



## **Comments Received on ICER's Value Assessment Framework**

*ICER opened a national call for proposed improvements to its value assessment framework to inform a planned 2017 update. ICER accepted comments on the framework from July 2016-September 2016. Over 50 sets of comments were received from patient groups, clinicians, life science companies, and other stakeholders. The following pages contain comments from those organizations that allowed us to make their comments public. Note that by clicking on an organization name in the Table of Contents you will be taken to that group's submission.*

**October 3, 2016**

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BIO: Biotechnology Innovation Organization

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PhRMA: Principles for Use of Evidence-Based Medicine: Advancing Patient Care and Health Care Value

Patients Rising

Quorum Consulting

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Sanofi

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St. Jude Medical

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September 12, 2016

Steven D. Pearson, MD, MSc, FRCP  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

***RE: ICER National Call for Proposed Improvements to its Value Assessment Framework***

Dear Dr. Pearson:

The Academy of Managed Care Pharmacy (AMCP) thanks the Institute of Clinical and Economic Review (ICER) for the opportunity to provide comments in response to the national call for suggestions on how to improve its value assessment framework released on July 14, 2016. AMCP appreciates the work of ICER in developing its value assessment framework and believes that it is important and critical to help move health care in the United States towards a value-based model, and further applauds ICER for seeking public feedback on how it can be improved. ICER's value assessment framework is one of the many tools utilized by managed care pharmacists and other health care providers in their comprehensive and holistic approach to evaluating the totality of evidence in determining whether medications and other health services are appropriate for the patient populations they serve. AMCP offers comments on the following elements of the ICER value assessment framework that it believes should be re-examined to further enhance the utility and relevance of the value assessment framework:

- Transparency, adaptability, and usability of the economic model
- Incorporation of real-world evidence and patient-reported outcomes
- Stakeholder representation on voting panels

AMCP is a professional association of pharmacists and other practitioners who serve society by the application of sound medication management principles and strategies to improve health care for all. The Academy's 8,000 members develop and provide a diversified range of clinical, educational, medication and business management services and strategies on behalf of the more than 200 million Americans covered by a managed care pharmacy benefit.

## **The Economic Models Used in the ICER Value Assessment Framework Should be Made Available to Managed Care Pharmacists and Other Health Care Providers**

While AMCP appreciates that the general components considered in the ICER value assessment framework are transparent, the economic models used to evaluate treatments are currently not made publicly available. AMCP supports economic models that when appropriately used, should be transparent, disclosed, reproducible, accurate, and valid. Furthermore, AMCP believes economic models should be made available to managed care pharmacists and other health care providers to download, audit, and test the model by modifying the assumptions of the model based on their perspectives and their covered populations.<sup>1</sup> Specifically, the availability of the economic models would, at minimum, allow for the following:

- Realistic adoption rates that accurately reflect the anticipated uptake of a medication based upon utilization management programs and/or the relevance to the population served;
- Consideration of an appropriate quality-adjusted life year (QALY) threshold after consultation with available literature or an organization's bioethics committee;
- Adjustment of the cost of a medication to more accurately represent the actual acquisition cost;
- Flexibility to extrapolate the data for a short-term (one year) versus long-term (five years) forecast to better understand the immediate budget impact versus overall value of the medication;
- Adaptability for rare diseases or precision medications; and
- Validation that the economic model is applicable to the relevant patient population.

In addition, AMCP urges ICER to consider a process by which stakeholders could be given an opportunity to test and validate the economic models when in draft format and provide feedback on how they can be improved prior to finalization. With this approach, the economic models are more likely to reflect current real-world conditions.

In supporting the need for transparent economic models, AMCP also recognizes that it is important to ensure that individuals who have access to the models have the appropriate training and qualifications to properly evaluate and modify the model. Therefore, AMCP recommends that ICER consider a free licensing process that would allow ICER to evaluate the qualifications of the requestor prior to releasing the economic model, similar to the approach used by the National Institute for Health and Care Excellence (NICE). Many managed care pharmacists have considerable expertise in pharmacoeconomics and therefore, AMCP recommends that ICER work with AMCP and other stakeholders to develop the list of criteria to use in selecting eligible recipients of the economic models and the creation of a process to minimize barriers to access.

## **The ICER Value Assessment Framework Should Incorporate Real-World Evidence and Patient Reported Outcomes**

AMCP commends ICER for reviewing and incorporating a diverse catalog of studies in its value assessment framework. However, AMCP urges ICER to develop a process for incorporating real-world evidence (RWE) and patient reported outcomes (PROs) into the catalog of evidence that informs the economic models for its value assessment framework. Furthermore, AMCP urges ICER to include managed care pharmacists as a key stakeholder during this process because many are pharmacoeconomic experts and have been collecting, analyzing, and using RWE in their practice settings for many years. In addition, pharmacists are easily accessible to patients and collect PRO data through the provision of pharmacy services such as academic and non-academic outcomes research, payer clinical programs and disease management, medication therapy management, and patient counseling.

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<sup>1</sup> AMCP Partnership Forum: FDAMA Section 114—Improving the Exchange of Health Care Economic Data. *Journal of Managed Care & Specialty Pharmacy* 2016 22:7, 826-831

**Voting Panels for ICER Value Frameworks Should Include Broad Stakeholder Representation with Pharmacoeconomic and Clinical Expertise**

AMCP urges ICER to ensure voting panels include managed care pharmacy representation, clinical experts in the specific disease state being evaluated, other health care providers, and the patient perspective. Finally, AMCP urges ICER to develop a transparent process and minimal qualifications to ensure that voting panel members have an appropriate knowledge of what pharmacoeconomic information is, understand the concept of overall value versus cost, and can evaluate the economic models for credibility.

AMCP appreciates your consideration of the concerns outlined above and looks forward to continuing work on these issues with ICER. If you have any questions regarding AMCP's comments or would like further information, please contact me at 703-683-8416 or [scantrell@amcp.org](mailto:scantrell@amcp.org).

Sincerely,

A handwritten signature in black ink, appearing to read 'S. Cantrell', with a stylized, flowing script.

Susan A. Cantrell, RPh, CAE  
Chief Executive Officer



September 12, 2016

Steven D. Pearson, MD, MSc, FRCP  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

Re: Institute for Clinical and Economic Review Call for Stakeholder Feedback

Dear Dr. Pearson,

The Advanced Medical Technology Association (AdvaMed) is pleased to provide the following comments in response to the Institute for Clinical and Economic Review's (ICER) request for stakeholder input.

AdvaMed is the national association of manufacturers of medical devices and diagnostics. AdvaMed member companies develop and manufacture the medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatments. AdvaMed members range from the largest to the smallest medical technology innovators and companies. We are committed to ensuring patient access to life-saving and life-enhancing devices and other advanced medical technologies in the most appropriate settings.

As the United States health care system moves more services and care from a volume-based system to risk-based value system, the need for more and better resources to understand value are important. This shift offers the promise to improve the quality of care, become more patient-centered, and slow healthcare cost growth. Medical technology companies are acutely focused on these issues and seek to be partners with patients, physicians, hospitals, other providers and payers to support high quality, patient-centered care in new risk-based value approaches.

We appreciate ICER's goal to help provide value assessments of new services and biopharmaceutical and medical products. We also appreciate ICER's recent efforts to engage with other stakeholders and its request for feedback on its value framework approach. We believe assessing value has to be a flexible process that is continually responding to improvements in science and service delivery and we are encouraged by ICER's openness to address stakeholder concerns in its framework.

In general, we believe ICER's current framework is not well suited for the wide variation and heterogeneity of medical technology products and their associated value propositions. We recommend that ICER make significant changes to its approach and engage the medical technology industry directly to improve and potentially develop more customized frameworks that more appropriately assess different categories of medical technology and diagnostic products.

More specifically, our letter provides comments on the following topic areas: (1) Price versus value; (2) Appropriate evidence for demonstrating the value of medical technologies; (3) Patient access; (4) Timeframes for considering value; (5) Stakeholder engagement; and (6) Transparency. Additionally, we have also attached a letter from Hal Singer, Ph.D., a Principal at Economists Incorporated, an Adjunct Professor at Georgetown University's McDonough School of Business, and a Senior Fellow at George Washington University's Institute for Public Policy. We asked Dr. Singer, to conduct an independent analysis of ICER's framework.

### **ICER's framework relies too heavily on estimating the cost per Quality Adjusted Life Year (QALY) gained**

With its strong emphasis on budget-impact analysis to attribute value to new innovations, in particular medical devices and diagnostics, ICER takes too narrow a view of what determines the value of a medical technology. Medical technologies can offer value for multiple parties within the health care system—improved health for patients, improved productivity for clinicians and staff, and potentially reduced expenditure for payers. Multifaceted value cannot be based predominantly on the incremental cost per QALY achieved, as the ICER framework seems to suggest.

AdvaMed believes medical technology assessment should encompass multiple categories of “value” which should be used in any evaluation of the value of a medical technology. Assessment of value should include clinical impact, non-clinical patient benefits, care delivery economics, and societal benefits. Each of these categories is a relevant value measure at a time when the nation's health care system, reflected in both public and private payer programs, is undergoing rapid transformation, and where patient preference, patient engagement in decision-making about a specific course of treatment, personalized medicine, and broad population health are major goals that stakeholders desire to see in the new system.

While ICER's model references comparative clinical effectiveness, incremental cost per outcomes achieved, other benefits or disadvantages, and contextual considerations, the broader determinants of value we highlight above are not adequately factored into ICER's calculation of cost per QALY achieved. Nor does the ICER framework take into account that value is prioritized differently by stakeholder group and by individual patients within a given patient stakeholder group. The ICER model's use and overemphasis on “value-based price benchmarks” diminishes the variation in prioritization that different stakeholders will consider for determining value drivers. With its emphasis on incremental cost per QALY estimate, individual patient preference and physician clinical expertise about the appropriateness of a particular treatment



option for patient care are inappropriately diminished. In this regard, ICER's assessments can have serious negative consequences for patients' access to all appropriate treatment options that should be available for an individual patient's medical condition because, in part, health plan use of ICER recommendations could lead to significant gaps in access to new technologies.

**Evidence demonstrating value of medical technologies must rely on multiple sources and go beyond RCTs**

In its individual value assessments, ICER has relied heavily on randomized clinical trials (RCTs) as the most appropriate evidence for demonstrating value. In fact, ICER's calculation and heavy reliance on Quality Adjusted Life Year (QALY) as a measure of value overweighs use of RCTs which is challenging for many medical technologies and diagnostics. While RCTs are a useful tool, practical and ethical barriers due to a lack of clinical equipoise often make it impossible for RCTs to be used for certain medical devices and diagnostics, particularly when concurrent skilled medical interventions such as surgery are a required element of their use. A practical barrier in this instance would involve the RCT demand that neither the patient nor the clinician know whether the patient has been assigned to the study or control group. An ethical barrier would involve, for example, exposing patients to ineffective surgeries from which they cannot benefit and which entail significant risk. The FDA recognizes these concerns, which is why it does not require RCTs in such circumstances.

Evidence that is considered appropriate for assessing value of medical technologies will vary for an industry characterized by a heterogeneous mix of therapeutic and diagnostic medical technologies and their primary users. Medical technologies range from implantable orthopedic and cardiovascular devices to minimally invasive surgical instruments to imaging and radiation therapy equipment, and drug delivery devices and point of care diagnostic tests. Devices and diagnostic tests also vary widely in their levels of complexity and degrees of risks and benefits for patients and care providers. Given this diversity, a "one size fits all" set of guideline principles or a specific checklist for evidence generation encompassing such a broad range of technologies is both inappropriate and impossible to develop.

Many medical technologies are also embedded in complex processes of patient care, where patient, provider, and institutional factors can have a significant impact on clinical and economic outcomes and complicate the perceived value of the technology itself. Medical device effectiveness is very often affected by how well they are deployed. Operator expertise and patient care setting have been shown to affect surgical outcomes but appropriate methods for taking them into consideration often are not incorporated into evaluations. As a result, it can be difficult to separate multiple confounding effects from the measurement of the technology intervention and costs. In addition, a learning curve effect in which the measured effectiveness of an intervention improves over time as a result of improving clinical proficiency of the physician and care delivery site experience can confound comparison between one intervention and another. Evaluations of clinical and economic impact must be carefully constructed and timed in order to control for confounding factors, with the recognition that study designs for these types of interventions are more complex than some other traditional interventions.

Furthermore, medical technology innovation often proceeds incrementally and continuously. After devices come to market, product improvements continue to accumulate over time, altering their clinical and cost-effectiveness. Therefore early assessments may underestimate effectiveness, and assessment conclusions may quickly become out-of-date as devices and their uses evolve. Any framework that evaluates clinical and economic value of a medical technology should include provision for regular review to ensure incremental improvements and innovation are adequately considered.

Diagnostic and imaging technologies present their own special analytic challenges. The core challenge is that the value of a diagnostic technology lies in enabling improved clinical decision-making and therapy selection, distinct from the value of the underlying therapy intervention itself. Additional clinical evidence development following product launch may be essential to driving adoption of these technologies and demonstrating their value.

Because of these unique characteristics, value assessment should acknowledge a range of types of evidence and associated methodologies that are appropriate for assessing the value of different types of medical technologies.

One broad alternative approach to RCTs for generating evidence for medical technologies is the use of various types of observational studies that may produce equally or more relevant data for medical technology value assessment. Circumstances when observational studies may be relevant for generating evidence of value for medical technologies include situations when evidence can only be provided through large or long-term studies, when treatment adherence varies among different technologies, when the only alternative to one treatment approach is an alternative such as surgery for which crossover designs are not possible, when providers have different levels of training that may affect patient care outcomes, or when a new technology's value lies in the process efficiency it brings to the health system. Observational studies have an important role to play in generating data that are collected under real-world practice circumstances and can include several different designs: retrospective and prospective studies, cohort studies, case-controlled studies, and cross-sectional studies.

Registries, another broad category of research, generally use observational study methods to collect uniform data, both clinical and other data, to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose. Registries are used for collecting data on long-term patient follow-up or for patient longitudinal studies. Certain registries, which combine patient data and archived medical samples, have provided for breakthroughs in the understanding of disease diagnosis, progression, and treatment, especially in oncology.

AdvaMed recommends that evidence required for value assessment should use all of the appropriate, sound, and high quality evidence that is available at the time of assessment, including evidence from outside the U.S. Value assessments should also incorporate flexibility to accommodate limited evidence available at approval or launch to allow a novel product with high expected value to be available for patient care.

Finally, many new to market and breakthrough or disruptive technologies can often be proven safe and effective for FDA approval, but still be in the process of developing more data needed for value assessment. These can often be low volume or slowly diffused technologies. In cases that show great promise for treating diseases in new ways or disrupting care patterns, but that may have limited data, ICER should refrain from reviewing these technologies until adequate information is available and outcomes in real-world practice become more widely available. A decision to rate a new technology as low value, simply because it is a new device that is still developing evidence is inappropriate and could have significant impact on patients and the ability to fulfill the promise of care improvement the technology offers.

### **Cap on annual spending for innovative medical devices/diagnostics will lead to compromised patient access to these products**

The ICER model is built on an assumption that spending on new medical devices and diagnostics should increase overall health care spending by not more than the anticipated growth in national Gross Domestic Product (GDP) + 1%. The budget cap puts medical devices and diagnostics at an unfair disadvantage in two ways. First, as long as device spending as a share of total national health care spending is lower than that for prescription drugs, the cap for device and diagnostic spending will always be lower than the cap for prescription drugs. This means that if two technologies, one drug and one device, are launched at the same time for the same indication, with the same effectiveness and the same net price, the device could fall above the cap allowed for devices and not be eligible for coverage and the drug below the cap for drugs and eligible for coverage. By essentially making all new devices and diagnostics coming out in a year compete for revenue under a GDP cap, wrong conclusions about its value will be made. A new device or diagnostic should be compared to the standard of care that is already on the market. If it is cost-effective and has a better budget impact than the standard of care, this new product should be used, regardless of how many other products also have similar cost-effectiveness that year.

The cap concept also sets up an untenable target for innovative medical devices and diagnostics, for which there are literally thousands of Food and Drug Administration (FDA) approvals in a given year. For devices and diagnostics in 2015, FDA approved 43 original pre-market approvals (PMAs), 829 additional PMA supplemental approvals, and 3,047 510(k) clearances. FDA recently released that there are 175,000 devices used in the US. Spending for medical devices and diagnostics as a percent of total national health care expenditures has been about 6.0 percent for the past 20 years, while prices for medical devices have actually grown far more slowly than the Medical Consumer Price Index or even the overall Consumer Price Index. Over the period 1989 to 2013, medical device prices have increased at an average annual rate of only 0.9 percent, compared to 4.5 percent for the MC-CPI and 2.7 percent for the CPI. While spending increases and decreases for various technologies, the consistency in national health spending, combined with low price growth, shows the high degree of interaction and replacement of products in the market and indicates an industry that is highly competitive. ICER's budget impact criterion is unnecessary for medical technologies and a veiled attempt to artificially drive down prices.

Even if ICER's budget impact concept is intended to be applied only to original PMAs, it assumes that the "value" of a new product in the last analysis is defined fundamentally by its incremental cost per QALY achieved—and that all new medical technologies are accompanied by high costs that need to be controlled. Linking the value of a new product primarily to its cost per QALY does not recognize the impact the innovation can have on improved health outcomes. Nor does it recognize that the innovative product can represent an improvement, both in terms of efficiency and quality, over the current standard of care. As a result, patient access to innovative care may be compromised because payers will translate cost into non-coverage decisions, and company interest in finding innovative approaches to health care conditions may be discouraged. As we have argued above, the value of medical technologies is multi-dimensional and any framework that is applied to individual products should reflect this reality. Additionally, a value framework for diagnostic tests will completely differ from that for a medical device, particularly as it relates to the necessary evidence.

In addition, the assumptions ICER makes regarding market uptake and use for a new technology can dramatically swing estimates for the price benchmarks. ICER has not shown any sensitivity analysis in its reports on the various use rates and has vastly overestimated technology use in previous studies. With the majority of new technologies, physician education and training needs often leads to slow diffusion of the new technology and often only a small portion of the eligible patient pool can actually receive a new technology. This is because physicians may be unaware of the technology, not be trained to use the technology, or be in a facility where the technology is unavailable. It is very difficult to fully understand the uptake rate of a new technology upon approval and applying this budget constraint with limited data and without showing the range of estimates is highly problematic.

In the medical technology industry, the life cycle of a product can be very short and competing products or updated generations of a given product enter the market much more quickly, driving up competition and lowering prices. Additionally, most technologies understand that the Medicare program and many private payers will seek to fit a new technology into existing payment mechanisms such as inpatient Medicare Severity-Diagnosis Related Groups (MS-DRGs) or outpatient ambulatory payment classification (APCs) which naturally creates downward pressure on prices as these technologies enter the market. ICER's artificial mechanism is unnecessary and highly inappropriate.

With the multitude of highly uncertain factors determining both the rate of diffusion and the price dynamics, ICER should eliminate the budget impact criterion from its value framework.

Given the relatively slow medical technology diffusion rates, difficulty measuring use rates, and the problems in setting a spending "limit" on new devices, the notion that ICER's model needs to reflect an "alarm bell" is flawed and should not be a part of the assessment process.

**5-year period for limit on value is inappropriate for many medical technologies that provide value over many more years**

The ICER model considers cost and value of an innovation only over a short timeframe—5 years. In so doing, it does not recognize that many medical devices and diagnostics have value for much longer period of time, e.g. 20 years for joint replacements, or even for the lifetime of the patient. With diagnostics, for example, long-term outcomes may depend on a variety of treatment decisions throughout a complex care pathway. With the improved negative predictive value of screening tests, such as the HPV screening assay, recommended screening intervals are being lengthened to 5 years and beyond for some screening programs. A model that limits value to 5 years would be inadequate to account for multiple 5-year intervals of screening and thus would be insufficient for public health decision-making. Therefore, applying the full price/cost of a new technology in the short term without accounting for longer term benefits creates a lower value estimate that is inappropriate for many new technologies.

ICER's framework, if applied as drafted, would thus reward a calculus that trades a higher-priced device that needs only be implanted or used once, for a lower-priced device requiring replacement at 5-years' time. Such a choice for short-term low-price over long-term value may ultimately harm health care budgets. ICER should take care that the frameworks it creates does not inadvertently reward short-term innovation dynamics at the expense of health care value and patient care over the longer term. AdvaMed recommends that ICER consider a time-horizon for devices that considers long-term durability of the product and patient longevity.

### **Process for stakeholder engagement**

ICER's processes must allow for all relevant stakeholders to engage in the development of its value assessments and to make meaningful contributions to these reports. Meaningful engagement, as a policy, is imperative, particularly where ICER's assessments focus on diseases or conditions, or on specific medical technologies requiring particular knowledge or expertise. Value, actual or perceived, will very likely differ across a wide range of stakeholders, including patients and patient advocacy groups, providers, payers, and manufacturers of the medical technologies and diagnostic tests.

ICER should incorporate a process for stakeholder engagement that includes not only ample opportunity for stakeholders to provide comments and insights regarding the technology being assessed, but also that explains whether and how those comments were considered in the development of the final report. Clinicians with expertise in the area of assessment should be included in the analysis. A meaningful comment period should be at least 45 – 60 days, in order to allow stakeholders enough time to develop comments that are relevant and useful to ICER. Often, stakeholders are challenged to replicate ICER's analysis, to understand particular assumptions made by ICER, including assumptions about indirect benefits and costs, and perhaps to perform independent analysis and provide feedback within the comment period.

