in-time assessment of value.* Another way in which ICER's value framework contains inherent biases against innovation is its use of single point-in-time assessments of value. Some of the outcomes which ICER acknowledges as important, such as likelihood of some patients to have long-term response within average equivalence, often will not be available at the time of a drug's launch.

Consideration of Differences Among Patients

ICER's calculation of value based on net health benefit (NHB) is likely to overlook differences in patient needs and values. While we appreciate that ICER has acknowledged the importance of considering patient differences, we are concerned the value framework model is moving in the opposite direction of precision and patient-centered medicine. Issues with the limitations of NHB in recognizing patient heterogeneity recently were acknowledged by the American Society for Clinical Oncology, for example, in its development of a draft value framework for cancer drugs.

Recently, stakeholders have called for a "move beyond traditional approaches to comparative effectiveness research and health technology assessments to achieve better alignment with patient needs and values, as well as with the emerging science." Ultimately, the goal should be to help patients understand trade-offs presented by the range of health care or treatment options and how population-level data applies to them as an individual.

Patients are a heterogeneous group with variable circumstances and preferences. Even assuming that patients assess treatment options on the same dimensions of value, individual patients will weight each dimension differently according to their individual circumstances. For example, a study published in *Health Affairs* asked patients to compare two treatment regimens for melanoma that, statistically speaking, yielded equivalent survival gains. However, when one regimen provides assurance of a shorter survival gain, and one offers a 50 percent chance of twice the survival gain, a large majority of cancer patients chose the latter.⁴ Such choices are not easily captured in a value framework like ICER's which may evaluate these regimens as equivalent. Heterogeneity of comorbidities and physical condition may also drive varied patient preferences; these factors will have a direct impact on patient outcomes and should also be accounted for in ICER's value framework.

⁴ Lackdawalla, D., et al. How Cancer Patients Value Hope And The Implications For Cost-Effectiveness Assessments Of High-Cost Cancer Therapies. *Health Affairs*. April 2012.

Transparency in Model Design and Assumptions

PhRMA recommends that ICER improve the transparency of the overall model design and assumptions. This information is necessary in order for stakeholders to effectively evaluate the reliability and validity of the model. Given the “black box” structure of Markov models, providing sufficient transparency with respect to assumptions and parameters is important in order for stakeholders to ascertain whether both the modeling strategy and the subsequent results are reasonable. ICER should consider releasing a working copy of the model so the assumptions and calculations can be examined in more detail. In addition, ICER should provide a more robust discussion and technical appendix to accompany its reports so that stakeholders can validate the value framework’s methodology for determining care value.

Identification of the Relevant Patient Population

The identification of the potential patient population for a new medical technology, including the evaluation of differences in risks and benefits in different patient subpopulations, has critical implications for how a value assessment tool evaluates the efficacy of the technology. If this initial step is flawed, it undermines the results of the analysis, and could result in misinformed decision-making by patients, providers, and payers. We are concerned that ICER’s method may lead to overestimates of the population of patients who will receive a new test or treatment.

There are several examples of such issues in ICER’s report regarding PCSK9 inhibitors. For example, it appears that in the PCSK9 inhibitor report, there are several problems with the methodology used to identify the potential familial hypercholesterolemia (FH) patient population that skew the results of the value assessment, including the age range chosen for the baseline patient cohort. ICER censors the baseline patient cohort to patients between the ages of 35 to 74, even though the risk of CVD-related events increases dramatically with age. In the future, ICER should take care to accurately represent the relevant patient population in analyses, and engage stakeholders who have expertise related to the specific indication of the drug evaluated, including patient advocates and health economists.

Flawed Parameter Assumptions

PhRMA recommends that ICER, as part of its value framework methodology, ensure that its assumptions are consistent with research found in published literature. For example, in the PCSK9 inhibitors report, ICER estimates six years of discounted life-years gained per death. This estimation is at odds with the recent U.S. burden of disease report from the Institute of Health Metrics and Evaluation, which suggests an underestimation of 12 life years gained per death averted.⁵

This discrepancy suggests that the values of the interventions are being underestimated by the methodological approach being taken. To prevent decision-makers from undervaluing medicines,

⁵ Murray, C.J., et al., The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. *JAMA*, 2013. 310(6): p. 591-606.

and potentially limiting patient access to appropriate treatments based on information that is inconsistent with widely-accepted research, PhRMA strongly encourages ICER to ensure that its methodology for evaluating new medicines is consistent with peer-reviewed, respected literature involving similar analysis.