The process could be greatly improved by incorporating the input of relevant stakeholders earlier in the process. AdvaMed has previously commented that the ICER review process could be improved through meetings with interested parties prior to drafting its reports, or at least prior to releasing the initial draft report to the public. Such meetings could promote discussion of specific

topics relevant to the review and evaluation, and could uncover issues that ICER may not have considered in advance or during the development of the report. Additionally, the regional affiliated organizations that use ICER reports (CTAF, Midwest CETAP, and New England CETAP) should change their processes to allow real stakeholder input, opportunity for comment, and stakeholder participation.

### **More transparency needed in ICER value assessment methodologies**

Embedded within value frameworks should be a commitment to transparency about the methods used for technology assessment. ICER needs to be more transparent about the models it uses for value assessment, making available to the public the assumptions that are used in the models and results of sensitivity analyses. AdvaMed also recommends that ICER make available the calculations, and coding required making the calculations, it uses for comparative effectiveness analysis.

AdvaMed appreciates the opportunity to provide this feedback to ICER and ICER's willingness to continue to work with stakeholders to improve its processes for assessing value in health care. I believe we share the common goal of improving the quality of care and services available in the US and we are committed to working with you to ensure that patients have access to high quality, life saving and life-enhancing technologies.

We would be pleased to answer any questions regarding these comments and appreciate any opportunities to work with you on these important issues in the future.

Sincerely,

A handwritten signature in black ink, appearing to read "Donald May". The signature is fluid and cursive, with a long horizontal stroke extending from the end.

Don May  
Executive Vice President  
Payment and Health Care Delivery



September 12, 2016

Institute for Clinical and Economic Review  
Steven D. Pearson, MD, MSc, President  
Two Liberty Square  
Ninth Floor  
Boston, MA 02109

RE: ICER National Call for Proposed Improvements to Value Assessment Framework

Dear Dr. Pearson,

The Asthma and Allergy Foundation of America (AAFA) is pleased to provide input on the 2017 update to Institute for Clinical and Economic Review (ICER)'s Value Assessment Framework. AAFA ([www.aafa.org](http://www.aafa.org)), a not-for-profit organization founded in 1953, is the leading patient organization for people with asthma and allergies, and the oldest asthma and allergy patient group in the world. AAFA is dedicated to improving the quality of life for people with asthma and allergic diseases through education, advocacy and research.

As noted by ICER and many other organizations, rising health care costs, as well as changing benefit designs, place increased pressure on care access and affordability. In this environment, it is more important than ever to address the issue of value, and to make sure these efforts are centered on care and outcomes that matter most to individuals, their families and caregivers.

One important element of this is making sure that patients, providers and other decision-makers have sound information and decision-support tools available to them. Understanding and defining the value of health care treatments and interventions is a national priority. AAFA is eager to take part in the value discussion. Patient perspectives on value often integrate considerations beyond clinical outcomes and cost, such as a treatment's ability to help patients achieve personal goals.

AAFA recognizes ICER's recent efforts to engage the patient community by, for example, appointing a patient representative to the governance board and by outlining a plan for gathering patient input in the scoping documents that inform ICER's reviews. However, we urge ICER to adopt a more open and collaborative process for identifying and appointing additional patient representation as well as create other opportunities for patient engagement.

Patients are critical members of the health care, drug development and innovation, research and policy making teams, and they must be given the opportunity to work side by side as equal partners with clinicians, researchers, payers, and policymakers in order to achieve the outcomes that are most important to them. Solving the challenges and problems of living with chronic diseases such as allergies and asthma requires active engagement of patients, families, and caregivers, in all issues relating to clinical discoveries and interventions, clinical trials, medical devices, regulation of drugs and devices, and their uses. Value



methodologies should consider diverse patient perspectives based on their unique circumstances, needs, treatments and life goals.

AAFA offers comments in the four areas ICER has identified as the highest priorities for potential revision to the framework.

***1. Methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value intended to fall in the current value framework within “additional benefits or disadvantages” and “contextual considerations”***

We commend ICER for recognizing the importance of integrating patient perspectives as a high-priority area to improve ICER’s value assessment framework. AAFA believes that there is a significant gap in appropriate, validated methods to integrate patient and clinician perspectives into value assessments and appreciates ICER’s effort to solicit more input in this area. AAFA is concerned, however, that the scope of this priority as articulated in the call for comments is too narrow and assumes that relevant patient-centered data is widely available for assessment. Specifically, the current scientific literature does not adequately incorporate patients’ perspectives, which underscores the need for a paradigm shift in how research is designed, conducted and evaluated. To imply that the current literature in any way includes appropriate incorporation of patient perspectives misrepresents the state of the field and, unfortunately, downplays the underlying need for gathering and considering these perspectives and the potential impact their inclusion can have on value assessments.

Therefore, AAFA encourages ICER to partner and collaborate directly with patients and patient advocacy groups and incorporate the patient voice in its value assessment process. We encourage ICER to acknowledge the fundamental deficiencies, gaps, and challenges in capturing and recognizing patient perspectives of value. We urge ICER to develop a more robust, systematic process for incorporating the patient perspective into its reviews and to make the process transparent and understandable to patients. Doing so will greatly improve and lead to greater credibility of ICER’s work.

AAFA recommends that ICER develop a more formalized patient-engagement process as part of its value assessment framework to ensure that the process and results are informed by patients, their families and caregivers. AAFA recommends that as part of each assessment, ICER describe how patient input and preferences were considered and incorporated to ensure accountability to patients, demonstrate responsiveness to patient input, and help patients better understand the information ICER uses.

AAFA recommends that ICER consider ongoing work that addresses the need for capturing the patient perspective including work undertaken by the National Health Council (NHC) and





the Partnership to Improve Patient Care (PIPC)<sup>1</sup>. The NHC, with stakeholder input, has created a Value Model Rubric to help evaluate the patient centeredness of value models and to guide value model developers on the meaningful incorporation of patient engagement throughout their processes.<sup>2</sup> PIPC held a roundtable discussion about value assessments with organizations representing diverse patients and people with chronic conditions and disabilities. The PIPC roundtable report elicits and captures diverse perspectives on patient-centeredness in value assessment. AAFA participated in these activities and shares the concerns noted in the PIPC report and supports ICER's use of the NHC's Patient-Centered Value Model Rubric.

***2. Incremental cost-effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures***

AAFA recognizes the importance of evaluating treatments and services to understand their comparative clinical and cost effectiveness. However, we stress that the appropriateness of outcomes selected is critical to the relevance and accuracy of determining value to patients. ICER should better reflect patient-centered outcomes. Quantifying value in a way that is useful and meaningful to individuals, their families and caregivers requires a basic understanding of their values and preferences. Doing so will benefit the patient and other stakeholders as they identify and integrate the appropriate patient-centered criteria in assessing the value of treatments for a particular condition. ICER's assessments should not conflate value considerations at the population level with value considerations experienced at the individual level, where real-world personal, clinical, outcomes and financial considerations differ from population-based models.

Again, input from the appropriate patient group for identification of outcomes that are important to them is critical to support a value assessment approach that is meaningful and has utility for individuals, their families and caregivers.

***3. Methods to estimate the market uptake and “potential” short-term budget impact of new interventions as part of judging whether the introduction of a new intervention may raise affordability concerns without heightened medical management, lower prices, or other measures.***

We are concerned that this ICER priority appears to focus solely on identifying methods that would help assess short-term affordability from the payer perspective and results in restricted access to care and treatments as an unintended consequence for patients. AAFA

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<sup>1</sup> PIPC ROUNDTABLE SUMMARY: ASSESSING VALUE TO THE PATIENT June 17, 2016  
[http://www.pipcpatients.org/pipc-admin/pdf/a19d1a\\_PIPC%20Roundtable%20Summary%20-%20Value%20to%20the%20Patient.pdf](http://www.pipcpatients.org/pipc-admin/pdf/a19d1a_PIPC%20Roundtable%20Summary%20-%20Value%20to%20the%20Patient.pdf)

<sup>2</sup> The Patient Voice in Value: The NHC Patient-Centered Value Model Rubric  
<http://www.nationalhealthcouncil.org/value>



urges ICER to also consider long-term outcomes and impacts from the patients' perspective. While interventions may have notable short-term budget impacts, they may not only greatly improve patient outcomes but can reduce the costs for a patient and the health care system over a longer period of time by reducing the likelihood of more costly interventions and/or poorer outcomes such as frequent emergency department visits, hospitalizations and/or surgeries.

Focusing on short-term (5 years or less) budget impacts in isolation, de-coupled from approaches that consider longer-term impacts over a person's lifetime, is not an appropriate or meaningful patient-centered approach to assessing the impact and value of interventions and services. As currently described, ICER's priority appears to focus too narrowly on the short-term impact for payers on siloed costs.

***4. Methods to set a threshold for potential short-term budget impact that can serve as a useful “alarm bell” for policymakers to signal consideration of whether affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.***

AAFA has concerns with ICER's focus on short-term budget impact models. We urge ICER to acknowledge that the measure of value to patients inherently extends beyond the short-term perspective that payers and other stakeholders often adopt. We are concerned that emphasizing the budget impact of treatments using assumptions and arbitrary thresholds for short-term budget impact will be and is used as a rationale to restrict patient access to evidenced based care and treatment, particularly when they are established without the context of any offsetting long-term benefits that are important to individuals, their families, and caregivers. Chronic conditions such as asthma and allergies impact individuals throughout their lives. Furthermore, we offer the following suggested revision for your consideration to the above wording: *Methods to set a threshold for potential short-term budget impact that can serve as a useful tool for policymakers to consider when affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.*

AAFA is eager to assist in any way that we can, to help further inform ICER's discussions. If you require additional information or clarification, please do not hesitate to contact me at [csennett@aafa.org](mailto:csennett@aafa.org) or Meryl Bloomrosen, AAFA's Senior Vice President Policy, Advocacy, and Research at [mbloomrosen@aafa.org](mailto:mbloomrosen@aafa.org).

Regards,

Cary Sennett, MD, PhD  
President and CEO

September 12, 2016

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

Dear Dr. Pearson:

The [Alliance for Aging Research](http://www.agingresearch.org) is the leading non-profit organization dedicated to accelerating the pace of scientific discoveries and their application to improve the experience of aging and health. The Alliance believes that advances in research help people live longer, happier, more productive lives and reduce health care costs over the long term. On behalf of the Alliance, thank you for the opportunity to comment on the Institute for Clinical and Economic Review's (ICER) Value Assessment Framework.

We understand that ICER's framework and similar value assessment tools are frequently used by payers to determine coverage of new treatments. As conversations around the value of new treatments intensify and coverage decisions impact patients' ability to access them, the Alliance seeks to ensure that the needs of older adults suffering with chronic diseases and terminal illnesses are meaningfully considered. We are concerned that ICER's current value framework does not accurately reflect the preferences and heterogeneity of older patients and could limit their access to new treatments. Our recommendations below are intended to better incorporate the perspectives of older adult patients into ICER's framework moving forward as the institute evaluates the value of treatments for use by this population.

### **Recommendation One: Engage Patients Earlier in Assessment Development**

We understand that one of the more challenging aspects of developing a value framework is knowing when to include the patient perspective. While the Alliance appreciates ICER's efforts to engage patient groups by their inclusion during the "other benefits/disadvantages" and "contextual consideration" phases of its value framework, we firmly believe that this is too late in the process. We recommend the inclusion of patients and patient groups during the initial scoping phase of individual assessment projects.

The scoping phase involves conversations over a seven-week period between ICER, treatment manufacturers, clinical experts, and insurers. At this point, the fundamentals for data collection and other considerations for a treatment's value assessment are established. Patients, patient groups and other members of the public only have three weeks after the initial scoping phase to respond to a pre-determined draft scoping document. This does not leave time for the breadth of

views from affected communities to be sought in a way that substantially alters the direction of a treatment's assessment.

We feel strongly that ICER should proactively reach out to patients, patient groups, family caregivers, and clinicians in the disease/condition area during the initial scoping phase of a value assessment. Family caregiver outreach is particularly essential when a chosen disease area's symptoms include cognitive impairment. Foundational conversations like these would better inform the assumptions used in the assessment, shape the underlying questions being considered, and create a common lexicon between ICER and the affected patient population. ICER should take extra care to include the views of older adults aged 65+ and those with the disease/condition who are also affected by co-morbid conditions at this point. Those with multiple chronic conditions make up a substantial portion of patients. The CDC reports that one in four Americans has multiple chronic conditions, those that last a year or more and require ongoing medical attention or that limit activities of daily living. That number rises to three in four Americans aged 65 and older. When possible, ICER should explain how early engagement with patients and patient groups ultimately informed the conclusions in its final report.

To enhance these conversation, we recommend that ICER provide templates to guide patients and patient groups in sharing their perspectives with a specific disease/condition. These materials should be developed with the intent of providing ICER with a fundamental understanding of the values and preferences among an affected patient population.

### **Recommendation Two: Delay Consideration of Specific Diseases/Conditions**

Currently, patients, patient groups, and clinicians are asked about the benefits or disadvantages offered by a new treatment under ICER review based on a research study that has already been conducted. Because ICER focuses on new treatments shortly after the time of FDA approval, their assessments must rely on clinical trial data. This a problematic approach for assigning value of a new treatment for use in a broad patient population because older adults and other subgroups are largely omitted or severely underrepresented in Randomized Controlled Trials (RCT).

A 2005 study published in *Pharmacotherapy* by Linnebuer et. al, highlighted low participation of older adults in investigational drugs trials for Alzheimer's disease, cardiovascular disease and other chronic conditions, who are also those most disproportionately impacted by chronic disease as they age. Looking at oncology alone, over 50 percent of all cancer cases are diagnosed in people ages 65 and older but only 25 percent of clinical trial enrollees are from that age group. This vast under-enrollment of older adults is due to many factors including a high likelihood of comorbidity exclusion, perceived financial issues, transportation barriers, and a fear of the science and the system. Also playing a large role is a lack of awareness about what clinical trials are and how they work.

Any assessment that solely uses RCT data for a disease/condition that disproportionally affects older adults is a fundamentally limited and we feel that special consideration should be given in these cases. ICER should allow a new treatment sufficient time on the market for a disease/condition that disproportionally affects the elderly before selecting that treatment for an

individual value assessment. This delay would allow for collection of data on how the treatment is performing in older patients as well as other with comorbidities. ICER could also suggest the establishment of patient registries to develop alternative data sets to RCT data for future analysis that are more representative of the patient population.

### **Recommendation Three: Enhance Transparency on Study Limitations**

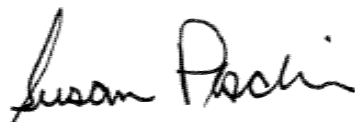
The Alliance recommends increased transparency about the limitations, model design, and evidence used for ICER's value assessments. The validity and reliability of ICER reports can be difficult to determine because the inputs used are often opaque. We believe that ICER should release the model used in its value assessments so that the calculations and assumptions can be examined in depth.

Our previous recommendation noted that RCT data does not reflect the efficacy of new treatments in older adult patients because clinical trials often exclude individuals of advanced ages and those with comorbidities. Evidence gaps like these in treatment value assessments should be easier to identify in ICER's final reports. If there are significant evidence gaps around specific populations, such as older adults, they should be published prominently in individual ICER reports. Also, if there is insufficient evidence to determine the value of a new treatment for such a significant population, ICER should publish in its final report what it expects a reasonable period of time to be in which they will revisit additional data and revise their report.

Finally, we encourage ICER to reach out to relevant patient groups for a "stamp of approval" prior to the release of its reports. Such an approval could reassure stakeholders that ICER reports are sufficiently patient-informed and used data that accurately reflected the preferences and values of patients.

Thank you again for the opportunity to comment on ICER's Value Assessment Framework. The Alliance looks forward to serving as a resource as you take steps to improve the framework and we would be pleased to answer any questions on our proposed recommendations. Inquiries can be directed to the Alliance's Public Policy Associate, Ryne Carney, at (202) 293-2856 or by email at [rcarney@agingresearch.org](mailto:rcarney@agingresearch.org).

Sincerely,



Susan Peschin, MHS  
President and CEO



Cynthia Bens  
Vice President, Public Policy

## Amgen Response to ICER's Call for Comments on its Value Assessment Framework (September 12, 2016)

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In response to ICER's "Call for Comments on its Value Assessment Framework," Amgen directs ICER to the extensive comments that we have provided over the past 14 months in response to other ICER comment documents, through ICER/manufacture calls and our public comments at the New England CEPAC (September 2015) and Mid-West CEPAC (May 2016) meetings. ICER does not explicitly state that it endeavors to employ rigorous, transparent, and completely objective scientific methods in its assessments, and our experience suggests that these principles are substantially lacking in ICER's framework, as highlighted below:

- **Full Transparency:** We have been unsuccessful in our efforts to replicate ICER's model results. The ICER models remain black boxes that cannot be replicated by the groups ICER thinks should consume and consider them. Although ICER has made some effort to share high-level model specs, the process remains far from fully transparent.

Recommendation: Make research methods, assumptions, data inputs, and equations available in a completely transparent manner, such that results are fully reproducible by third parties.<sup>1-3</sup> This is a critical first step towards becoming a *trusted* organization.

- **Patient Centricity:** ICER does not protect patient interests by paying special attention to data that patients can uniquely provide. In addition, ICER does not use studies on patient Willingness to Pay (WTP) to inform its thresholds.

Recommendation: Keep the patient at the center of the analysis by having a lower threshold for incorporating data derived directly from patients, such as survey data and health related quality of life studies, using effects that are more meaningful to patients, and performing extensive sensitivity analyses that invoke common sense patient benefits which may have been omitted or impossible to collect in clinical trials.<sup>1-3,5,6</sup>

- **Flexible Willingness to Pay Thresholds:** ICER's current assessments apply the threshold range of \$100,000 to \$150,000 per quality-adjusted life year (QALY). A "one-size-fits-all" cost-per-QALY threshold is known to be inherently biased against the oldest and sickest patients, as well as those with the rarest diseases. Further, ICER applies a cost-per-QALY threshold that has not been validated in the US, much less shown appropriate across every disease, patient group, and medical situation.

Recommendation: Inform thresholds with data, as it is available (e.g., literature-based QALY estimates for cancer treatment in the US). The cost-per-QALY thresholds should be flexible and appropriate to the society and the condition being treated.<sup>2,3,6</sup> Special considerations such as upwardly skewed age distribution, excessive discounting of life years based on sicker patients, or orphan disease status must be included in the analysis.

**Amgen Response to ICER's Call for Comments on its Value Assessment Framework  
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- **Budget Impact is Not “Value”:** ICER positions its “Potential Health System Budget Impact (Short-Term)” as an assessment that directly informs “Provisional Health System Value”. Although ICER has slightly modified its framework regarding the place of budget impact, the framework still indicates that ICER considers budget impact as the main determinant of health system value. Budget impact analyses poorly reflect value as they treat healthcare spending as a consumption rather than an investment, and do not take into account any long-term health benefits, cost savings, or improved productivity.<sup>8</sup>

Recommendation: Remove budget impact as a key driver of the conversation around “Health System Value” and make it clear that budget impact is a completely separate construct from value and not a measure of value. Instead of budget impact, ICER should provide its Policy Roundtable with a more multi-factorial view that comprise “value” as an investment that provides long-term returns.

- **Valid Budget Impact Methodology:** ICER’s budget impact methods utilize arbitrary caps, exaggerated adoption rates, and focus on short-term time horizons (1-year and 5-year). Arbitrary budget caps place an inflexible threshold on healthcare spending based on the status quo, and short-term time horizons do not take into account any long-term health benefits.<sup>8</sup>

Recommendation: Use non-judgmental budget impact methodology that avoids arbitrary budget caps and reports objective findings.<sup>1,2,5,6</sup> ICER should also (1) utilize realistic adoption rates using real-world adoption rates from reasonable analogs, and perform extensive sensitivity analysis; (2) use real costs, not artificial prices; and (3) focus on multiple time horizons, including those that incorporate longer-term offsets due to patent expiration.<sup>1,5</sup>

- **Provision of Context and Uncertainty:** ICER simplifies its answers to easily misunderstood absolutes and averages, without context or quantification of uncertainty.

Recommendation: Present results as ranges, with extensive sensitivity analyses, rather than absolutes based on average treatment effect.

- **Contextual Considerations:** ICER buries important determinates of value into “Contextual Considerations” where they have much less visibility, do not influence the quantitative analysis, and are never reported.

Recommendation: Include varied and flexible valuation methods in the framework that synthesize the value from all of the areas ICER currently recognizes as important but fails to formally consider in the value analysis.<sup>1,2</sup>

**Amgen Response to ICER's Call for Comments on its Value Assessment Framework  
(September 12, 2016)**

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- **Relevance to Clinical Practice:** ICER does not consider less “convenient” sources of data that may be more externally valid (i.e., representative of real-world situations in clinical practice) such as real-world evidence, registries, actual price vs list price, etc.

Recommendation: Ensure full consideration and use of data that may be more generalizable to clinical practice (e.g., more generous use of and validation against real-world data).<sup>1-5</sup> ICER should also run more extensive alternative analyses (e.g., probabilistic sensitivity analyses) with such data and collect new data as needed to best address the decision problem being considered. Similarly, the choice of comparators, place in therapy, and utilization assumptions need to be informed by real-world data and extensive input from experts in the field.<sup>3,5</sup>

- **Multi-Stakeholder Perspective (Expert Opinion):** ICER's mission indicates that its process supports “a broader dialogue on value in which all stakeholders can participate fully.” Unfortunately, this is not the case. While there has been increased opportunities for manufacturers to engage with ICER, feedback that is provided is often not incorporated or reflected in ICER's output, including expert opinion.<sup>1,2,4,7</sup>

Recommendation: Reflect expert input from opinion leaders, patient advocates and manufacturers into models and analyses. ICER should also include expertise on specific disease conditions and representatives from patient advocacy organizations specific to the conditions on its voting panels for the CTAF, New England CEPAC, and the Mid-West CEPAC. While ICER has made modest changes to update its Policy Roundtable, it is critical to have appropriate representation on ICER's voting panel that will deliberate on the evidence and vote on the “Care Value” of these important treatments for patients.

- **Heterogeneity of Treatment Effect:** ICER does not adequately consider how heterogeneity of treatment effects and differences between patients regarding the value of outcomes will influence the results.

Recommendation: Report how the results may differ under scenarios where patients respond differentially to alternative treatment options and value the various outcomes achieved.<sup>1-3</sup>

We believe these principles represent best practice for value assessments and ICER should adopt our detailed and focused guidance on these points. US patients deserve no less when the value and potential access to life-altering therapies is being publically challenged. ICER's current approach to value assessment falls well short of these best practices on many dimensions, and we will continue to remind ICER of the importance of objective and rigorous scientific analyses that must form the basis of any quality improvements in health care. Done in any other way, ICER risks having the opposite effect on the health care system.



**Amgen Response to ICER's Call for Comments on its Value Assessment Framework  
(September 12, 2016)**

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September 12, 2016

Steven Pearson, MD, MSc  
President, Institute for Clinical and Economic Review  
Boston, MA 02109 USA

**RE: ICER National Call for Proposed Improvements to Value Assessment Framework**

Dear Dr. Pearson,

On behalf of the 52.5 million adults and more than 300,000 children in the United States with doctor-diagnosed arthritis, the Arthritis Foundation appreciates the opportunity to provide comments to ICER on the *National Call for Proposed Improvements to Value Assessment Framework*. The term arthritis encompasses more than 100 rheumatic diseases and conditions that affect joints, the surrounding tissue and other connective tissues. Arthritis is a complex, chronic disease that is often difficult to treat because it is systemic and can affect multiple organs. As such, each person with the disease has a unique set of experiences with symptoms and treatments. People with RA often do not fit the profile of an “average patient,” which can make comparative effectiveness analyses and value frameworks difficult to design for this population. A treatment that works well in one patient might not work in another patient with seemingly identical disease characteristics, leading to two critical conclusions: a robust cross-section of patient representation must be included in the design of value frameworks and policy decisions; and patient and prescriber access to a broad range of treatment options must be available to adequately treat people with this disease.

The Arthritis Foundation believes robust stakeholder engagement is a critical component of any value framework that will have a direct impact on people with arthritis and the providers who treat them. Information from clinicians who have daily contact with this patient population is also an important component of developing a robust stakeholder engagement process. We hope our comments will inform ICER’s value framework methodology and help to ensure the treatment needs of the people who suffer from arthritis are met. Please find our specific comments on the value assessment framework in the subsequent sections.

**Timeline.** We appreciate the opportunity for patient advocacy group engagement in the comment process. However, we are concerned that the comment deadlines are too short for many patient and provider groups. We understand that ICER’s timeline is based on the Food and Drug Administration’s review and approval process, in addition to payers making coverage decisions. We urge ICER to re-evaluate the processes and timelines given to the patient advocacy and provider communities for feedback. Allowing more time for comments would allow for more detailed patient-centered input.

**Value Assessment Inputs.** The Arthritis Foundation is concerned that patient advocacy groups were not adequately represented during the original framework creation and we urge ICER to

engage patient advocacy groups for input in the future. Hearing one patient story is only one patient story and patient advocacy organizations are in a unique position to gather robust data about the patient experience. As an advocacy organization, the Arthritis Foundation maintains regular contact with a broad cross-section of patients, and uses this data to inform public policy affecting people with arthritis. The key to success in ensuring health policy reflects the needs of patients is routine interactions with the people living with the disease through mechanisms such as patient surveys, focus groups and story-banking. Like many patient advocacy organizations, the Arthritis Foundation routinely engages with people with arthritis in these ways and wants to be a valuable resource to ICER. In order to fully integrate the patient perspective, it is critical to forge patient partnerships, provide transparency to patients, include patient perspectives, acknowledge the diversity of patient populations, include outcomes important to patients and utilize patient-centered data resources. In the current value framework, ICER includes areas for descriptive/qualitative data input, and we ask that ICER elaborate on how patients, caregivers and providers will be engaged, what methods will be utilized and how that input will be presented quantitatively. For these reasons, we urge ICER to incorporate feedback from patients, patient advocacy organizations, care givers, and provider panels in the design of the value framework and throughout the evaluation process.

**Comparative Clinical Effectiveness.** The current value framework states that patients will inform opportunities for using or generating real world evidence (RWE). We urge ICER to provide more transparency on the methods by which patient groups will be involved in the comparative clinical effectiveness category of the framework. We are concerned that the current scientific literature does not adequately incorporate patient, caregiver and provider perspectives. ICER should rely on additional means for capturing information, for example by partnering with patients and patient groups who can provide robust information on the patient experience. The Arthritis Foundation would welcome the opportunity to partner with ICER on this initiative.

The Arthritis Foundation supports the collection of meaningful data for metrics with an emphasis on the quality of the evidence. We recommend that data from patient reported registries (PROs) should also be part of comparative clinical effectiveness, with robust input from patient and provider stakeholders.

**Incremental Costs.** ICER has deemed a standard of 100-150k per quality adjusted life years (QALYs). We urge ICER to consider whether this calculation is generalizable, and seek further clarification on the specific processes used to calculate QALYs for different populations and disease groups. As ICER continues to refine this section of the value framework, we encourage you to develop mechanisms to determine whether a QALY and the subsequent data are from relevant patients and populations. Relying on population-based assessments that do not reflect the heterogeneity of disease subpopulations, patient treatment responses and patient preferences increases the risk of mischaracterizing the value of the treatments being compared. ICER should recognize that no single QALY threshold estimate can or should be generalizable to all populations, and that QALY thresholds vary by decision-maker, population and disease. Further, we seek clarity on how specific indirect and direct costs and caregiver costs are calculated. Many

patients with arthritis also suffer with comorbidities such as cardiovascular disease, mental health conditions, infections and malignancies<sup>i</sup>. Of adults diagnosed with arthritis, 47% also have at least one of the previously listed conditions and as many as 40% of people with rheumatoid arthritis (RA) experience significant symptoms of depression, which can lead to more physical function problems, higher disease activity, poorer health overall and an increased need for medical care<sup>ii</sup>. We urge ICER to elaborate on how comorbidities will be accounted for in the incremental costs outcome measures, including disability, quality of life, mental health and mortality.

**Other Benefits or Disadvantages.** Objectivity is important in any evaluative process. ICER mentions the use of independent public appraisal committees; we seek clarity on who comprises the committees and the methodology they utilize. We are concerned this approach may be insufficient to incorporate the impact of important patient-centered factors, such as prescribing patterns, treatment adherence, patient preference and work limitations. The voting panel may not have the expertise or appropriate context to meaningfully evaluate this category. We urge ICER to develop a formalized patient engagement process, including patient and provider panels that will engage and provide feedback during all facets of the framework.

Treatment adherence and off-label prescribing are major issues for patients. A study by Cush and Dao (2012) found that off-label use (OLU) accounted for 21% of all drug use. Further, agents closely aligned with rheumatologic care including immunosuppressant's, gabapentin, corticosteroids, anti-spasmodics and sleep medicines were often prescribed off-label. For groups like oncology, it is estimated that 50-60% of patients are using drugs off-label<sup>iii</sup>. We seek clarity on the process ICER will use to account for off-label prescribing and medication adherence.

Patient preference must be taken into account when evaluating treatment value, as there are multiple reasons a patient may prefer a certain drug. For example, some patients are not able to self-inject, and therefore prefer infused drugs. The many factors contributing to medication adherence should also be taken into account, and range from affordability to access issues for people living in rural areas, drug synchronization for people on multiple drugs and a lack of education about the importance of completing a drug regimen.

More than 43.2% (22.7 million) of the 52.5 million adults with doctor-diagnosed arthritis report limitations in their usual activities due to their arthritis. Further, 31% (8.3 million) of working age adults with doctor-diagnosed arthritis report being limited in work due to arthritis<sup>iv</sup>. Therefore, we seek additional transparency on methods used to judge worker productivity not included in the comparative effectiveness category.

**Contextual Considerations.** These considerations include ethical, legal or any other issue that influences the relative priority of illness and interventions. We seek clarity on the methods ICER will utilize when new classes of drugs like biosimilars come onto the market. Two biosimilar medications for RA have already been approved by the FDA, and these drugs may come to market as soon as the fall of 2016. Robust details explaining how the framework will be revised

when biosimilar introduction occurs is needed to understand the full economic impact of disease groups and medications. Again in this category, ICER mentions the use of independent public appraisal committees, and we seek clarity on who comprises the committees, the methodology they utilize and how the patient voice will be integrated and documented in these deliberations.

**Care Value.** Keeping patients stable on the right medication is critical to maintaining positive health outcomes and greater productivity for patients. There are parts of the care value equation that could threaten a medically stable patient, such as the absence of patient, caregiver and provider input as well as the non-disclosure of the precise equations used in the evaluation. We seek full transparency on the equations used to calculate care value, specifically how ICER will quantify patient involvement and impact as it relates to the significant benefits or contextual factors in the care value calculation.

**Budget Impact.** Focusing budget impact on the short-term payer timeline can result in patients having restricted access to life changing treatments. We urge ICER to consider long-term outcomes and impacts from the patient and payer perspective. In some instances, cost savings may not be realized for several years, as with the introduction of biologic medications. Biologics for arthritis did not immediately show cost savings. From 1993 to 2008, after the introduction of biologics to treat inflammatory diseases, there has been a 32% reduction in joint replacement procedures<sup>v</sup>. For people with chronic disease, their disease state does not exist in 1-year increments; therefore the current approach to assessing budget impact is too narrowly focused and can miss potential cost savings over a lifetime horizon.

**Value-Based Price Benchmarks.** Calculations in this category of the ICER framework are based on the list price of drugs. The list price does not adequately reflect the actual price paid for the drug. Further clarity is warranted on the specific methods used to calculate the discount and rebate rates. We urge ICER to consider third party data and existing research when available to help provide a more realistic estimate of the industry-wide discount rate.

**Other Frameworks.** The value discussion is of vital importance to patients who are directly challenged by barriers to treatment and limitations in their daily life that impact quality of life. The majority of current value frameworks aim to help payers with formulary decision-making and may leave out the patient and caregiver perspective when determining value. For a framework to be comprehensive, it is critical to incorporate robust patient input, especially if these models are used to inform decisions that affect access to treatments for patients. We are concerned that the methodology for the incorporation of the patient voice is unclear in the current ICER framework. We urge ICER to not only provide a clear process for integrating the patient voice, but to also work with patient advocacy organizations and others such as the National Health Council (NCH) to ensure the updated framework is comprehensive.

Overall, the Arthritis Foundation wants to ensure people with arthritis have access to the medications they need to function in daily life. Attempting to make decisions about the value of a drug without robust supporting data from patients and providers in daily contact with patients



is a questionable practice. We ask that ICER consider its current process to evaluate and make decisions regarding treatments. Further, as new treatments and more robust information about these treatments becomes available, we urge ICER to consider a protocol for how these decisions will be revised in the future. The Arthritis Foundation cannot support any value based recommendations that could result in a patient on a stable drug no longer having access to that drug. To that end, we urge ICER to consider the critical need for adherence to drug regimens, and the perspective of patients, caregivers and other stakeholders to ensure that their working value assessment framework has the broadest possible relevancy.

Again, thank you for the opportunity to comment on the *National Call for Proposed Improvements to Value Assessment Framework*. Please contact Sandie Preiss, Arthritis Foundation National Vice President of Advocacy and Access, at 202-887-2910 or spreiss@arthritis.org with questions or for more information.

Sincerely,



Sandie Preiss  
Vice President, Advocacy and Access  
Arthritis Foundation

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**EXECUTIVE DIRECTOR**

Christian G. Downs, JD, MHA

September 12, 2016

Steven D. Pearson, M.D., M.Sc., FRCP  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

Dear Dr. Pearson:

Thank you for the opportunity to comment on the Institute for Clinical and Economic Review's (ICER's) Value Assessment Framework. The Association of Community Cancer Centers (ACCC) is a membership organization whose members include hospitals, physicians, nurses, social workers, and oncology team members who care for millions of patients and families fighting cancer. ACCC represents more than 23,000 cancer care professionals from approximately 2,000 hospitals and private practices nationwide, and it is estimated that 65 percent of cancer patients are treated by a member of ACCC. We are committed to preserving and protecting quality cancer care for our patients and our communities, including access to the most appropriate cancer therapies, and we support efforts to better understand, and define, the value of that care.

High and rising health care costs certainly drive – and perhaps demand – meaningful conversation about the value drug therapies and other health care interventions bring to our patients. As cancer care specifically becomes increasingly cost-prohibitive for cancer patients and their families, we appreciate the work of organizations to facilitate this important and often difficult conversation when it is done in an evidence-based and patient-centered manner. Yet while the value discussion remains fairly conceptual to most on-the-ground clinicians caring for cancer patients every day, ACCC has significant concerns about the growing attention ICER's value assessments have received by payers and policymakers. Particularly as certain methodologies for assessing value emerge at the forefront for payers, ICER must recognize the enormity of their decisions and the significance of developing precise, accurate assessments of treatments that could make the difference between life and death for a cancer patient.

In response to ICER's national call for proposed improvements to its Value Assessment Framework, ACCC asks ICER to consider the following changes:

**Better stakeholder engagement:** While we appreciate this opportunity to comment, and recent efforts by ICER to educate the public on their process, we remain concerned that ICER has yet to meaningfully engage and incorporate stakeholder perspectives in their methodology and process. Given the growing attention payers and policymakers are giving ICER recommendations, it is critical that your organization broadly incorporate feedback from patient groups, clinical experts, and life science companies to make appropriate value assessments about cancer treatments.

**Limit voting members in drug and health intervention reviews and on panels such as the Comparative Effectiveness Public Advisory Council (CEPAC) to subject matter experts:** To ensure the clinical accuracy of their assessments, we urge ICER to limit voting members of panels to subject matter experts in the health interventions and disease areas being reviewed, including requirements that a supermajority of voting panel members be board certified in the area of concern and actively remain involved with treating patients and/or conducting research in that specific disease area. Particularly for complex conditions such as cancer, only clinical experts can be expected to keep pace with the continual evolution of the standard of care and the nuance of individual clinical decision making.

**Better account for patient preferences and individualization:** We share the concerns of several stakeholders that the development of a universal, one-size-fits-all model to quantify the value of one health care intervention or drug therapy over another is in direct contrast with an increasingly individualized approach to cancer care. Scientists have made great strides in recent years in understanding the genetic and molecular make-up of various cancers, giving clinicians a new set of tools to diagnose and treat patients through personalized medicine. Value, therefore, is a nuanced, multi-dimensional concept, and the tradeoff between the efficacy of a drug and subsequent quality of life is highly individualized for each patient, which raises questions about whether the quality-adjusted life year (QALY) used by ICER accurately captures the full value a therapy offers an individual patient, particularly as studies including the 2013 ECHOUTCOME project have indicated that “the underlying assumptions of the QALY calculation model are not in line with behavior from a real-life population.” Therefore, we support incorporating more patient-centric measures in ICER’s methodological approach and also ask ICER for more clarity around how clinicians can interact with this framework. While various approaches to assessing the value of one therapy over another can help guide a patient’s decision-making process, ultimately, the final decision about treatment should remain between the patient and their provider. Our members are looking for sound, easy-to-understand tools to help facilitate meaningful conversations with their patients about various treatment options given their individual treatment goals.

**Provide more information about how value assessments will evolve and not stifle innovation:** It remains unclear how ICER chooses specific therapies to evaluate and how value determinations will be updated as new evidence and data emerges and the standard of care evolves. As of now, ICER reviews are static, putting newer, innovative therapies with less published data at a disadvantage, including cutting edge immunotherapies that have proven to have great promise for cancer patients. ICER has not been transparent about how therapies in rapidly evolving areas such as ImmunoOncology will be continuously reviewed as new data emerges, or how ICER will manage updates of its recommendations in these contexts. ICER’s reports have not been consistent in how abstracts and other emerging data are incorporated into



recommendations, which is of particular importance for new therapeutic areas. We are also very concerned that ICER's approach favors therapies that have been on the market for some time and have more data, which could have the unintended consequence of stifling innovation. The short-term budget impact window also puts innovative therapies, with higher upfront costs but long-term benefits, at a disadvantage.

**Ensure that ICER's methodologies and evaluations adhere to the scientific standards of transparency and peer review:** ICER has not made its methodologies for clinical evaluation or economic evaluation completely transparent in a way that outside researchers could test and validate its approaches. Furthermore, these methodologies have not been subject to peer-review or published in a scientific journal. Given the rapid evolution of some of the therapy areas ICER evaluates, as well as ongoing debates in the health policy and economics communities regarding issues including appropriate use of the QALY and best practices for the development of budget impact models, ICER should ensure that its approaches are transparent and peer-reviewed.

As ICER continues to have a voice in conversations about value and cost in our health care system in a manner that could significantly impact public health and access to innovative therapies, ICER has a major responsibility to account for the nuances of value to the patient, health care system and to society, the complexities of different diseases, and the rapidly changing cancer landscape and continual evolution of evidence for different health care interventions. ACCC and ICER share a common goal to ensure therapies are used appropriately, efficiently and effectively, and we look forward to working with the broader health care community to achieve this goal. We urge ICER to continue to work with stakeholders to refine their methodology, and we look forward to continuing the dialogue.

Thank you for the opportunity to comment. If you have any questions, or need additional information, please feel free to contact Leah Ralph, Director of Health Policy, at [lralph@accc-cancer.org](mailto:lralph@accc-cancer.org) or (301) 984-5071.

Respectfully submitted,

A handwritten signature in black ink, reading "Jennie R. Crews". The signature is fluid and cursive, with the first name "Jennie" being the most prominent part.

Jennie R. Crews, MD, MMM, FACP

President

Association of Community Cancer Centers



September 12, 2016

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

Re: Institute for Clinical and Economic Review's Call for Proposed Improvements to its Value Assessment Framework

Dear Dr. Pearson,

Astellas appreciates the opportunity to provide feedback to the Institute for Clinical & Economic Review (ICER) in response to ICER's July 14, 2016 call for proposed improvements to its Value Assessment Framework (VAF). An innovative company with global headquarters in Tokyo, Japan, Astellas is among the top 20 global research-based pharmaceutical companies and its presence continues to grow in the United States. Our fundamental goal is to use our expertise in select therapeutic areas to advance the Triple Aim of better care, lower costs, and improved health for patients by developing and offering treatments that help to address unmet medical needs. Our United States product lines focus on the therapeutic areas of immunology, oncology, infectious disease, cardiology, and urology.

We applaud ICER's solicitation of comprehensive stakeholder feedback on improvements to its VAF, as well as the efforts ICER has made to extend the public comment periods on draft reports and facilitate stakeholder input generally. Initial and ongoing stakeholder feedback is essential to help ensure that the VAF is a relevant and useful tool for assessing value. Astellas has long supported policies that recognize the need for healthcare decisions to be patient-centered and founded on the best available data.

**Astellas Pharma US, Inc.**

1 Astellas Way, Northbrook, IL 60062  
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Our comments are designed to supplement those being submitted by the National Pharmaceutical Council (NPC), the Pharmaceutical Research and Manufacturers of America (PhRMA), and the Biotechnology Innovation Organization (BIO). Chiefly, they highlight Astellas' specific concerns with ICER's current methods for determining long-term cost effectiveness and its use of short-term budget impact in assessing value.

\* \* \* \* \*

## I. The Use of "Quality Adjusted Life Year" Should be Informational Only

The Quality Adjusted Life Year (QALY) is an important tool for measuring health improvement, as expressed by length and quality of life. However, QALYs have a number of significant limitations, as described in detail by our colleagues at NPC, PhRMA, and BIO. Using a cost-per-QALY threshold as the sole determinative basis of the "care value" metric for all health conditions and within a healthcare system that is financed through a complex system of multiple payers is not appropriate. While attractive for its simplicity, a QALY cannot adequately capture the full value that an innovative therapy offers to individual patients, especially since individual characteristics, preferences, and needs vary. The significance of patient heterogeneity will only increase as medical science advances toward personalized medicine, which will further reduce the utility of a single QALY as the measure of health improvement -- especially when being used by individual patients and their physicians to inform decisions about the individual's treatment.

Thus, while we do not object to the use of QALYs or cost-per-QALYs as part of a comprehensive, multi-faceted cost-effectiveness analysis, we encourage ICER to recognize that no single threshold can or should be universally applicable across different populations, diseases, and treatments. Accordingly, ICER should revise its methodology so that cost-per-QALY is not the sole determinative of "care value."