Consideration of Patient-Centered Outcomes

In any value assessment tool, whether it is intended for use by patients or not, it is imperative that the patient's perspective is at its center. Although ICER has stated that its value framework accounts for "contextual consideration" and "other benefits/disadvantages" of medicines, it is unclear what specific patient-centric endpoints are accounted for and how those facets of value are incorporated into its findings. In its 2013 report, "Delivering High Quality Cancer Care: Charting a New Course for a System in Crisis", the Institute of Medicine notes that patient-reported outcomes are widely accepted by authoritative regulatory bodies such as the FDA and the European Medicines Agency. This is particularly true for validated PRO instruments. The report also notes that patients often report different outcomes for treatments than providers and researchers.⁶ It is important that stakeholders continue to find ways to collect such data, and PhRMA encourages ICER to ensure that data based on patient-centric endpoints are included in its value framework, if they are not already accounted for.

Undervaluation of Long-Term Benefits of Medicines

PhRMA recommends that ICER expand the time horizon of its value framework in order to better account for the long-term benefits offered by innovative medicines. Spending on health care is akin to an investment, and is valuable in part for the benefits it provides over time and in the future. ICER's focus on total cost alone within a five year time span, with no attention to benefits that a therapy may offer long-term in the form of improved outcomes and savings in other areas of health care, will not lead to sensible decision-making by health care stakeholders. PhRMA recommends ICER revise its approach so as not to undervalue medicines that may require an investment up front, but result in significant future benefits to patients and the health care system.

Misrepresentation of Drug Prices

PhRMA is concerned that ICER value assessments will inevitably lag price discounts that are driven via negotiations between manufacturers and payers in the private sector, particularly since discounts are frequently significant, proprietary, and occur rapidly after initial introduction. This dynamic was evident with new medicines for treating hepatitis C infection, for which private purchasers rapidly drove significant discounts, requiring ICER to issue a press release acknowledging that its initial assessment did not reflect discounts that had already been

⁶ Institute of Medicines. Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis. September 10, 2013.

negotiated.⁷ ICER should adjust its methodology for calculating “provisional health system value” so it better reflects actual prices for new medicines, and may want to consider waiting for a period of time after a new product is first introduced to permit collection of more accurate price data.

Use of Flawed GDP-Based Threshold

PhRMA has concerns regarding the “GDP + 1” – based threshold ICER’s value framework uses to assess health system value. The concept of imposing budgetary threshold that pays no attention to the value of medical innovations is fundamentally flawed, regardless of the threshold ICER sets. Additionally, if ICER does not appropriately set its budget threshold, there is greater risk that innovative treatments will violate that threshold, which may result in reduced patient access than would be the case with more widely accepted assumptions on the growth rate of the GDP. PhRMA has particular concerns about the “GDP + 1” budget threshold used in the value framework, and encourages ICER to continue to revise its approach to calculating the budget impact of innovative medicines.

- *Potential issues with estimations of GDP growth.* GDP growth varies substantially over time and predictions of GDP growth can vary among sources. There is potential for volatility in the cap over time and it will swing with changes in the business cycle. Therefore, whether a new drug is challenged by stage two of the ICER methodology may depend on when the drug happens to be ready for introduction, and when ICER most recently updated its budget impact threshold. Additionally, several estimations of GDP growth, including those by the Congressional Budget Office and the Center for Medicare and Medicaid Services are higher than the estimates used by ICER.
- *Volatility in the number of new drugs introduced.* In the budgetary phase of the ICER value framework, the methodology calls for dividing a number that represents allowable growth in national drug spending by the average over the past two years of the number of newly approved drugs per year. Although that number was 34 over 2013 to 2014, the number varies widely over time. In 1998, the two-year average would have been 46. In 2004, it would have been 19. Even looking at decade-long averages, the number of new drugs introduced varies substantially over time. Such methods would result in significant variations in the cap over time and capricious changes in access to innovative drugs.
- *Setting allowable spending growth amount per new drug.* Because ICER’s value framework calls for calculating its cap on health care spending growth by dividing their allowable growth in drug spending by the average number of annual drug introductions over the previous two years, more new drug introductions result in a lower future cap and vice versa. Thus, ICER risks generating perverse incentives for the biopharmaceutical industry.

⁷ Institute for Clinical and Economic Review. “New Lower Prices for Gilead Hepatitis C Drugs Reach CTAF Threshold for High Health System Value.” <http://www.icer-review.org/new-lower-prices-for-gilead-hepatitis-c-drugs-reach-ctaf-threshold-for-high-health-system-value/>

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If the industry is more productive in terms of new introductions, the cap becomes more severe in the future, making it more difficult for patients to get access to newly introduced drugs in the future.

PhRMA and ICER have a mutual interest in promoting informed, evidence-based shared decision-making by stakeholders at all levels, including payers, policymakers, physicians and patients. We appreciate ICER's engagement with the biopharmaceutical industry in the development its value framework, and hope that you continue to incorporate our feedback as the framework evolves.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Randy Burkholder', with a long horizontal flourish extending to the right.

Randy Burkholder
Vice President, Policy & Research