## II. Short-term Budget Impact is Not Relevant in Assessing Value

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ICER's VAF currently includes a short-term budget impact metric, "to sound an 'alarm bell' if the short-term costs [of a new drug] might increase overall health care spending significantly faster than the US national economy is growing."<sup>1</sup> This metric indicates that -- regardless of an intervention's value -- policymakers and insurers should be concerned about the short-term budget impact and "consider whether special measures should be put into place to help manage the possible short-term squeeze on health budgets."<sup>2</sup> Incorporating short-term budget impact into a value assessment is inappropriate because it (1) is unrelated to value, (2) risks distorting assessments of value, and (3) is of limited utility since payer entities vary greatly in their ability to shoulder additional short-term costs -- and to shift spending from lower-value to higher-value uses.

First, as the term "value assessment framework" suggests, the VAF should focus on a therapy's value, i.e. (1) the comparative clinical effectiveness of a therapy, taking into account individual quality-of-life considerations, as well as public health considerations, and (2) the long-term costs to the healthcare system. By applying an arbitrary budget cap, ICER's "affordability threshold" methodology mistakenly assigns a "desired" value on a medicine and does not fully account for the clinical effectiveness (comparative or otherwise) of a therapy and is, thus, unrelated to health economic value.

Second, incorporating short-term budget impact into a value assessment necessarily distorts the assessments of value -- potentially causing confusion about the meaning of ICER's determinations -- and in turn stifling innovation. It also risks creating a systematic bias against interventions that have higher upfront cost but create reduced overall healthcare spending over the longer term due to improved patient outcomes. Put differently, this budget cap metric may favor lower-value treatments -- those that are either inexpensive and have less clinical benefits over a longer period of time or that are used by a small patient population -- over higher-value treatments -- those that may be more expensive, but result in better clinical outcomes and lower health care

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<sup>1</sup> ICER, Addressing the Myths About ICER and Value Assessment.

<sup>2</sup> Id.

expenditures over a longer period of time. The potential to shift spending toward lower-value treatments is a perverse result for a “value assessment framework.” These short-term budget considerations have no place in a value assessment framework. Assessing the “value” of a medicine is complicated and often contentious -- yet the basic concept of “value” is widely shared: it is a way of comparing the medicine’s benefits and costs, not a way of summing its total costs over a five-year period.

The distortion created by ICER’s budget impact metric is particularly evident when it is worked into the price that ICER suggests for a new drug. Chronic disease and its symptoms manifest and develop over long periods of times, sometimes over the lifetime of the patient. Treatments that properly manage those conditions can have significant long-term value, both by improving the quality of patients’ lives and by preventing more serious conditions. Reliance on short-term affordability thresholds might inappropriately encourage insurers to restrict access to those treatments irrespective of their value to patients and the health system over time.

ICER’s examples of value-based price benchmarks underscore this point. ICER concluded that PCSK9 drugs show “intermediate to high value” when priced between \$5,405 and \$7,735, yet the price threshold that ICER says should set off the affordability “alarm bell” for insurers and policymakers (the “price at short-term affordability threshold”) is only \$2,177 -- just 40% of the price at which ICER determined PCSK9s to have high value. This large discrepancy highlights the fact that a drug’s budget impact is unrelated to its value, and could be used inappropriately to constrain access to medicines that are, by ICER’s own analysis, high value.

Finally, ICER’s budget impact metric has limited utility and is unnecessary. The ability of a given budget (be it governmental, insurer, family, or individual) to accommodate additional costs will vary greatly depending on the entity or individual. As a result, no single affordability threshold will be applicable, and the “alarm bell” analogy is not apt. The goal of the ICER VAF should be to provide information to patients, insurers, and policymakers about the value of a new medicine, so that they can make more informed decisions regarding treatment, coverage, and healthcare policy, each taking into account

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their own unique budget considerations. Policymakers and insurers are experienced budgeters and have significantly more knowledge about their own budgets -- including what new costs those budgets can handle -- than ICER. Similarly, patient preference and choice should not be jeopardized. As informed consumers, patients can make decisions about the affordability of a given treatment based on their personal financial situation and cost-sharing liability, especially when armed with appropriate information about the value of the particular intervention.

\* \* \* \* \*

In conclusion, Astellas appreciates the opportunity to share our specific concerns, and again emphasizes our support of the comments being submitted by NPC, PhRMA, and BIO on the ICER VAF. We are grateful for the opportunity to provide feedback, and welcome the opportunity to discuss the points raised in these comments.

Please feel free to contact me at 224-205-8687, or Karen Lencoski, JD, MBA, Director, Therapeutic Area Government Strategy, at 224-205-8560, if you have any questions about our comments.

Sincerely,

James Spalding, PharmD, MS, MBA  
Senior Director, Specialty Products  
Health Economics & Clinical Outcomes Research

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Jason Bhardwaj  
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Boston, MA 02118

August 1<sup>st</sup>, 2016

ICER's Value Assessment Framework Team  
publiccomment@icer-review.org

**Greater prominence of “Novel Therapy Value” beyond patent protection is needed to balance short-term “Health System Value” assessments**

In my opinion, the work ICER is doing to create a transparent assessment of value is an important mission and service for our health system and our country in general. I applaud the open call for feedback on the assessment framework, which I realize must remain pragmatic in order to form an actionable, balanced, and context-rich judgment based on the best (but often imperfect) data available.

This proposal is to synthesize and increase prominence of a long-term “Novel Therapy” value assessment that provides important balance to the “Health System Value” assessments, and that together enables a more balanced decision on coverage and reimbursement. As I understand it, the “Health System Value” assessments address the potential risk that a large increase in overall health system costs will limit availability of more affordable (and presumably “higher QALY return”) health interventions. Entresto was the apt example offered of a drug whose individual benefits could have merited a significantly higher price point, but at those levels would be well beyond a reasonable benchmark level of posing access challenges.

I agree it is possible for new therapies (e.g., Hep C) to create access-to-care implications for budget-constrained health plans, so especially in its modified format I agree it is valuable to include that factor – as important context accompanying the “Care Value” assessment. But, it's worth pausing to remember how many of those low-cost, high-value therapies – to which we agree maintaining access is important – came to be in the first place: novel interventions that have come off patent protection (e.g., generic drugs, commoditized medical devices, etc.) and now meaningfully advance our standards of care. A balanced framework should also include, with similar prominence, the degree of longer-term value creation a therapy offers.

In a similar vein, I believe that incorporating full lifecycle (i.e., post-patent protection) pricing was under consideration, to some degree, as part of the “Care Value” / QALY assessments. For the reason mentioned above, I believe this long-term view is critical to consider. However, I suspect ICER may find that their approach must address two key challenges: (1) a timeframe mismatch, and (2) industry strategies to extend pricing protections.

First, the timeframe for “Care Value” is not a good fit for post-patent pricing. Although ICER refers to the “Care Value” assessment as the long-term view of value (vs. the short-term “Health System Value”), in my opinion as currently constructed it is more of a “medium-term view”. Although additional timeframe expansion required would only be moderate – typical protections are lost ~10-12 years post-marketing once development timeframes are deducted – it may be quite difficult to align on a single approach to calculate long-term therapy price (e.g., discounted value calculation).

Second, based on market factors, some manufacturers are able to develop “bells and whistles” versions of their original therapies in order to enable premium pricing for a longer timeframe (e.g., cardiac defibrillators with new monitoring capabilities, injectable versions of existing drugs). These marginal updates do not create the same broader value as their initial versions and need to be assessed differently.

Addressing these two challenges, including a new, prominent assessment of the degree to which a new therapy offers a novel mechanism of action or addresses major unmet needs, will showcase its potential amplified value over a longer timeframe. In addition to the rationale above, this is also important because novel innovations are by nature more highly correlated with greater technology risk and/or smaller populations. Without this view, many potential technologies would be difficult to develop and commercialize. For example, even if a new therapy only offers “at-threshold” per-patient value in its “Care Value” assessment, it may meaningfully advance medical science which could outweigh other concerns. Today ICER's framework, in my opinion, only lightly addresses these value drivers in its “Contextual Considerations” bucket – because it is associating them only with tomorrow's, and not all future generations of, patients.

This proposed addition might be of lesser interest to a managed care organization trying to address a projected budget shortfall next quarter. However, if the ICER mission is to not only incorporate broad points of view (to this the ICER team is clearly dedicated), but also assemble them into a balanced framework addressing broader societal goals (e.g., for CMS), this change is important.

I believe the novel nature of a therapy is highly assessable by the experts that are part of ICER's process. If this idea is of interest, I would be happy to further contribute thoughts to more tactical potential methods of assessment.

Sincerely,

Jason

**Disclosure:** I work for a clinical-stage neuromodulation company that is investigating a novel therapy for Major Depressive Disorder.



September 12, 2016

Steven D. Pearson, M.D., M.Sc. FRCP  
President  
Institute for Clinical and Economic Review  
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***BY ELECTRONIC DELIVERY***

**RE: National Call for Proposed Improvements to its Value Assessment Framework**

Dear Dr. Pearson:

The Biotechnology Innovation Organization (BIO) appreciates the opportunity to provide feedback in response to the Institute for Clinical and Economic Review's (ICER's) National Call for Proposed Improvements to its Value Assessment Framework (the "Framework").<sup>1</sup> BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place. In that way, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes, but also have reduced healthcare expenditures due to fewer physician office visits, hospitalizations, and surgical interventions.

BIO appreciates the efforts ICER has made over the last several months toward improving the public comment process associated with each step of a Drug Review, including the current national call for feedback on the underlying Value Framework methodology. The responsibility to take into account broad stakeholder perspectives and address stakeholder concerns is increasingly important given the emerging evidence that ICER Reviews have the potential to impact patient access to needed medicines.<sup>2</sup> However, while ICER has taken steps to improve the ability to collect stakeholder feedback, the Institute's stated goal of "work[ing] collaboratively with patient groups, clinical experts, and life science companies" requires a much clearer understanding with regard to how stakeholder input is meaningfully incorporated.<sup>3</sup> In this letter, BIO addresses this and other outstanding issues and responds to the four major categories of issues ICER identifies in the call for comments.

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<sup>1</sup> ICER. 2016 (July 14). *ICER Opens National Call for Proposed Improvements to its Value Assessment Framework*, available at: <https://icer-review.org/announcements/improvements-value-framework/> (last accessed August 1, 2016).

<sup>2</sup> JCP Editors. 2016 (June). *Conferences: Perceptions of ICER Reports and Health Technology Assessments in the United States*. *Journal of Clinical Pathways*, available at: <http://www.journalofclinicalpathways.com/article/perceptions-icer-reports-and-health-technology-assessments-united-states> (last accessed August 31, 2016).

<sup>3</sup> ICER. 2016. *Addressing the Myths About ICER and Value Assessment*, p. 2, available at: [http://icer-review.org/wp-content/uploads/2016/08/icer\\_myths\\_facts.pdf](http://icer-review.org/wp-content/uploads/2016/08/icer_myths_facts.pdf) (last accessed August 31, 2016).

Though the majority of the methodological concerns BIO has raised in the past persist,<sup>4</sup> and are reiterated throughout this letter, we continue to raise several primary issues that must be resolved in the new iteration of the Framework.

- First, ICER should not continue to conflate the impact of a therapy on patient health outcomes, including quality of life, with the potential budget impact to any individual payer or group of payers. To clarify, BIO supports the concept of assessing the value of different therapies to an individual patient to facilitate the right medicine getting to the right patient at the right time. However, we also adamantly assert that the final decision of which therapy, or combination of therapies, is most appropriate for a patient must be left to the patient working with his or her provider; consider the *individual* clinical circumstances of the patient; and assess the impact of a therapy on a patient over the long term. The updated Framework should facilitate—not hinder—this aim.
- Second, we continue to strongly urge ICER to ensure that the Framework relies on robust and validated methodological standards and applies them consistently and transparently.
- Third, we appreciate and agree with ICER’s stated goal of undertaking a value assessment that, among other aims, seeks to “fairly reward innovators for the value they bring to patients, and provide them ample incentive to pursue the investments and research that will lead to the innovative treatments of tomorrow.”<sup>5</sup> However, the Framework does not work to achieve this aim. For example, it does not address significant concerns with regard to the potentially negative impact on the innovation ecosystem, nor does it attempt to quantitatively account for the need to sustain innovation. Moreover, the current structure of the budget impact threshold penalizes increased regulatory efficiency that results in bringing more therapies to market each year.
- Fourth, while we acknowledge ICER’s progress with respect to broader stakeholder engagement (e.g., evidenced by the extended duration of certain public comment opportunities), we strongly urge the Institute to establish a robust engagement strategy with patients in particular. The Institute should work with patients to identify how their input can inform each step of the process, how to standardized engagement with this community, and identify the primary point of contact at the Institute for patients who may have questions outside of an official comment period.

These issues, as well as related methodological and process concerns, are discussed in detail throughout the remainder of this letter. We urge ICER to address each of these issues—and BIO’s accompanying recommendations—in an updated version of the Framework, or, describe why ICER believes these changes were not warranted.

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<sup>4</sup> BIO. 2016 (May). *Follow-Up on BIO’s Comments in Response to the ICER Value Framework*, available at: <https://www.bio.org/letters-testimony-comments/follow-bio%E2%80%99s-comments-response-icer-value-framework> (last accessed August 31, 2016).

<sup>5</sup> ICER. 2016. *Addressing the Myths About ICER and Value Assessment*, p. 2, available at: [http://icer-review.org/wp-content/uploads/2016/08/icer\\_myths\\_facts.pdf](http://icer-review.org/wp-content/uploads/2016/08/icer_myths_facts.pdf) (last accessed August 31, 2016).

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**I. Persistent Operational Considerations: ICER should clarify critical facets of its process for operationalizing the Framework that remain opaque to most stakeholders.**

BIO reiterates our appreciation of changes ICER has made over the course of the last several months to increase the duration of public comment periods tied to certain elements of the Drug Review process. We encourage ICER to continue to dialogue openly on this issue and reassess whether the duration should be further extended to allow a broader audience to participate. As we have noted previously, public comment periods shorter than 30 days—for draft scoping documents—and 60 days—for more dense documents like the draft evidence review—are recognized standards for public comment periods.

Despite this progress, BIO continues to express concern that aspects of the ICER Drug Review process remain opaque to stakeholders. The process for Reviews is not consistently standardized, leaving many stakeholders to devote significant resources to engaging ICER, and effectively prohibiting those stakeholders without such resources from being able to offer feedback in the first place. The following areas are key examples of the need for great clarity in how each element of the Drug Review process functions:

- The process for choosing therapeutic areas/clinical indications to study and obtaining input from clinical experts;
- Whether and how completed Drug Reviews can be updated based on emerging evidence;
- Which stakeholders ICER engages in the development of a Draft Scoping Document and how the feedback received is taken into account;
- The timeline and notification process for posting detailed model analysis plans; and
- Sufficient details with regard to the data relied on and the model assumptions made to allow stakeholders to reproduce the Value Framework methodology as applied to an individual Drug Review.

First, it remains unclear how ICER chooses which therapeutic areas will be studied: while BIO appreciates ICER's release of a list of disease and conditions likely to undergo a review at the beginning of 2016, stakeholders have little insight into the criteria used to compile the list, what stakeholders had input into the list, and how often the list will be updated. Stakeholder input is important insofar as it could inject practical considerations into this process, including preemptively identify methodological concerns with the study of certain therapies. A prime example is BIO increasing concern with ICER's aim to assess therapies that have not yet been approved by the FDA. As a result, these therapies often lack sufficient clinical effectiveness data to allow the therapy to be considered are not yet priced to be able to be included in economic models, and those for which there are limited data to study off-label use.

For example, ICER's review of obeticholic acid for treatment of nonalcoholic steatohepatitis (NASH) preceded FDA approval for this therapy, and concerns were raised by those in the patient and provider community that it preceded a clinical consensus on standard of care for these patients.<sup>6</sup> FDA is the national regulatory authority responsible for judging clinical safety and efficacy and bases approval decisions on a robust body of evidence that has been specifically submitted to the Agency for this purpose. While in some cases, robust clinical evidence already exists at the time of FDA review of an off-label use of an approved medicine—for example, in the form of inclusion in nationally recognized clinical guidelines documents—this is not always the case (exemplified by the obeticholic acid example). In the absence of such evidence, any effort to pre-judge the appropriateness of a therapy to treat a specific clinical indication before a planned FDA review has been completed inappropriately supplants the Agency's authority. Thus, in the future, BIO strongly urges ICER to omit any therapies currently under review by FDA from a Framework evaluation until such a time as the Agency has ruled on approval.

Following ICER's choice of a topic of study, it is also unclear whether the Institute seeks input from clinical experts to identify the comparative clinical effectiveness questions that are most relevant to patient care. This is a critical component of the development of an assessment of the comparative value of health interventions, which can help ensure the result is relevant to patients and their providers. BIO appreciates that ICER identifies the "Expert Report Consultants" who contributed to each Draft Evidence Report, but we encourage the Institute to identify specifically: when in the Drug Review development process ICER engages clinical experts to obtain input on the scope and direction of the clinical comparative effectiveness review sections of the Review; what process is utilized to engage and obtain input from clinical experts; and how that input is considered and incorporated, or not, into the various draft documents associated with a drug review (for additional discussion with regard to this issue, see section II(B)).

Second, BIO continues to be concerned that ICER has not acknowledged whether, and through what process, the Institute will update a Drug Review in the face of an evolving standard of care and/or new evidence. This is of particular concern given that these reviews are conducted in the absence of a full picture of a therapy's benefits and disadvantages and that these reviews will continue to be relied upon by other stakeholders even after additional data (e.g., real-world evidence) emerge. When BIO has voiced this issue previously, it has been based on the concern the reality of clinical practice results in an ever-burgeoning body of evidence that is added to continuously; a stark contrast to ICER's static estimate. In this letter, we also note the shorter-term example of the consequences of failing to take into account the most recent evidence in a drug review that is underway.

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<sup>6</sup> For example, see *Statements of Donna Cryer, President and CEO, Global Liver Institute, to the New England Comparative Effectiveness Public Advisory Council (New England CEPAC)*, available at: <https://icerwatch.org/comments/cepac-public-comments-obeticholic-acid-donna-cryer-jd> (last accessed August 1, 2016).

For example, the Draft Evidence Report for ICER's Rheumatoid Arthritis Review is scheduled to be released in the midst of the American College of Rheumatology's annual meeting.<sup>7</sup> Annual academic medical conferences are routinely the venue in which manufacturers and academic researchers publish novel data and the latest evidence in a field. In fact, these stakeholders plan their publication development and release schedules around these annual meetings, and it is very difficult, if not impossible, to accelerate or change course with regard to such releases on short notice. In the case of the Rheumatoid Arthritis Review, the timing of the release of the Draft Evidence Report deprives the initial report of this updated evidence. Though it is our assumption that ICER's updated Final Evidence Report would take into account these novel data, there is a significant benefit to including these data from the beginning to allow all stakeholders to review and respond to a more complete dossier of evidence.

Third, BIO raises concerns with the information available at the time of the public release of draft scoping documents. The draft scoping document is the first indication of how ICER intends to approach a specific topic. We appreciate that ICER has noted increased outreach to stakeholders to seek guidance in drafting this document, and that ICER has created a new "Open Input" period to inform the drafting of the scoping document. However, we urge ICER to clearly identify which groups it engages, how stakeholders can get involved in this early stage of planning if such opportunities exist outside of the "Open Input" period, and to what extent stakeholders' feedback is incorporated in the draft scoping document.

Fourth, there is not a consistent timeline for posting detailed model analysis plans, and ICER does not uniformly announce when such plans have been posted. Despite the ICER's publishing of the *Manufacturer Engagement Guide*, BIO members report that this guidance is not uniformly applied to topics currently under study.<sup>8</sup> For example, with regard to the Non-Small Cell Lung Cancer Review, stakeholders did not know when to expect a detailed model analysis plan to be available after a revised scoping document had been released. The availability of this plan, with sufficient time to allow stakeholders to review and reproduce it, is critical to stakeholders' ability to provide meaningful comments on the model ahead of—or in response to—a draft evidence report. Based on the resources required to analyze such models, BIO recommends that this detailed model analysis plan be available to stakeholders no less than 30 days before the draft evidence report is released.

Moreover, while ICER alerts stakeholders to documents newly posted on the various Public Advisory Council boards' websites, the Institute does not regularly alert stakeholders that new documents have been posted on the Open Science Framework website. For example, ICER does not always update its "Topics" page when new documents or notices are announced related to a previously announced topic. While this may seem like a relatively benign issue, it

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<sup>7</sup> According to ICER's current Drug Review schedule, the Draft Evidence Report will be released on November 14, 2016, see ICER. 2016. *Arthritis*. Key Dates, "Draft Evidence Report," available at: <https://icer-review.org/meeting/arthritis/> (last accessed September 1, 2016). The American College of Rheumatology's annual meeting is scheduled to take place November 11 through 16, see American College of Rheumatology. 2016. *Annual Meeting*, available at: <http://www.rheumatology.org/Annual-Meeting> (last accessed September 12, 2016).

<sup>8</sup> ICER. 2016 (July). *Manufacturer Engagement Guide [Updated]*, available at: [http://icer-review.org/wp-content/uploads/2016/02/ICER\\_Mfr\\_Engagement\\_Guide\\_070816.pdf](http://icer-review.org/wp-content/uploads/2016/02/ICER_Mfr_Engagement_Guide_070816.pdf) (last accessed August 31, 2016).



contributes to diminishing the efficiency of the comment process for both stakeholders and ICER. ICER should also consider making explicit their decision process in incorporating feedback at various stages in the review process (i.e., identifying comments received in response to the draft scoping document and later documents, and providing a rationale for including or not including comments), a persistent issues.

Fifth, ICER should provide sufficient detail to allow stakeholders to reproduce the Framework methodology as applied to an individual Drug Review. For example, an analysis of ICER's Multiple Myeloma Drug Review found that "a major technological drawback of the ICER report is the inability for fellow stakeholders to re-create their exact analysis given that the report is a static pdf document. In addition, some methods are not described in detail in the evidence report."<sup>9</sup> Similarly, with regard to the application of the Value Framework to the Non-Small Cell Lung Cancer Draft Evidence Report, it remains unclear: the exact methodology used in the network meta-analysis (NMA) and comparative effectiveness analysis (CEA), given the lack of a sufficiently detailed research protocol (e.g., the Draft Report did not consistently identify whether constant or time-varying hazard ratios were used, or present alternatives considered to the NMA models mentioned); the clinical rationale for all of the modeling assumptions (e.g., rationale for the model choices in NMA and CEA); and the full details regarding the results (e.g., model fit statistics for all models assessed).<sup>10</sup> ICER should ensure that all future applications of the Framework are reproducible, as this is important as a principle of the scientific method as well as key to ensuring that stakeholders can provide ICER with the most relevant, useful feedback in response to comment opportunities.

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<sup>9</sup> This analysis goes on note that: "[m]ost meta-analyses require data points to be accompanied by variance measures or 95% confidence intervals (CIs). This is the case with the network meta-analysis (NMA) found in the ICER evidence report. Two direct comparisons failed to report the variance or 95% CI for the hazard ratio in the reference studies. However, the ICER NMA reported these measures and did not include a replicable source and/or methodology. The calculation of these missing values is within the realm of reasonable data configuration, however it is important that these manipulations are made transparent within the ICER report methods. It is important to note the authors did mention, 'When 95% confidence intervals were not available, uncertainty ranges were based on plausible values from the published literature' (pg. 74). However, without further clarification, the validity of these data should be approached with caution." (emphasis added) See. Husain, F., Y. Kuang, A. Grijalva, B. Kerr, R. Saad, C. Whittington, and T. Feinman. 2016 (May). Growth Replicator: ICER Multiple Myeloma. *Doctor Evidence*, available at: <http://growthevidence.com/wp-content/uploads/2016/05/Final-GROWTH-Replicator-ICER-Multiple-Myeloma-Replication-Report.pdf> (last accessed September 9, 2016).

<sup>10</sup> See ICER. 2016 (August 19). *Treatment Options for Advanced Non-Small Cell Lung Cancer: Effectiveness and Value*, available at: [https://icer-review.org/wp-content/uploads/2016/08/MWCEPAC\\_NSCLC\\_Draft\\_Evidence\\_Report\\_081916.pdf](https://icer-review.org/wp-content/uploads/2016/08/MWCEPAC_NSCLC_Draft_Evidence_Report_081916.pdf) (last accessed September 12, 2016).

**II. Integrating Patient and Clinician Perspectives and the Role of Cumulative Innovation into the Framework: ICER should ensure that the Framework does not shortchange the impact of innovative medicines on individual patients.**

**A. ICER must capture information that is meaningful to patients more holistically in the Framework's summary metrics.**

The first category of issues on which ICER requests specific input is “[m]ethods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value intended to fall in the current value framework within ‘additional benefits or disadvantages’ and ‘contextual considerations’[.]”<sup>11</sup> BIO appreciates ICER’s recognition that there should be a more rigorous inclusion of this type of information than the Framework currently allows. We agree that this is necessary to better reflect and incorporate the information that is important to patients and caregivers. While the full text of an ICER Drug Review may include a narrative discussion of patient and clinician perspectives, there is a continued reliance on summary metrics that obscure any nuance and detail that may have been captured in the Review text. In particular, the summary metrics may obscure important differences in the preferences and clinical characteristics of patient subpopulations, both of which may be better taken into account with improved and meaningful patient engagement in applying the Framework. Moreover, these summary metrics, like Care Value, oversimplify and reduce to an “average” the impact of innovative therapies on the full range of a patient’s quality of life and on the healthcare system as a whole.

An example is the often qualitative review of “additional benefits or disadvantages” in comparison to the quantitative dollar per quality-adjusted life year metric, which drives the Care Value metric. Additionally, this metric does not uniformly incorporate the impact of a therapy on a patient’s ability to return to their daily routines, and does not take into account the full impact on society, including through improvements to worker productivity and the broader impact of a healthier population. One mechanism to address this issue that ICER should employ is to incorporate indirect costs or cost-savings into economic models as sensitivity analyses to assess the impact of these “contextual considerations” on any cost-effectiveness ratio.

Not only should ICER more comprehensively take into account patient perspectives in the Framework, but also, BIO notes the importance of ensuring that patient perspectives are represented on the Public Advisory Councils, which are responsible for reviewing and voting on the content in the final Drug Reviews. While we appreciate ICER’s recent announcement of the appointment of a patient advocate to the ICER Governance Board, this does not replace the need for true subject matter expertise—including with respect to patients’ perspectives—on the Councils themselves.<sup>12</sup>

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<sup>11</sup> ICER. 2016 (July14). *ICER Opens National Call for Proposed Improvements to its Value Assessment Framework*, available at: <https://icer-review.org/announcements/improvements-value-framework/> (last accessed September 6, 2016).

<sup>12</sup> ICER. 2016 (July 21). *ICER Elects Patient and Consumer Advocacy Experts to Governance Board*, available at: <https://icer-review.org/announcements/icer-gov-board/> (last accessed July 22, 2016).



B. ICER must recruit subject matter experts to participate on the health technology assessment (HTA) panels that review, and vote on, the Drug Reviews.

To improve clinical accuracy of their assessments, ICER should include clinicians who have expertise in the disease area and are currently treating patients and/or conducting research in the disease area. Especially in the case of chronic, complex conditions, only clinical experts can be expected to keep pace with the rapid evolution of the standard of care and the nuance of individual clinical decision making. Not only should subject matter experts be involved in vetting the comparative clinical effectiveness questions that a drug review identifies (discussed above, see Section I), but it is important that they have a role in reviewing and validating the model inputs in any clinical and cost-effectiveness analyses. The inclusion of clinical experts on the HTA organizations that ultimately review the Framework's application and vote on the Care Value metric will also improve ICER's ability to update drug reviews based on emerging evidence.

There are several models ICER can emulate to address this recommendation. For example, the National Comprehensive Cancer Network (NCCN) establishes individual panels of clinicians and researchers that share a specific expertise to develop and update the NCCN Guidelines for oncology care.<sup>13</sup> These experts utilize their clinical expertise and existing evidence to make recommendations, and routinely update these recommendations based on emerging evidence. A similar example can be found in the statutory requirement that the Patient-Centered Outcomes Research Institute (PCORI) establish expert advisory panels to consult on the funding of research that is related to rare diseases and clinical trials.<sup>14</sup> In fact, the inclusion of a requirement for subject matter expertise as a statutory provision demonstrates that this is a standard with regard to comparative clinical effectiveness.

Yet another example is the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC), which maintains a pool of up to 100 experts in various fields and, from that advisory group, chooses "no more than 15 members with knowledge specific to the topic in question to serve on the panel for each MEDCAC meeting."<sup>15</sup> MEDCAC also has an established mechanism to "recruit non-MEDCAC members who have relevant expertise to provide additional input to panel members and invite experts to make formal presentations to the MEDCAC for a particular meeting."<sup>16</sup> While BIO has raised issues with MEDCAC's application of the model in practice in the past, the general structure of their process can serve as

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<sup>13</sup> National Comprehensive Cancer Network. *About the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)*, available at: <https://www.nccn.org/professionals/default.aspx> (last accessed on August 22, 2016).

<sup>14</sup> See ACA § 6301(d)(4). It is worthwhile to note that, while statute only identifies the topics of "clinical trials" and "rare disease" as the subject of required PCORI expert advisory panels, it permits the formation of others, and PCORI has established 7 such panels on the following subjects: assessment of prevention, diagnosis, and treatment options; improving healthcare systems; addressing disparities; patient engagement; clinical trials; rare disease; and communication and dissemination research. See PCORI. 2016 (June). *Join an Advisory Panel*, available at: <http://www.pcori.org/get-involved/join-advisory-panel> (last accessed September 1, 2016).

<sup>15</sup> Centers for Medicare and Medicaid Services. 2016. *Medicare Evidence Development & Coverage Advisory Committee*, available at: <https://www.cms.gov/Regulations-and-Guidance/Guidance/FACA/MEDCAC.html>.

<sup>16</sup> *Id.*

an example nonetheless.<sup>17</sup> No matter how ICER decides to implement this recommendation, we strongly urge the Institute to do so immediately such that ongoing reviews benefit from the participation of subject matter experts.

C. The Framework should reflect the role of cumulative innovation in improving the treatments available to patients over time.

BIO continues to raise the concern that the Framework does not consider the impact of cumulative innovation, which could be accomplished through an expansion of the “contextual considerations” category in each Review. Cumulative innovation describes the concept that relatively modest improvements in patient outcomes that result from individual innovative therapies build on each other to advance the scientific field forward, and result in major advancements on the standard of care over time. Each individual advance is important to the overall improvement in treatment for these patients. For example, the cancer death rate has fallen by 20 percent since 1991, in large part due to medicines.<sup>18</sup> The survival rate among children with cancer is approximately 83 percent compared to 58 percent in the mid-1970s. Yet, despite this reality, the ICER Framework does not take into account cumulative innovation, and thus, shortchanges the value of innovative therapies to the detriment of patient access.

III. **Replacing Metrics That Obscure the Impact of Personalized Medicine: ICER should not rely on metrics that do not take into the impact of innovative medicines on individual patients.**

A. ICER must ensure that the Framework relies on robust methodological standards and applies them consistently.

ICER’s second category of particular interest for stakeholder input is the structure of the Framework’s incremental cost-effectiveness ratios, specifically the appropriate threshold to set, and best practices in capturing health outcomes through quality-adjusted life years (QALYs). However, as a threshold matter with regard to ICER’s evidence review, this subsection reviews BIO’s increasing concerns with the assumptions that are used to identify comparators in a given clinical comparative effectiveness review and to assess clinical effectiveness and comparative clinical effectiveness.

Regarding the former, BIO identifies a lack of objectivity when determining the comparators in the draft scoping document, which is not necessarily based on systematic literature review of treatments in the disease area or actual utilization data on most commonly used treatments. For example, the draft scoping document for primary progressive multiple sclerosis (PPMS) included only ocrelizumab (not yet approved by the FDA at the time of the

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<sup>17</sup> BIO. 2014 (August 29). *Comments in Response to the Proposed Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) Charter*, available at: <https://www.bio.org/advocacy/letters/bio-submits-comments-hhs-regarding-proposed-medicare-evidence-development-and-cover>.

<sup>18</sup> PhRMA. 2014 (May 14). *Five Facts About the Value of Innovative Cancer Medicines*, available at: <http://catalyst.phrma.org/five-facts-about-the-value-of-innovative-cancer-medicines> (last accessed September 12, 2016).

release of the draft scoping document) and rituximab, while other more commonly used disease modifying therapies (DMTs)) for PPMS were not included.<sup>19</sup> For NSCLC, ICER mentioned the evaluation of cancer immunotherapy use in the first-line setting, but included atezolizumab, which did not have clinical data in first line.<sup>20</sup> Wherever possible, draft scoping documents should be supported by systematic literature review and the viewpoints of subject matter experts.

Regarding clinical effectiveness assessments, BIO identifies the following example as illustrative of our concerns: in defining a threshold for response in rheumatoid arthritis in the revised scoping document, there is a simplistic assumption made that meeting the ACR20 threshold directly translates to a 20 percent improvement in physical function;<sup>21</sup> instead, this multidimensional outcome measure requires at least a 20 percent improvement in a core measures set, and benefits from the use of a regression model across a data set to infer comparative clinical effectiveness.

To address this issue, at least in part, BIO recommends that ICER incorporate the International Society For Pharmacoeconomics and Outcomes Research's (ISPOR's) Multi-Criteria Decision Analysis (MCDA) methods to improve the quality of the Framework's assumptions and its application to drug reviews by providing structure, consistency, and transparency to this effort. Moreover, we urge ICER to consistently assess the uncertainty of any cost-effectiveness analyses that may be incorporated in the updated version of the Value Framework through deterministic or probabilistic sensitivity analyses.<sup>22</sup> In addition to taking into account variances in clinical effectiveness and cost, such analyses also should consider the impact of existing policies that can impact patient access, which, when considered across a population, could subsequently impact any global assessment of cost effectiveness. The results of these sensitivity analyses and key assumptions and drivers of the model should always be emphasized—including in any reported summary metrics—rather than just the base case ratio.

ICER also could address these issues by submitting the methodology for each drug review through a peer-reviewed process to act as an external arbiter of the validity and reliability of the assumptions made to evaluate clinical comparative effectiveness. While we recognize and appreciate that the methodology used to assess PCSK-9 inhibitors was peer reviewed recently, the Value Framework methodology has evolved since this 2015 review was conducted.<sup>23</sup>

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<sup>19</sup> ICER. 2016 (September 6). *Disease Modifying Therapies for Relapsing-Remitting and Primary Progressive Multiple Sclerosis: Effectiveness and Value Final Addendum to Background and Scope*, available at: [https://icer-review.org/wp-content/uploads/2016/09/CTAF\\_PPMS\\_Final\\_Scope-Addendum\\_090216.pdf](https://icer-review.org/wp-content/uploads/2016/09/CTAF_PPMS_Final_Scope-Addendum_090216.pdf) (last accessed September 12, 2016).

<sup>20</sup> ICER. 2016 (August 19). *Treatment Options for Advanced Non-Small Cell Lung Cancer: Effectiveness and Value: Draft Evidence Report*, available at: [https://icer-review.org/wp-content/uploads/2016/08/MWCEPAC\\_NSCLC\\_Draft\\_Evidence\\_Report\\_081916.pdf](https://icer-review.org/wp-content/uploads/2016/08/MWCEPAC_NSCLC_Draft_Evidence_Report_081916.pdf) (last accessed September 12, 2016).

<sup>21</sup> See ICER. 2016. *Rheumatoid Arthritis: Revised Scoping Document* [and accompanying analysis model], available at: <https://icer-review.org/topic/arthritis/>.

<sup>22</sup> Caro JJ, Briggs AH, Siebert U, et al. 2012. Modeling good research practices - overview: A report of the ISPOR-SMDM modeling good research practices task force-1. *Value Health* 15:796-803.

<sup>23</sup> Kazi, D. S., et. al. 2016. Cost-effectiveness of PCSK9 Inhibitor Therapy in Patients With Heterozygous Familial Hypercholesterolemia or Atherosclerotic Cardiovascular Disease. *The Journal of the American Medical Association* 316(7):743-753.

Submitting each Drug Review analysis—or at a minimum, each iteration of the Value Framework—for peer review can improve and help to ensure its methodological rigor, and will provide sufficient detail such that stakeholders can understand how a review was conducted and, as a result, any implications for patient care.

- B. ICER should not use a QALY-dependent clinical comparative effectiveness threshold, as it shortchanges the impact of innovative medicines on individual patients and undermines efforts to support personalized medicine.

As a threshold matter, BIO urges ICER not to include a cost-per-benefit threshold as a feature of the Care Value metric in the updated Value Framework. We raise serious concerns with the premise of imposing an average cost-per-benefit metric in a value assessment framework as it inherently obscures the benefits of increasingly personalized medicines to individual patients. This type of metric will not be able to distinguish between the costs and cost offsets of a therapy to different stakeholders (e.g., a patient, a provider, a payor, and/or the federal government). In fact, a cost-per-benefit threshold does not reflect the importance of assessing a therapy's comparative impact on patient health outcomes separately from the budget impact to any given stakeholder, discussed in the introduction of this letter in more detail.

BIO specifically urges ICER not to use QALYs—and by extension, QALY-based thresholds—in the updated version of the Value Framework. We recognize that a clinical comparative effectiveness review is a key feature of the Value Framework, but posit that such an assessment can be undertaken without the use of the QALY summary metric. If ICER chooses to explore other mechanisms, we urge the Institute to convene experts from diverse perspectives to assist in identifying an alternative (or potentially several alternatives to be applied depending on the disease or condition to be studied).

Our opposition to the continued use of the QALY is based on our concern that the reliance on QALYs is not meaningful in the context of a multi-payer insurance system, as we have in the U.S. Here, in contrast to countries with a single payer system, there is no single budget against which to determine “willingness to pay” over the lifetime of the patient. More importantly, QALYs cannot adequately capture the comprehensive value an innovative therapy offers individual patients, the healthcare system, and society. QALYs are arbitrary and do not holistically assess the value of a therapy to an individual patient.<sup>24</sup> Additionally, it is unclear to what extent changes in quality of life as measured by changes in QALYs are meaningful to patients. Assessing the individual impact of a therapy on a patient is increasingly becoming the premise of clinical care as medical science advances toward personalized medicines that take into account patients' individual characteristics, including their genetics, and the disease

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<sup>24</sup> For example, QALYs are not able to distinguish between net gains (or losses) that are driven by a small gain (or loss) to a large number of patients or a large gain (or loss) to a small number of patients. For a broader discussion of this issue, see BIO. 2007 (October 25). *The Complexities of Comparative Effectiveness*. Appendix Two: Conversion to a Common Metric, p. 24, available at: <https://www.bio.org/articles/complexities-comparative-effectiveness> (last accessed August 5, 2016).

pathophysiology. ICER has yet to address the well-documented disadvantages of using QALYs to assess the value of a therapy.<sup>25</sup>

Among those disadvantages is the fact that QALYs may be particularly ill-suited for determining the utility of the change in quality of life to patients with certain types of chronic conditions—including autoimmune conditions. The variability of outputs resulting from different assumptions under the QALY methodology for these types of patients makes direct comparisons under the Framework infeasible. Moreover, the cost-per-QALYs paradigm is biased against certain types of therapies, such as those that treat complex, chronic conditions, and those that treat diseases that affect only small populations. In both instances, medicines can often have higher associated costs per individual. Therapies that treat rare diseases may never meet this threshold, which would ostensibly indicate that biopharmaceutical developers should not invest in bringing these therapies to market. Yet that conclusion does not match the societal view of the importance of these medicines (e.g., as evidenced by the passage of the Orphan Drug Act into law).

The National Institute for Health and Care Excellence's (NICE's) "highly specialised technologies programme" was developed on the basis of this bias, and NICE has recognized exactly this failing of the cost-per-QALY threshold, noting that:

Given the very small numbers of patients living with these very rare conditions a simple utilitarian approach, in which the greatest gain for the greatest number is valued highly, is unlikely to produce guidance which would recognise the particular circumstances of these very rare conditions. These circumstances include the vulnerability of very small patient groups with limited treatment options, the nature and extent of the evidence, and the challenge for manufacturers in making a reasonable return on their research and development investment because of the very small populations treated.<sup>26</sup>

Additionally, assessments that rely on QALY comparisons may inherently attribute a higher value to therapies for which overall survival data are available (though we recognize that QALYs can take into account quality of life associated with other outcomes, such as

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<sup>25</sup> For example, concerns have been raised with regard to: the assumption that health status/utilities can be measured on a cardinal scale; the assignment of utility weights to disease states can be done in a way that captures the various perspectives of patients with a certain disease; the narrow range of health benefits captured by QALY measurements; testing the theoretical assumptions attributed to the use of QALYs; whether QALYs are the same regardless of to what stakeholder they accrue; equity-weighted utility maximization; and the use of condition-specific measurements in QALY analyses. For additional information, see Whitehead, S. J., and S. Ali. 2010. Health outcomes in economic evaluation: the QALY and utilities. *British Medical Bulletin* 96(5-21); see also Griebsch, I., J. Coast, and J. Brown. 2005. Quality-adjusted life-years lack quality in pediatric care: a critical review of published cost-utility studies in child health. *Pediatrics* 115(5):e600-614.

<sup>26</sup> National Institute for Health and Care Excellence (NICE). 2013. *Interim Process and Methods of the Highly Specialised Technologies Programme*. Paragraph 36, p. 8, available at: <https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/Highly-Specialised-Technologies-Interim-methods-and-process-statements.pdf> (last accessed August 31, 2016).



progression-free survival, response rate, albeit with varied weight). This too may bias a QALY-based comparative assessment between older therapies—for which these data are more likely to be available—and therapies recently on the market, especially those that received approval through an accelerated approval pathway (e.g., breakthrough therapy designation). A more detailed discussion of this issue is included in the next section (III(C)).

In light of concerns we identify throughout this section, BIO continues to strongly urge ICER not to rely on the QALY metric. However, if the Institute continues to use QALYs as the key feature of its cost-effectiveness analysis despite this opposition, we urge ICER to address all of the issues described in this section of the letter. Additionally, we urge ICER to routinely incorporate sensitivity analyses around QALY measurements and to reflect these analyses in any summary metric. ICER should recognize the limitations of a QALY-based analysis in each drug review, both in the narrative discussion sections and as part of the summary metrics.

If, in spite of opposition, ICER continues to use a cost-per-QALY threshold to drive the Care Value metric, we strongly urge ICER to develop a range of thresholds specific to the disease or condition under study. The current iteration of the Value Framework applies a one-size-fits-all threshold of \$100,000/QALY or \$150,000/QALY without regard to the condition. As described above, certain conditions—based on the complexity and time course of the disease and/or the size of the patient population—have higher associated per-patient costs, and a static cost-per-QALY threshold inherently penalizes therapies that treat these conditions. In establishing thresholds for a certain disease or condition, or even a patient subpopulation within a disease or condition, ICER should clearly identify the evidence on which it relies and obtain feedback from various stakeholders—in particular patients—to inform its thinking.

C. The static nature of ICER's evidence review inherently disadvantages newer-to-market therapies, for which there may not be as much published evidence as may exist for therapies that have been on the market longer.

BIO is committed to the use of high-quality evidence in the assessment of the value of any health intervention, as the outcome of the assessment is only as valid as the data inputs. That said, we recognize that the timing of the application of the Framework to drug reviews—namely, as close to FDA approval of a new therapy—creates a distortion in the relative amount of available data for review and analysis. Specifically, therapies that have been on the market longer—and thus have more data available for analysis—may be at an advantage compared to newer-to-market therapies. This distortion is exacerbated by the absence of a process to update drug review findings based on emerging evidence. ICER must account for this difference in available published data when calculating Care Value to avoid summarily penalizing newer therapies under the Framework. One way to accomplish this is to establish explicit data quality standards, as many medical specialty societies do in advance of their clinical landscape reviews.<sup>27</sup> This mechanism would allow ICER to rely on a variety of high-quality evidence, not

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<sup>27</sup> For example, the American College of Rheumatology (ACR) has published Policy and Procedure Manual for Clinical Practice Guidelines, in which ACR clearly identifies how evidence will be rated. See ACR. 2015 (January). *Policy and Procedure Manual for Clinical Practice Guidelines*. Guideline Development, Phase 2: Development, Use of GRADE to Evaluate the Evidence and Develop Recommendations, pp. 14-15, available at:

just published literature, when applying the Framework to individual drug reviews. BIO acknowledges that this is not the only mechanism to address the distortion created by ICER's current static value assessment, and we encourage ICER to engage stakeholders to explore other approaches to address this pressing issue.

**IV. Overhauling the Price and Product-Update Assumptions and Restructuring the Short-Term Budget Impact Measure: ICER should ensure that all assumptions rely of robust evidence reflective of marketplace realities, and completely restructure the short-term budget impact measure to ensure that it reflects the impact of innovative medicines on individual patient care.**

**A. ICER's assumptions around the price and uptake of new-to-market therapies should reflect the realities of the marketplace.**

The third category of issues on which ICER is seeking specific comment is methods to estimate the market uptake and potential short-term budget impact of new interventions that “may raise affordability concerns without heightened medical management, lower prices, or other measures.”<sup>28</sup> In response, BIO reiterates our concerns with the Framework's two primary uptake assumptions. First, as BIO has noted in previous comments to ICER, the use of the wholesale acquisition cost (WAC) is problematic.<sup>29</sup> WAC does not reflect the discounts and rebates that are widely negotiated in the marketplace, nor does it reflect the rebates required by federal healthcare programs (e.g., Medicaid, 340B drug discount program, and the Coverage Gap Discount Program that applies to Medicare Part D). Thus, WAC is misleading with regard to the “cost” of the therapy to any individual payer, and does not reflect the costs to a patient. While we understand that the exact rebate amounts are not available to be used, this does not absolve ICER of the responsibility to use evidence-based estimates of actual spending in the base case (e.g., since the government is the largest payer, ICER could start by applying the average rebate percentage applicable to government healthcare programs to WAC as the base case).

Second, we continue to question ICER's assumption of unrestricted access to a new therapy in the first five years it is available on the market. This assumption is not reflective of

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[http://www.rheumatology.org/Portals/0/Files/ACR%20Guideline%20Manual\\_Appendices\\_updated%202015.pdf](http://www.rheumatology.org/Portals/0/Files/ACR%20Guideline%20Manual_Appendices_updated%202015.pdf) (last accessed August 31, 2016).

<sup>28</sup> ICER. 2016 (July14). *ICER Opens National Call for Proposed Improvements to its Value Assessment Framework*, available at: <https://icer-review.org/announcements/improvements-value-framework/> (last accessed August 1, 2016).

<sup>29</sup> In BIO's May 2016 comments, we raised concerns that not only is the use of WAC in an inaccurate reflection of the cost of therapies given the market realities of the U.S. healthcare system, but also, ICER does not appear to use the same metric for all drug reviews. For example, the Review of therapies treating high cholesterol and severe asthma with eosinophilia utilized WAC, while the Review of therapies treating congestive heart failure utilized WAC minus a calculated discount, and it is unclear what measure was utilized by the Review of therapies treating diabetes (ICER lists “annual drug costs” simply as “calculated”). In the absence of a consistent and transparent measure of cost to different stakeholders, including to patients individually, the Framework is missing a critical element of the calculation of value. See CTAF. 2016 (March 14). *Insulin Degludec (Tresiba®, Novo Nordisk A/S) for the Treatment of Diabetes: Effectiveness, Value, and Value-Based Price Benchmarks*. Table 7, p. 30, available at: [https://icer-review.org/wp-content/uploads/2016/03/CTAF\\_Degludec\\_Final\\_Report\\_031416.pdf](https://icer-review.org/wp-content/uploads/2016/03/CTAF_Degludec_Final_Report_031416.pdf) (last accessed September 12, 2016).

reality and negatively skews the assessment of therapies that treat large patient populations.<sup>30</sup> In assuming unrestricted patient access, ICER's application of the Framework does not comply with internationally-accepted guidelines on calculating budget impact established by ISPOR.<sup>31</sup> Moreover, such an assumption does not reflect reality: one study estimates that payers impose utilization management restrictions on over 70 percent of covered therapies that treat certain diseases/conditions in certain segments of the health insurance market.<sup>32</sup> A recent study suggests that ICER may be grossly overestimating the budget impact of new therapies and therefore present misleading information to its stakeholders. For example, researchers found that based on the initial quarters of reported sales, the actual one-year cost of the two novel PCSK-9 Inhibitors studied reached \$83 million, or 1.2 percent of ICER's predicted \$7.1 billion.<sup>33</sup> Thus, the Framework must reflect the realities of market uptake of a new therapy, either by delaying the study of a therapy until real-world evidence is available or used market uptake assumptions that are justified based on examining real-world utilization data of previous drug launches in the disease area (e.g., from claims databases or other sources).

It is also unclear why ICER takes a "health system perspective" in establishing cost-effectiveness models in some Reviews (e.g., the Review assessing high cholesterol therapies) but takes a payer perspective in others (e.g., the Review assessing severe asthma with eosinophilia therapies).<sup>34</sup> The perspective ICER assumes is important because it dictates the inclusiveness of the cost offsets that ICER considers, which, in turn, impacts the value-based price benchmark. To address this, and considering BIO's broader recommendations throughout this letter, we

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<sup>30</sup> For a more detailed discussion on issue, see BIO. 2016 (May). *Follow-Up on BIO's Comments in Response to the ICER Value Framework*. Section III(A): Utilization, in the context of the Provisional Health System Value metric, is assessed inconsistently and biases Reviews against therapies that treat large patient populations, pp. 6-7, available at: <https://www.bio.org/letters-testimony-comments/follow-bio%E2%80%99s-comments-response-icer-value-framework> (last accessed August 1, 2016).

<sup>31</sup> ISPOR. *Principles of Good Practice for Budget Impact Analysis*, available at: [http://www.ispor.org/workpaper/BudgetImpactAnalysis/BIA\\_TF0906.asp](http://www.ispor.org/workpaper/BudgetImpactAnalysis/BIA_TF0906.asp) (last accessed August 31, 2016).

<sup>32</sup> Avalere Health. 2014 (March 24). *Consumers Face More Hurdles to Accessing Drugs in Exchange Plans Compared to Employer Coverage*, available at: <http://avalere.com/expertise/life-sciences/insights/more-controls-on-drug-access-in-exchanges> (last accessed August 31, 2016).

<sup>33</sup> An upcoming study, described by researchers in a news piece on August 11, 2016, found "that predictions of health care costs made prior to the introduction of new drugs are often dramatically overestimated." One example provided was ICER's assumptions on unmanaged utilization of PCSK-9 Inhibitors in the 2016 Drug Review of these therapies. According to the report, the researchers found that, based on the initial quarters of reported sales, the actual one-year cost of the two novel PCSK-9 Inhibitors reached \$83 million, or 1.2 percent of ICER's predicted \$7.1 billion. See PR Newswire. 2016 (August 11). *Billion Dollar Blunder: On the 1-Year Anniversary of a New Class of Cholesterol Medicines, Study Finds Actual Cost of New Drugs Is Billions Less than Predicted Independent analysis of pre-launch predictions of 14 new drugs finds predicted cost many times the true cost*, available at: <http://www.prnewswire.com/news-releases/billion-dollar-blunder-on-the-1-year-anniversary-of-a-new-class-of-cholesterol-medicines-study-finds-actual-cost-of-new-drugs-is-billions-less-than-predicted-300311969.html> (last accessed August 31, 2016).

<sup>34</sup> See ICER. 2015 (November 24). *PCSK9 Inhibitors for Treatment of High Cholesterol: Effectiveness, Value, and Value-Based Price Benchmarks: Final Report*. Section 6.2 "Incremental Costs per Outcomes Achieved," p. 30, available at: <https://icer-review.org/wp-content/uploads/2016/01/Final-Report-for-Posting-11-24-15-1.pdf> (last accessed September 12, 2016); see also ICER. 2016 (March 14). *Mepolizumab (Nucala®, GlaxoSmithKline plc.) for the Treatment of Severe Asthma with Eosinophilia: Effectiveness, Value, and Value-Based Price Benchmarks: Final Report*. Section 6.3 "Incremental Costs per Outcome Achieved," p. 20, available at: [https://icer-review.org/wp-content/uploads/2016/03/CTAF\\_Mepolizumab\\_Final\\_Report\\_031416.pdf](https://icer-review.org/wp-content/uploads/2016/03/CTAF_Mepolizumab_Final_Report_031416.pdf) (last accessed September 12, 2016).



recommend that ICER take a holistic, societal perspective when considering benefits, costs, and cost offsets. At a minimum, ICER should standardize the perspective used across drug reviews, and/or describe why one perspective is considered to be more appropriate for a specific review.

**B. ICER's Provisional Health System Value metric is not meaningful in the context of clinical care and relies on an inappropriately short time frame for the review of new therapies.**

As a threshold matter, BIO continues to urge ICER to disaggregate the assessment of clinical comparative effectiveness and budget impact to specific payors. At a minimum, ICER should rename the “provision health system value” metric to identify its focus on short-term budgetary impact (i.e., revise the name to “short-term budgetary impact” metric).

BIO continues to express concern with regard to ICER's continued use of only a five-year measurement window to assess budget impact (i.e., Provisional Health System Value). This is especially true since ICER has, and continues to, target chronic conditions for its Reviews, including rare diseases. These conditions manifest over multiple years or even decades, and can have a differential impact on patients depending on their personal (including genetic) characteristics. Especially in the case of rare diseases, this impact can be challenging to study given the size of the patient population. Thus, the five-year assessment window and the metrics of “average” value, which are not unique to individual patient experiences, are inadequate to capture the full range of benefits, costs, and cost offsets of an innovative therapy to individual patients, the healthcare system, and society.

If ICER does not expand the time horizon over which budget impact is considered, the Institute may contribute to stifling the innovation ecosystem by systematically undervaluing therapies that have relatively high upfront costs but represent significant improvements in the standard of care and can improve longer-term patient health outcomes and decrease longer-term healthcare system expenditures. If ICER insists on continuing to utilize the 5 year budget impact window, we urge the Institute to model—and report as summary metrics—budget impact at several time intervals, including 7 and 10 years to more adequately demonstrate the potential impact of cost offsets across the course of a patient's disease. An expansion of the modeling in this manner will be particularly relevant to certain types of payors, including those in integrated healthcare systems, large employers (e.g., those likely to see lower rates of turnover in their beneficiary populations), and federal healthcare programs (e.g., Medicare).

**V. Discontinuing the Use of the Budget Impact Threshold: ICER should not continue to employ the budget impact threshold as it is not meaningful in the context of clinical decision-making and obscures the nuance and detail of the impact of an innovative therapy on an individual patient.**

The fourth issue category on which ICER specifically requests feedback is the structure of the threshold for a potential short-term budget impact that “can serve as a useful ‘alarm bell’

for policymakers.”<sup>35</sup> BIO continues to question the premise of the budget impact threshold and its relevance to clinical decision making. This threshold applies a one-size-fits-all standard to therapies regardless of their impact on patients’ lives and the overall healthcare system, and is not meaningful in the context of clinical decision-making between patients and providers. In this way, it is anchored to the status quo of current innovation, which does not reflect society’s call for better treatments and cures (e.g., evidenced by the Cancer Moonshot and Precision Medicine Initiatives).

Moreover, the budget impact threshold is based on the narrow assumption that annual spending on novel prescription drugs should not exceed gross domestic product (GDP) growth plus one percent, without a thorough analysis of the impact of this spending on U.S. GDP. In particular, ICER does not account for the potentially positive aspects of a growth in prescription drug spending that result in healthier patients and improved efficiency and effectiveness in the system. For example, healthier patients may be more productive, which positively contributes to GDP growth.<sup>36</sup> Similarly, there also is no consideration of the observation that rising income leads to higher expenditures on health (which could mean that patients are finally able to obtain the care they need).<sup>37</sup> Thus, artificially tying annual spending on new prescription drugs to GDP growth may result in unintended consequences that introduce inefficiencies into the healthcare system, not least of which through decreasing patient access to needed therapies. BIO agrees with the commentary in a 2016 research article, which discusses the policy implications of budgetary caps on prescription drug spending, that “[i]t seems neither fair nor efficient that patient access to new therapies should now swing with the vagaries of the business cycle or the choice of forecasting agency.”<sup>38</sup>

Additionally, BIO questions why ICER has focused on estimating the sum total cost of a therapy to all healthcare payers when this is not a meaningful metric in our multi-payer health insurance system. The threshold was established, in part, to mirror the “acceptable” growth formula established for the Independent Payment Advisory Board (IPAB) under the Affordable Care Act. Yet employing this benchmark is inappropriate given that the IPAB has jurisdiction only over the Medicare program, whereas ICER applies its threshold collectively across all payors. Additionally, a “global” approach to assessing costs and cost offsets ignores the specific costs to the patient, which research has shown directly impacts adherence to therapy and downstream healthcare system spending.<sup>39</sup>

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<sup>35</sup> ICER. 2016 (July14). *ICER Opens National Call for Proposed Improvements to its Value Assessment Framework*, available at: <https://icer-review.org/announcements/improvements-value-framework/> (last accessed August 1, 2016).

<sup>36</sup> Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation (ASPE). *The Effect of Health Care Cost Growth on the U.S. Economy*, available at: <https://aspe.hhs.gov/sites/default/files/pdf/75441/report.pdf> (last accessed August 29, 2016).

<sup>37</sup> Id. at 9-11.

<sup>38</sup> Goldman, D. P., D. N. Lakdawalla, J. R. Baumgardner, and M. T. Linthicum. 2016 (January). Are Biopharmaceutical Budget Caps Good Public Policy? *The Economists’ Voice* [ed. By Cragg, M., J. Stiglitz, and J. Zwiebel.] ISSN (Print) 2194-6167, Section 8, p.10.

<sup>39</sup> Eaddy, M. T., C. L. Cook, et. al. 2012. How Patient Cost-Sharing Trends Affect Adherence and Outcomes: A Literature Review. *Pharmacy and Therapeutics* 37(1):45-55.

The so-called “alarm bell” also directly influences ICER’s value-based pricing benchmark summary metric, which detracts from the nuance of treatment decisions and the impact of innovation on patients, the healthcare system, and society as a whole. The threshold is driven by the inaccurate assumptions of uptake and cost used to construct the Provisional Health System Value metric (discussed in an earlier section of this letter), and therefore, inherently disadvantages the assessment of therapies that treat large patient populations. This bias against therapies that treat large patient populations appears to exist regardless of the value such medicines may have to individual patients and the healthcare system. Ultimately, such a bias can support inefficient, inappropriate healthcare choices, by discouraging the utilization of medicines that may offer significant health benefits, and diminish investment in treatments and cures for large patient populations, resulting in missed opportunities to help reduce overall health expenditures. Thus, ICER should not continue to employ a budget impact threshold in the Framework, but instead, significantly restructure the narrative discussion of the potential short- and long-term financial impact of a therapy on specific stakeholders in each drug review.

## **VI. Conclusion**

BIO appreciates the opportunity to provide comments on the underlying Framework methodology, but remain concerned that this is the first such opportunity to do so in the year since the methodology was revised and used to conduct almost a dozen drug reviews. Moving forward, ICER must establish a formal process for soliciting and incorporating stakeholder feedback on the underlying methodology in a more timely fashion as the standard for value assessment evolves.

We reiterate the need for ICER to identify how stakeholder feedback is incorporated in each stage of the drug review process, and, in particular, provide greater clarity around the Institute’s efforts to incorporate the patient perspective into each review. We reiterate our recommendation that ICER reform the summary metrics of the Value Framework through the recommendations discussed in this letter to avoid obscuring the nuance of treating patients with complex, chronic conditions.

Finally, we urge ICER to more clearly state that its work is only a single input into the broader discussion on improving the efficiency and effectiveness of healthcare decision making. The Institute also should emphasize the limitations of the drug reviews and support the importance of individual patient/provider decision making in any discussions that address payers’ coverage and reimbursement determination processes. As a substantive contributor to the discussion of value, ICER has a responsibility to ensure that its process is inclusive, its methodology is reflective of the realities of patient care, and its findings are interpreted in the appropriate context.

BIO looks forward to opportunities to contribute to ICER's ongoing work, and continues to encourage the Institute to refine the Framework to ensure that it promotes, rather than acts at odds to, patient-focused health care. Please feel free to contact me at (202) 962-9200 if you have any questions or if we can be of further assistance. Thank you for your attention to this very important matter.

Respectfully submitted,

/s/

Laurel L. Todd  
Vice President  
Healthcare Policy and Research

Kristin Viswanathan  
Director, Health Policy and Research

September 12, 2016

Steve Pearson, MD  
Institute for Clinical and Economic Review  
Two Liberty Square  
Ninth Floor  
Boston, MA 02109

RE: Call for Proposed Improvements to the ICER Value Assessment Framework

Dear Dr. Pearson,

On behalf of Boehringer Ingelheim Pharmaceuticals, Inc. (BI), we are pleased to submit comments on ICER's Value Assessment Framework. BI is a leading global research organization with extensive expertise developing therapies to treat a variety of chronic and life threatening diseases. BI supports ICER's continued efforts to improve the quality of evidence for decision-makers through its value assessment process and commends ICER's efforts to update and improve its framework. We believe that collaboration, transparency, and open dialogue throughout the development of value assessment frameworks is critical to ensuring that they are appropriately and accurately evaluating the treatments according to what patients and other stakeholders value. We therefore particularly appreciate the opportunity to provide feedback to ICER on this important issue.

Below, we focus our comments and recommendations on the following:

- Ensuring indirect treatment comparisons are rigorous with transparent methods
- Separating budget impact analyses from assessments of Health System Value
- Removing budget impact thresholds
- Considering longer-term time horizons in budget impact analyses
- Ensuring drug costs used in cost-effectiveness and budget impact analyses are reflective of the intended audience
- Differentiating cost-effectiveness thresholds
- Engaging patients and incorporating their perspectives
- Ensuring continued transparency and collaboration with stakeholders

## **Ensure indirect treatment comparisons are rigorous with transparent methods**

BI acknowledges the need for indirect treatment comparisons (ITCs), particularly in the context of comparing different treatments for which direct head-to-head comparison trials may not be available. However, we emphasize that the methodology used to conduct ITCs must be rigorous and based on internationally-accepted standards, such as those endorsed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR).<sup>i</sup> As the results from ITCs are critical inputs to cost-effectiveness analyses, we request that ITC methods and results be clearly and comprehensively presented in the evidence reports along with any limitations of the analysis (e.g., differences in study design, heterogeneity in patient populations across studies, etc.).

## **Separate budget impact analyses from assessments of Health System Value**

BI acknowledges ICER's rationale for utilizing a budget impact analysis in assessment of "Health System Value," however, we remind ICER that budget impact analyses do not assess the value of a technology. We therefore recommend that, this should be viewed as distinct from the assessment of "Health System Value" and the determination of a "Value-based Price Benchmark." As defined by ISPOR, a budget impact analysis "addresses the expected changes in the *expenditures* of a health care system after the adoption of a new intervention," and provides information on "the *fiscal impact* of the adoption and diffusion of new health care interventions."<sup>ii</sup> This definition is echoed by the Academy of Managed Care Pharmacy (AMCP), and they further emphasize that "budget impact models are not intended to establish the overall *value* of health care technologies because they do not include the full impact of the technology on clinical and patient outcomes."<sup>iii</sup> We acknowledge that budget impact estimates provide valuable information to decision-makers when affordability is the underlying issue, but they do not inform decision-makers of what health outcomes are being achieved in return for the expenditure, which is the definition of value in health care.<sup>iv</sup> The approach is consistent with that of several well-established global health technology assessment organizations that evaluate and report budget impact but do not incorporate it into the determination of value.<sup>v,vi,vii</sup>

## **Remove the arbitrary budget impact threshold**

BI strongly recommends that ICER remove the single budget impact threshold that spans across all diseases and patient populations regardless of factors that could significantly affect how patients and other stakeholders perceive or weigh the value of a certain product or treatment. The concept of establishing a single budget impact threshold across all drugs in different therapeutic areas for different decision-makers with varying budgets, resources, and patient populations runs contrary to the principles of good practice by ISPOR; which states that "given the (health care) systems' *highly local nature* and *decision makers' varying perspectives*, a budget impact analysis cannot give a *single* estimate applicable to *all* decision makers." Defining a common budget impact threshold across all drugs also disincentivizes the development of drugs for highly prevalent diseases with unmet need, which is counterintuitive to maximizing public health.

Furthermore, there are several issues with ICER's derivation of their \$904 million budget impact threshold.

1. The "GDP +1%" benchmark is arbitrary and does not take into account the changing health care needs of an aging US population. In 2014, Americans aged 65 years and older accounted for 14.5% of the US population, with this figure expected to grow to 21.7% by 2040.<sup>viii</sup> Considering the greater health care needs of the elderly and increasing percentage of the aging population, it is unreasonable to assume the growth of health care spending will remain constant at GDP+1%. Furthermore, this approach opposes the concept of true innovation that may occur periodically rather than at a constant rate.
2. In fixing the contribution of drug spending to 13.3% of health care spending, ICER artificially isolates individual components of health care spending and fails to recognize the reduced utilization of health care services (and other aspects of health care spending) that may result from adoption of new innovative drugs. For example, the increased adoption of oral oncolytics has shifted care delivery away from more costly sites, such as hospitals and infusion centers, resulting in lower health care spending in these service areas.
3. In assessing the budget impact for adopting a new drug, uptake assumptions should be evidence-based to the extent possible. For marketed products, uptake rates should be based on an analysis of past market performance, while options for forecasting uptake of new drugs could include the use of analogs, as well as inputs from clinical experts regarding expected usage patterns. Payer utilization controls can also impact uptake, and these should be considered as well. Given the uncertainty associated with predicted uptake rates, sensitivity analyses should also be conducted for different uptake assumptions.

With considerations of all the limitations stated above, we recommend that ICER remove the budget impact threshold, and disassociate budget impact analysis from the determination of the "Value-based Price Benchmark".

### **Consider longer-term time horizons in budget impact analyses**

ICER currently assesses the budget impact of technologies over a five-year period. However, the benefits of a new intervention (for example, in terms of cost offsets from reduced health care resource utilization) may not be realized in the short-term. We acknowledge the delicate balance between near-term budget constraints and long-term resource allocation, and recommend that ICER considers using both short-term (i.e. one to five-year period) and longer lifetime time horizons in their budget impact analyses, which are sufficiently long enough to account for the long-term benefits and cost offsets of the treatment. Furthermore when using longer time horizons, lower medication costs that result as drugs become genericized should also be taken into account in the analyses.

## **Ensure drug costs used in cost-effectiveness and budget impact analyses are reflective of the intended audience**

The drug costs that are included in both the cost-effectiveness and budget impact assessments should reflect the perspective of the intended audience of the analyses<sup>ix</sup>. As recommended by ISPOR, analyses “performed from a payer perspective should use drug prices actually paid by the relevant payer *net of all rebates, copays, or other adjustments*” while those from a patient/consumer perspective should use “*total net out-of-pocket* payments for medications... as the drug cost measurement.”<sup>x</sup> Although the rebates paid to health plans by manufacturers are commercially confidential and likely to vary significantly from plan to plan, ICER could address this concern by developing and applying standard rebate assumptions in the base case. These assumptions should be different for primary care vs. specialty products and should take into account the novelty of the therapy under consideration and the number of competitors in the market. A plausible range of rebate assumptions should be tested in sensitivity analyses.

## **Differentiate cost-effectiveness thresholds for different perspectives, disease areas, and populations when evaluating care value**

BI recognizes that cost-effectiveness analyses are a key component of the “Care Value” assessment in the ICER framework; however, we recommend that ICER revisit the current cost-effectiveness thresholds in its value assessment framework, and consider varying thresholds for different perspectives, disease areas, and populations. Evidence suggests that the value of a treatment or product changes depending on the perspective from which it is assessed. The US healthcare system is highly fragmented, with multiple stakeholders paying for, delivering and receiving healthcare and defining value in different ways. The application of a single willingness-to-pay threshold in this context is misleading and ignores stakeholder preferences. For example, studies involving oncologists and cancer patients suggest willingness-to-pay thresholds in the region of \$300,000/QALY, much higher than the \$50,000-150,000/QALY thresholds commonly referenced by payers.<sup>xi,xii</sup> Cost-effectiveness thresholds can also vary for different disease areas and specific patient populations. This variation is acknowledged by the National Institute for Health and Care Excellence (NICE) in the United Kingdom that has adopted special provisions for oncology drugs (via the Cancer Drugs Fund), and for end-of-life treatment (supplementary advice has been provided to the Appraisal Committees).<sup>xiii,xiv,xv</sup>

## **Engage patients and include their perspectives in all aspects of the value framework development and assessment process**

In order for value assessments to advance the national dialogue on value in health care, frameworks like ICER need to systematically and consistently incorporate the patient voice. Engaging patients and patient groups in this work is necessary to fully understand how different populations and subpopulations determine value. Therefore BI believes it is critical to engage, inform, and actively listen to patients with chronic conditions throughout each aspect of these processes.



While BI is aware of ICER's initial attempts to engage patients/patient groups, below are some recommendations on ways to bolster and systematize this engagement:

- *Continual partnership with patients and patient groups:* Patients should be involved in every step of the value framework development and dissemination process. Currently patient engagement is limited to discrete portions of the evaluation process, however, it is not clear how patients' perspectives have been integrated into the framework, nor is it clear if patients have a role beyond the assessment in informing the communication and dissemination of the results. ICER should develop a clear process/guidance for how patients/patient groups can engage with during each part of the process.
- *Appropriate information sharing and transparency to patients:* ICER should disclose the assumptions and inputs into the value model itself to patients/patient advocacy groups in an easily understandable way. This will allow for richer dialogue between the patients and ICER.
- *Consideration for the diversity of patients/populations:* The value assessment should account for differences across patient subpopulations, trajectory of disease, and stage of a patient's life. Because many diseases change/progress over time, value definitions are likely to change dependent on the person's current state of health and life circumstances.
- *Incorporate outcomes that are important to patients:* The outcomes integrated into the economic models should include a portion of those that patients have identified as important and consistent with their goals, aspirations, and experiences.
- *Look for patient-centered data sources:* The value assessment should rely on a variety of credible data sources that allow for timely incorporation of new information and account for the diversity of patient populations and patient-centered outcomes, especially those from real-world settings and reported by patients directly.

To help guide these efforts, BI encourages ICER to look to patient-focused resources, including the National Health Council's Value Rubric. This paper helps to illustrate meaningful examples of patient engagement in many of these areas.

### **Ensure continued transparency and collaboration with stakeholders**

Lastly, BI would like to commend ICER for its recent efforts to enhance stakeholder engagement through actions such as lengthening the public comment periods for draft scoping documents and draft evidence reports. However, we encourage ICER to continue working to ensure sufficient time for stakeholders to review and provide input at all critical points throughout the assessment process, including when modeling inputs and assumptions are being determined. Seeking stakeholder input helps to ensure that the evidence and recommendations presented in the report are accurate and reflect the most current evidence base. As such, we urge ICER to continue to strive for a high degree of transparency and collaboration with stakeholders throughout the value assessment process.

BI appreciates the opportunity to comment on ICER's Value Assessment Framework. We look forward to working with ICER to improve care and treatment options for patients, and welcome the opportunity to discuss our comments further.

Sincerely,

SENT ELECTRONICALLY

A handwritten signature in purple ink, appearing to read 'Martina Flammer', with a long horizontal flourish extending to the right.

Martina Flammer MD, MBA

VP, Clinical Development & Medical Affairs Specialty Care  
Boehringer Ingelheim Pharmaceuticals, Inc.

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- <sup>i</sup> Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: Report of the ISPOR task force on indirect treatment comparisons good research practices – part 2. *Value in Health*. 2011; 14:429-437.
  - <sup>ii</sup> Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis – Principles of good practice: Report of the ISPOR 2012 budget impact analysis good practice II task force. *Value in Health*. 2014; 17:5-14.
  - <sup>iii</sup> The AMCP Format for Formulary Submissions, Version 4.0. Academy of Managed Care Pharmacy; April 2016.
  - <sup>iv</sup> Porter ME. What is value in health care? *New England Journal of Medicine*. 2010; 363:2477-2481.
  - <sup>v</sup> Guide to the methods of technology appraisal 2013. National Institute for Health and Care Excellence; 2013.
  - <sup>vi</sup> Guidelines for the economic evaluation of health technologies: Canada [3rd Edition]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2006.
  - <sup>vii</sup> Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee version 4.5. Pharmaceutical Benefits Advisory Committee; 2015.
  - <sup>viii</sup> Aging statistics. Administration for Community Living. US Department of Health and Human Services. [http://www.aoa.acl.gov/Aging\\_Statistics/index.aspx](http://www.aoa.acl.gov/Aging_Statistics/index.aspx). Accessed August 31, 2016.
  - <sup>ix</sup> Hay JW, et al. Good research practices for measuring drug costs in cost effectiveness analyses: issues and recommendations: The ISPOR Drug Cost Task Force Report—Part I. *Value in Health*. 2010; 13:3-7
  - <sup>x</sup> Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis – Principles of good practice: Report of the ISPOR 2012 budget impact analysis good practice II task force. *Value in Health* (2014); 17:5-14.
  - <sup>xi</sup> Nadler E, et al. Do oncologists believe new cancer drugs offer good value? *Oncologist*. 2006 Feb; 11(2):90-5.
  - <sup>xii</sup> Seabury SA, et al. Patients value metastatic cancer therapy more highly than is typically shown through traditional estimates. *Health Affairs*. 2012 Apr; 31(4):691-699.
  - <sup>xiii</sup> Cancer Drugs Fund. National Institute for Health and Care Excellence. <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/cancer-drugs-fund>. Accessed August 31, 2016.
  - <sup>xiv</sup> Process and Methods Guide Addendum A - Final amendments to the NICE technology appraisal processes and methods guides to support the proposed new Cancer Drugs Fund arrangements. National Institute for Health and Care Excellence. <https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/process-and-methods-guide-addendum.pdf>. Accessed August 31, 2016.
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## **BMS Response to ICER's Call for Improvements to its Value Assessment Framework**

BMS has taken on some of the most challenging health problems of our time and welcomes the opportunity to participate in ICER's national call for suggestions on how to improve its value assessment framework. BMS' pipeline is a reflection of the desire to cause the same transformation in cancer care as our research contributed to the transformation of HIV to a manageable chronic disease. As a leader in immuno-oncology research and innovation, we have delivered on the challenge of fighting cancer and developing lifesaving therapies. An evidence-driven approach to measuring treatment value is critical as we tackle the most challenging diseases of highest unmet need, but the science is progressing rapidly.

BMS will support the development of best practices in value assessment, but we disagree on the ICER framework's focus on cost-containment and care rationing as well as on many methodological details of how innovative and transformational treatments are currently being evaluated. We believe that value in healthcare should be measured in the longer, healthier lives of patients. We are aligned with society's desire to make major advances in cancer, which Americans overwhelmingly support.<sup>1</sup> However, by failing to account for disease and patient complexity, while also narrowly focusing on a single component of healthcare spend, ICER's value framework sidesteps an opportunity for appropriate assessment of value. BMS believes in and works to promote a comprehensive and current approach to value that incorporates key elements: a real-world approach, patient priorities, total health system value over a multi-year timeline, multi-stakeholder input and the most up-to-date clinical science.

We have reviewed ICER's list of the highest priority areas for potential revision and believe the ICER value framework could be improved in the following ways:

- Include more robust clinical expertise into the evaluation design
- Remove the budget impact threshold analysis
- Increase transparency and reproducibility of methodology and processes
- Improve care value methodology
- Incorporate stakeholder critiques into methodology and processes
- Define value from patient perspective, including recognition of the heterogeneity of treatment effects

We discuss each of these recommendations in greater detail in the following sections. Finally, we outline a more comprehensive approach to value assessment that defines value from the patient perspective and looks at the full range of patient experience with care.

### ***Include more robust clinical expertise into the evaluation design***

ICER's value assessment framework sidesteps an opportunity for a meaningful assessment of value by failing to account for the complexity of disease and patient experience. The goal of a cost-effectiveness analysis is to identify high value treatments for a specific patient population.



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To do so, extensive clinical expertise is needed to identify the population of interest, relevant treatments and key outcomes among other factors. Thus, it is imperative that ICER better incorporate clinical expertise into its value framework design and evaluations. In addition, a 21<sup>st</sup> century approach of value assessments should assess patient values in the real-world from resources, such as patient reported outcomes (PROs).<sup>2,3</sup> ICER utilizes a model similar to the National Institute for Health and Care Excellence (NICE) which was launched in 1999.<sup>4</sup> However, since NICE's inception, the healthcare community has seen major technological advances in clinical data-gathering that truly reflect the patient experience.

### **1. Clinical panel should represent a diverse group of disease area experts.**

To achieve the goal of including robust clinical expertise, ICER's voting panel should be well-rounded and include members with diverse areas of expertise. In particular, clinical panel members should have strong expertise in the therapy or disease area being evaluated, and ICER should ensure these members attend and participate in the meetings. Non-clinical experts should be briefed by clinical experts prior to the voting process to ensure all panel members have a strong understanding of the key clinical questions. Not only should clinical experts be used to inform the broader voting panel, but ICER should also involve clinical experts on its panel to provide input early on when the project scoping documents and protocols are developed. Clinical experts could even be required to sign off on the patient population and clinical question of interest before the project announcement and draft scope are released. For example, in the NSCLC therapy review announcement, the listed drugs were used to treat entirely disparate patient populations.<sup>5</sup> The input of NSCLC experts early in the review process likely would have prevented this oversight.

In addition to better incorporating clinical expertise into its voting panel process, ICER should also better incorporate clinical expertise from the broader provider community. ICER's new open input period is useful, but it is unclear if comments from the clinical community and other stakeholders will be used to inform the model. For ICER's rheumatoid arthritis review, for example, the due date for the open comment period was the same day as the release of the draft scoping document, which clearly did not leave sufficient time for ICER to carefully review and then incorporate clinical comments. As another example, ICER initially proposed to combine treatments for rheumatoid arthritis and psoriatic arthritis, however, these disease areas have different outcomes of interest.<sup>6</sup>

**2. Assessments should be timely and recognize the evolution of the value of medicines over time.** In the future, ICER should update its results and reports when new data or information is available. This will allow ICER's reports to reflect real-world practices and utilization patterns. For instance, new phase III trial evidence on daratumumab was released after ICER's final report on multiple myeloma.<sup>7</sup> Therefore, ICER should update its review of multiple myeloma therapies to reflect this new evidence. Specific areas of concern include:

#### ***Remove the budget impact threshold analysis***

ICER's budget impact framework arbitrarily establishes budget caps for societal expenditures on medical innovations and fundamentally ignores the value of innovation in healthcare and the value of care provided to individual patients.

1. **Deters innovation and access in areas of high unmet need.** Setting budget criteria instead will deter innovators from developing therapies that could benefit a broader patient population.<sup>8,9,10</sup> Nevertheless, treatments that provide significant benefits to a large number of patients are exactly the treatments most desired by society. It is fundamentally flawed to assume patients subjected to a cancer of high incidence or

prevalence are worth 'less' than patients who have a rarer form of cancer. Applying this threshold to past innovations, such as statins and anti-retrovirals, would have limited access to these drugs at the time they were introduced to the market.<sup>11,12</sup> Further, the short-term nature of the budget impact analysis ignores not only any health benefits to patients, but also ignores how improved patient outcomes can reduce medical costs in both the short and long run

2. **Sets an arbitrary threshold for one component of healthcare spending.** We believe the budget impact threshold ICER selected is highly arbitrary. First, the threshold focuses narrowly on one component of healthcare costs, with emphasis on medicines. The ICER budget cap limits allowable spending growth amount per new medicines. In essence, this practice implies that spending on new medicines should be frozen based on current patterns of care. Second, we believe that the ICER budget cap is based on flawed estimation of GDP growth, a highly volatile number of newly approved medicines each year, and an unrealistic adoption rate. There is no clear economic reason why drug spending should be limited to an excess cost growth of 1% (i.e., GDP + 1%). ICER states that this threshold is "embodied" in current federal and state legislation.<sup>13</sup> However, applying this threshold only to pharmaceutical spending assumes that the relative value of pharmaceuticals compared to the rest of the healthcare industry is constant over time. In practice, when new pharmaceuticals provide significant value to patients above the status quo, spending on pharmaceuticals treatments should increase relative to other type of health care goods and services; in periods of low or modest innovation, the share of the economy dedicated to drug spending should fall.

### ***Increase transparency of methodology and process***

ICER should increase the transparency of its reviews through three primary avenues: (i) refining topic selection and timing, (ii) provision of additional methodological detail, and (iii) inclusion of approaches for validation. The goal of a cost-effectiveness analysis is to identify high value treatment for a specific patient population.

1. **Topic selection and timing.** Although ICER has recently better outlined how its topics are chosen, the topic selection criteria are largely driven by the approval of new, high-cost treatments, rather than the goal of answering clinical questions for patients.<sup>14</sup> A new cost-effectiveness analysis is of most interest in a rapidly evolving treatment landscape, but topics should be based on clinical questions of interest rather than drug cost. BMS recommends greater alignment with clinical societies on relevant questions for research. Further, it would be beneficial to all stakeholders if they were made more aware of when ICER plans to evaluate its topics. Ideally, a schedule of topics would be released well in advance of the development of any draft scoping document, rather than allowing only a few weeks for preparation as part of the open comment period.
2. **Transparency of methodological detail.** In addition, ICER should make full details of its models publicly available for replication purposes. Cost-effectiveness modelling best practices indicate that models should be both transparent and valid to help researchers understand the results and have confidence in them.<sup>15</sup> This transparency includes the ability for other decision-makers to replicate a model and produce similar results. While ICER currently provides an overview of its methods online and has begun providing inputs and assumptions documents, these documents are not sufficiently detailed to allow for replication by interested stakeholders. For instance, in the ICER PCSK9 report, details were omitted with respect to the estimation of cardiovascular disease risk in the





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secondary prevention population.<sup>16</sup> ICER also should provide methodological details when it shares its preliminary analysis results with manufacturers.

3. **Peer reviewed methodology.** Peer-review of the model before it is finalized and applied in a review is recommended. Although ICER has submitted components of its reviews to peer-reviewed journals—such as publications on the treatment for familial hypercholesterolemia and the hepatitis C virus<sup>17,18</sup>—it has not published the complete evidence-based reviews of its topics. Publication of all reviewed topics should be common practice, and ICER's draft and final reports should reflect the rigor of the published manuscripts. Further, although ICER has begun to publish its protocol online, it should ensure that the details included allow for a full replication of the analysis.

### ***Improve care value methodology***

ICER could better incorporate all components of value, including those from patient and societal perspectives. Focusing primarily on medicines fails to take advantage of a much greater opportunity to evaluate value in the US healthcare system where a large majority of health spending remains unexamined.

1. **Incorporate patient priorities.** While ICER has begun to try to integrate patient and societal perspectives in the clinical-effectiveness phase of its evaluation, these perspectives generally are not included in ICER's care value modeling, even in more recent reviews such as those in the multiple sclerosis or rheumatoid arthritis. To address this shortcoming, ICER should consider adding other components of value to patients such as worker productivity and the value of durable survival gains. Treatments that improve patient or caregiver work productivity (i.e. through reduced absenteeism or presenteeism) should also be reflected in the value calculation, as health-related lost productivity is estimated to cost over \$260 billion to employers annually in the United States.<sup>19</sup> For example, a recent Cancer Support Community survey found quality of life and length of life were important factors when making a treatment decision.<sup>20</sup>

However, the patient's perspective on survival gains is not adequately accounted for in the ICER framework. As a study published in Health Affairs indicates patients place significant value in survival improvements in the tail of the distribution above and beyond treatments that improve median survival.<sup>21</sup> Patients surveyed were asked to compare two treatment regimens for melanoma that, statistically speaking, yielded equivalent survival gains. A large majority of cancer patients chose the regimen that offered a 50% chance of twice the survival gain over a regimen that provided assurances of a shorter survival gain. Although the "sure bet" regimen provides assurance of a shorter survival gain, and "hopeful gamble" offers a 50% chance of twice the survival gain, a large majority of cancer patients chose the latter. This value of hope cannot be ignored. In recognition of the importance of long term survival, the America Society of Clinical Oncology (ASCO) explicitly incorporates survival improvements in its revised value framework through tail of the survival curve bonus points.<sup>22</sup>

Finally, ICER should rely on a patient-centric approach for valuing treatments. For example, while the clinical efficacy of a psoriasis treatment could be similar across most patients, the value of an effective treatment to a given patient may depend on the location on the body where psoriasis manifests itself. For instance, patients who experience the disease on highly visible regions of their body are likely to place a significantly higher value on treatment than other psoriasis patients where the disease manifests itself more discretely. Using a single QALY measure obscures these patient specific preferences.

2. **Incorporate patient heterogeneity into methodology.** Further, ICER should better incorporate patient heterogeneity in its methodology. Although ICER does on occasion model certain subpopulations (e.g., line of therapy for non-small cell lung cancer [NSCLC]), in other cases it will not (e.g., separating patients with squamous and non-squamous NSCLC histologies). ICER's definition of a relevant patient population is broad and ignores significant patient heterogeneity resulting from different natural history and biology (NSCLC review). NCCN guidelines state "The generic term 'non-small cell lung cancer (NSCLC)' should be avoided as a single diagnostic term". NCCN specifically separates out treatment by histology type which is due to clinical trial findings that different treatments have different risk/benefit profiles based upon histology. Further, the FDA has recognized these differences during reviews and approvals of NSCLC therapies.

As another example, ICER's hepatitis C virus (HCV) model did not examine how treatment effects vary based on patient comorbidities such as HIV co-infection, diabetes, renal disease, and congestive heart failure. All of these comorbidities are known to impact and be impacted by co-infection with HCV, resulting in, for example, an increase in the rate of disease progression, complications, and mortality. More generally, when evaluating a therapy or disease area, ICER should strive to identify the highest value treatment for a given patient, rather than identifying the highest value treatment for only the average patient.

3. **Incorporate caregiver perspective.** Benefits to non-patients are also not adequately incorporated into ICER's baseline cost effectiveness models. Currently 3 in 10 American households provide unpaid caregiving to a family member.<sup>23</sup> Unpaid caregiving imposes a significant health and financial burden<sup>24,25</sup>, and treatments that can reduce this burden should be valued to reflect this. Further, non-patients also value new treatments due to their "insurance" value. Non-patients that do not suffer from the disease under consideration still value the availability of treatment advances, as these innovations act as a sort of "insurance policy" in the event these individuals contract the disease of interest in the future. The value of innovative treatments to non-patients can be quite large.<sup>26</sup>
4. **Prevent bias against interventions when data is not yet available.** Further, ICER's current approach is inherently biased towards finding that health care interventions are not cost-effective. ICER's general approach has been to assume that a treatment's benefits are valued at \$0 if there is no evidence available at the time of the review. This type of approach, however, is problematic as it systematically underestimates the value of a treatment at drug launch, as much of the information on potential treatment benefits (e.g., change in caregiver burden) has not yet been collected. ICER should consider incorporating plausible assumptions from other treatments or other diseases related to treatment costs and benefits when no data is available.
5. **QALY thresholds inappropriate for US healthcare system.** Further, ICERs use of a QALY threshold is premature given the lack of debate in the U.S. on society's willingness to pay for new treatment innovations. Whereas ICER uses a \$50,000-\$150,000 value of a QALY, a number of economic analyses find that the value of an additional QALY for cancer patients is closer to \$150,000-\$300,000.<sup>27,28,29</sup> Other research has demonstrated that patients near the end of their life have a higher willingness to pay for survival extensions compared to the average patient.<sup>30</sup> Arbitrary QALY valuations can alternatively make drugs seem either cost-effective or highly non-cost effective





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depending on these parameter assumptions. A broader discussion with stakeholders, including patients and other experts is needed before drugs are arbitrarily categorized as being cost-effective or not. In addition, understanding the total cost of care inclusive of therapeutic interventions and other healthcare spend (resulting in cost savings and medical cost offsets) is important to factor in.

6. **Significant uncertainty makes benchmark pricing unworkable.** Additionally, ICER should eliminate recommendations on treatment price when there is significant uncertainty in the treatment's value. In the multiple myeloma review, the differences between the low and high ends of the credible incremental cost effectiveness ratio ranges were greater than \$200,000 for some treatments. Further, changes to some basic assumptions changed the incremental cost effectiveness ratios for elotuzumab by more than \$200,000 between the draft and final reports. If one were to calculate prices based on the credible cost-effectiveness ranges presented, the resulting discounts would encompass such a large range that they would be—in many cases—practically meaningless.

Also, ICER's current approach inappropriately assumes that drug prices are static. Drugs that are viewed as "expensive" today inevitably decline in price, either after competing drugs enter the market or the loss of a drug's patent exclusivity. For instance, therapeutic competition from biosimilar drugs is estimated to lower biologic drug prices by as much as a third.<sup>31</sup> Failing to account for the likely price profile throughout the drugs lifecycle will underestimate the value to society. Finally, the "list price" that ICER assessments currently utilize does not represent the actual discounted price that is relevant to, and often negotiated, by payers.

#### ***Incorporate stakeholder critiques into methodology and process***

ICER should also better integrate stakeholder comments into its methodology and processes. From BMS' experience conducting research, extensive consultation with patients, caregivers, and providers helps manufacturers and other stakeholders determine what treatments are needed and what outcomes should be prioritized. For example, BMS' research process and post-market evidence generation efforts are aimed at improving survival, quality of life, and other areas of care that patients, caregivers, and providers have deemed valuable. In addition, BMS discusses value with payers every day and we lead active dialogue with payers on all aspects of value through submissions of extensive, high quality, and transparent clinical and economic research.

In order to allow for more meaningful input, ICER should dually lengthen its public comment periods and allow for more time to incorporate these comments into their models. To date, most of the revisions ICER has made in response to stakeholder comments have been minor fixes. Given the project timelines, there generally is insufficient time for ICER researchers to fundamentally revise its methodology or approach in response to valid comments; this constraint can be problematic when comments advise changes or clarifications to the evaluation's more time-consuming components, such as the network meta-analysis. As part of the comment process, ICER should also respond to stakeholders' comments directly as to why or why they were not implemented in ICER's approach in order to increase the transparency of ICER's methodology.



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## **BMS supports a more comprehensive and current approach to value assessment**

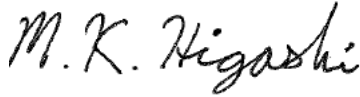
BMS believes in, and works to promote, a comprehensive and current approach to value that incorporates key elements: patient priorities, real-world evidence, total health system value over a multi-year timeline, multi-stakeholder input, and the most up-to-date clinical science. The value of medicines evolves over time with new understanding of benefits compared to risks and changes in the evidence base, such as long-term data that becomes available only after a medication's launch.

- 1. BMS supports defining value from the patient perspective considering patient preferences, goals, and experiences.** BMS is taking action to ensure the growth of value frameworks that consider patients' desires, goals, and experiences. We support the rubric developed by the National Health Council (NHC), which aims to assess value frameworks by considering their degree of patient partnership, engagement, transparency, inclusiveness, and diversity.<sup>32</sup> The rubric also supports the use of patient-centered data sources and patient-reported outcomes in line with BMS' push to use more real-world evidence in determining the value of rheumatoid arthritis and cancer therapeutics. In developing the rubric, NHC notes that "it is not apparent that individual patients or patient organizations were engaged throughout the creation" of new value frameworks like that of ICER.
- 2. BMS is committed to generating greater evidence to improve health care decision-making and the ultimate value of care provided to patients.** BMS believes value frameworks should take into account real-world evidence as it can better reflect a therapy's impact in the actual clinical setting. Overall, BMS participates in numerous pharmacoeconomic conversations and produces globally over 200 publications per year. For example, to better treat patients with rheumatoid arthritis (RA), BMS has published studies using real-world data from the Corrona, LLC RA registry to identify patient response to ORENCIA® based on key biomarkers.<sup>33</sup> Additionally, BMS has launched the ACROPOLIS (Apixaban ExperienCe Through Real-World Population Studies) program designed to generate evidence from clinical practice settings to help improve healthcare decisions in the prevention of stroke and embolism.<sup>34</sup>
- 3. BMS supports a comprehensive assessment of value that looks at the full range of the patient's healthcare experience.** BMS supports value assessments that broadly incorporate the patient's care journey, including examining healthcare delivery and reassessing the standard of care to ensure that treatment is up-to-date and reflects the most appropriate therapies available. Value assessment should consider the impact of making progress against costly conditions. As new medicines hold the promise to reduce costly healthcare utilization for non-drug services<sup>35</sup>, other contextual factors such as innovation should be considered to improve value in the long-run. In fact, many ex-U.S. health technology assessment bodies do consider innovation, extent to which a therapy addresses unmet medical need, societal preferences, and other relevant factors in their decision-making.<sup>36</sup> Lastly, pharmaceutical costs are only a modest share of overall health spending. In 2014, retail and non-retail pharmaceuticals accounted for 13.8 percent of national health expenditures<sup>37</sup> while hospital care, physician services, health insurance, and nursing care facilities accounted for 70 percent.<sup>38</sup> In 2010, labor costs accounted for 56% of total healthcare spending in the United States. The entire care continuum cannot be overlooked when researching the value of one component in the healthcare system.

## Conclusions

BMS appreciates the opportunity to comment and suggest improvements to ICER's value framework. BMS has outlined a number of areas in ICER's framework that, if improved, could strengthen ICER's methodology and approach. We hope that ICER incorporates these recommendations into their modelling and processes.

Sincerely,



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Mitch K. Higashi, PhD  
Head of US Medical Health Economics and  
Outcomes Research



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Wayne M. Sichel, JD  
Head of U.S. Federal Policy

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September 12, 2016



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**RE: National Call for Proposed Improvements to ICER Value Assessment Framework**

Dear Dr. Pearson:

The California Life Sciences Association (CLSA) appreciates the opportunity to provide feedback in response to the Institute for Clinical and Economic Review's (ICER) National Call for Proposed Improvements to its Value Assessment Framework (hereinafter "Framework"). CLSA is the statewide public policy organization representing California's life science innovators, including over 750 medical devices, diagnostic, biotechnology and pharmaceutical companies, research universities and private, non-profit institutes, and venture capital firms. CLSA's diverse membership represents the spectrum of organizations throughout California working to develop life-saving, and life-sustaining therapies and treatments in the innovation ecosystem.

CLSA is concerned that ICER's current Framework prioritizes the speed with which an assessment can be put before a "Public Deliberation Panel" (hereinafter "Panel") over taking the steps necessary to ensure sufficient evidence and stakeholder perspectives, particularly those of patients, are adequately incorporated into an appropriately rigorous Framework. Taking such steps will mean expanding the primary focus of an assessment beyond the short-term payer impact. The Framework's focus on treatments and cures as a short-term expenditure for a payer, as opposed to a long-term investment in a patient's health and wellbeing, discourages breakthrough treatments and technologies and is consequently a disservice to patients. The biggest cost-driver in healthcare going forward will be the growth in the underlying burden of disease, and therapies from biopharmaceutical and medical technology innovators can dramatically reduce that disease burden and the associated costs, while bringing the benefits of a healthier populace. These are also the benefits that matter most to the patients suffering from chronic and life-threatening diseases and conditions.

***Process-related Concerns and Recommendations***

First, we strongly believe that improvements in the ICER Framework should begin with increased and improved communication and information exchange with stakeholders. As it currently stands, numerous critical points in ICER's process remain a mystery to those affected by the process. These opportunities for greater dialogue and stakeholder engagement include:

- Outlining the process by which therapeutic areas are selected for further evaluation, including the criteria utilized, how such criteria was weighed, and which stakeholders helped determine the selections. This is a critical threshold decision for ICER, and



vetting these selections more transparently would only strengthen the integrity of the process.

- While we appreciate ICER's efforts with the "Open Input" period during development of the Draft Scoping Document, given the central importance of this document to the overall evaluation, we urge ICER to treat engagement and input from stakeholders similarly to public comments on the reports themselves, identifying how stakeholders can engage at this stage, the input provided from stakeholders, and the extent to which that input has been adopted and the rationale for such adoption.
- Related to the Draft Scoping Document, we urge that a more detailed discussion of the underlying assumptions to the analyses take place at this stage and that all such assumptions be outlined in the Draft Scoping Document. This would allow for adequate engagement and discussion of one of the more contentious aspects of any report.
- More broadly, we encourage uniform guidelines requiring meaningful engagement with stakeholders at all key points in the development of any reports, publicly noting the stakeholders, the input, and the extent to which such input was accepted or rejected.

Second, we are concerned with certain substantive elements of ICER evaluations, though, as discussed above, we remain unclear on why and how certain therapeutic areas are selected. Specifically, we strongly oppose inclusion of therapies or technologies that are not yet FDA approved or for which there is limited data available to study off-label use. We assert that such premature evaluation not only undermines the authority of the FDA as the federal regulatory authority, but means that ICER is attempting to finalize an Evidence Report prior to there being adequate evidence to make any such determinations. Moreover, not only may the data be limited or unavailable, but significant restrictions exist as to the data manufacturers are able or permitted to provide.

Third, as referenced above, we believe the Framework would be significantly improved with a broader, more transparent and inclusive engagement process including a variety of interested stakeholders. These efforts might include:

- Broadly soliciting patient and clinician perspectives on therapies or technologies under or being considered for evaluation. Engagement with stakeholders across the spectrum of manufacturers, patient advocacy groups, and providers must be meaningful (e.g., applicable input is documented and considered for incorporation or rejection). We assert that the critical perspectives of these key stakeholders must be represented throughout the process in order to have a Framework representing a true value assessment. For example, we would encourage ICER to consider the recommendations of the National Health Council's *Patient-Centered Value Model Rubric* in this regard.<sup>1</sup>
- We further recommend earlier engagement on the Draft Evidence Report with the manufacturers of therapies and technologies under review, as well as other interested stakeholders. In order to ensure stakeholders have adequate time to review the detailed model analysis plans, among other things, and provide meaningful feedback, we recommend the Draft Evidence Report be made available to stakeholders no less than 30 days prior to release. This earlier engagement would also serve to strengthen ICER's

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<sup>1</sup> National Health Council. The Patient Voice in Value: The NHC Patient-Centered Value Model Rubric (March 2016). Available at: <http://www.nationalhealthcouncil.org/sites/default/files/Value-Rubric.pdf>.

evaluations, because ICER would have more time to consider and incorporate stakeholder input. The underlying evidence could also be strengthened with this added lead time, as the manufacturer of a treatment under review will have more time to provide or vet further clinical data and any other potentially helpful or relevant references. This same dynamic should apply to the stakeholders' ability to respond to analyses and conclusions in any other significant documents in the process.

Finally, we urge ICER to modify how the Public Deliberation Panels (e.g., the California Technology Assessment Forum (CTAF)) compose their public meetings. At least as it pertains to our experience with CTAF, the roundtable policy discussion with various stakeholders answering questions from a moderator and the Panel Participants will clarify questions that arose during deliberation of the Voting Questions (where communication by Panel Participants with anyone outside of other panelists and the ICER moderator is discouraged by the structured discussion). On more than one occasion, we have witnessed a Panel Participant make remarks to the effect of "I wish I had known that before we voted."

We strongly recommend that the policy discussion roundtable portion of the meeting precede Panel Participants' votes on a therapy or therapies. Relative to the rigidity of the timed public comment period where questions from the panel can be rare, this more informal roundtable discussion among various stakeholders is often their first opportunity to assess the merits of different perspectives on value, the strength of evidence, and a treatment's likely reception in the marketplace, among many other things. To use an election season analogy, it would be a disservice to voters if the Presidential debates were held after voting day, and we believe the same logic should apply to the Public Deliberation Panels' public meetings.

Related to the Public Deliberation Panels' public meetings, we also recommend that manufacturers be permitted to present their own response to the Final Evidence Report immediately following ICER's presentation of the report and the presenter's discussion of public comments with ICER's response. On multiple occasions, for instance, the position of the manufacturer has been mischaracterized or key details of a clinical trial or a manufacturer's critique have been left out of ICER's presentation of public comments. This puts the manufacturer in the difficult position of having to use a portion of its scant few minutes of public comment time, which is the same as any other member of the public, to address heretofore unknown issues with, for example, a mischaracterization of the evidence or the manufacturer's position on a key point of dispute. We believe providing for a more substantial and substantive manufacturer response to the Final Evidence Report outside of, or in lieu of, the few minutes during the rigidly structured public comment period would make for a much more equitable and consequently intellectually rigorous deliberation.

### ***Methodology-related Concerns and Recommendations***

We urge ICER to take this opportunity to reevaluate a number of the methodological underpinnings of the current Framework.

First, not only are there inherent limitations and uncertainties in using quality-adjusted life years (QALYS) as a tool in cost-effectiveness analysis, but equating cost-effectiveness and "value" is misleading and fails to facilitate a truly patient-centered approach. Using QALYS to measure cost-effectiveness discounts crucial differences in individual patient needs and is consequently



an inappropriate tool to quantify the value that innovative therapies offer patients and the healthcare system, particularly when one looks over a longer time horizon where additional data on the therapy will become available.<sup>2</sup> Moreover, evaluating the cost-effectiveness or “value” of a single therapy or technology in a silo fails to account for the complexity of the condition or conditions from which a patient may suffer, as well as the ancillary healthcare services the individual patient requires. This is particularly true of chronic conditions and rare diseases.

Second, we assert that ICER should suspend use of the budget impact component of the Framework, as it prevents the appropriate evaluation of innovative therapies’ impact on individual patient care. Generally speaking, the “value” of a breakthrough treatment or technology, for instance, will always be skewed towards the long-term due to the benefits of enabling patients’ to live longer and healthier lives drawing out well beyond a five-year time horizon. Examining the long-term value of innovative therapies, furthermore, is necessary to measure the effectiveness of a treatment from a patient perspective. A focus on the short-term budget impact and the short-term costs to the payer of an innovative technology or therapy with long-term benefits to patients prevents any attempt to define real “value.” Should ICER return to using a budget impact component in the future, we urge the use of a substantially longer time horizon.

Third, despite the focus on the payer perspective, ICER calculates its short-term budget calculations using the wholesale acquisition cost (WAC). This use of WAC, however, is inconsistent with the payer’s perspective of drug-spending in the marketplace – that perspective being that the WAC is effectively meaningless in terms of a budgetary impact, as it is just a list price and not the net price. For instance, a payer’s actual drug spend accounts for the negotiated discounts, rebates, and other concessions on medicines, which offset, on average, four-fifths of any price increase on brand medicines in 2015 alone and reduced absolute invoice spending on brand medicines by 27.1 percent.<sup>3</sup> These offsets and reductions grow even larger when factoring in the required rebates of federal healthcare programs like Medicaid, as well as any negotiated supplemental rebates within those programs. As a result, the budget impact is not reflective of how the marketplace functions in a real world scenario, particularly as it relates to the payer’s perspective of WAC as little more than a reference point for the levels of discounts and rebates received.

Fourth, ICER should abandon the one-size-fits-all budgetary growth threshold of the “amount of net cost increase per individual new intervention that would contribute to growth in overall health care spending greater than the anticipated growth in nation GDP +1.” Any such standard must take into consideration the impact on the individual patient and account for the real world utilization of respective therapies, including the interaction of drugs and devices with other healthcare services and spending.

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<sup>2</sup> We believe the recommendations of the European Consortium in Healthcare Outcomes and Cost-Benefit Research with respect to use of QALYs can be helpful here, as they discuss the “major inconsistencies which irrefutably invalidate [QALYs’] use.” Available at:

[http://www.echoutcome.eu/images/Echoutcome\\_Leaflet\\_Guidelines\\_final.pdf](http://www.echoutcome.eu/images/Echoutcome_Leaflet_Guidelines_final.pdf).

<sup>3</sup> IMS Health. Medicines Use and Spending in the U.S. – A Review of 2015 and Outlook to 2020. Available at: <http://www.imshealth.com/en/thought-leadership/ims-institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2015-and-outlook-to-2020#form>.

Fifth, we urge ICER to abandon its use of only four potential uptake patterns and develop evidence-based uptake projections. We assert that the initial uptake patterns assigned by ICER to new therapies have resulted in a number of wildly exaggerated potential budget impacts. For instance, the Partnership for Health Analytics Research (PHAR, LLC) has concluded that ICER overshot the budget impact of PCSK9 inhibitors by \$7.1 billion (actual costs of \$83 million compared to ICER's projection of \$7.2 billion).<sup>4</sup> We recommend that ICER develop a more granular approach (e.g., beyond just assigning a therapy to four arbitrary uptake patterns, but an evidence-based estimate or range of estimates) to estimating uptake patterns among those patients most likely to receive the therapy or technology under payers' likely utilization management controls.

Finally, we suggest the Framework should be modified in several respects when evaluating medical devices, and we encourage ICER to deliberately engage the medical device community separately in an effort to more thoroughly understand the appropriate Framework modifications to more accurately evaluate medical devices and technologies. Recommended modifications include:

- *Reducing Market Uptake Assumptions for Devices or Making Them Evidence-Based:* Market uptake assumptions for devices generally should differ significantly from those used in biopharmaceuticals, as devices are not adopted in the same manner as drugs and result in significantly smaller volumes.
- *Accept Evidence from a Broader Range of Clinical Trial Designs:* Evaluating the strength of supporting clinical data should also differ for medical devices, as not all drug evaluation concepts are equally applicable to devices. As the United Kingdom's National Institute for Health and Clinical Excellence (NICE) has recognized, stating, "Clinical evidence on technologies, in particular new technologies, is often limited, especially comparative studies against appropriate alternative treatments or methods of diagnosis."<sup>5</sup> In other words, randomized control trials are often exceedingly more difficult to undertake for new devices and may be infeasible on account of ethical issues. The evidentiary standards related to the evaluation of medical devices and technologies should be modified to reflect these challenges.
- *Any Budget Impact Analyses Must be Long-Term:* Any focus on short-term budgetary impact is also problematic for many medical devices, as they often see significant clinical and economic improvements over time, as future device iterations become available, competition in the market increases, and overall clinical and operator experience/expertise with the technologies advance.

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<sup>4</sup> The Partnership for Health Analytics Research (PHAR, LLC). "Billion Dollar Blunder: On the 1-Year Anniversary of a New Class of Cholesterol Medicines, Study Finds Actual Cost of New Drugs Is Billions Less than Predicted" (August 11, 2016). Available at: <http://www.prnewswire.com/news-releases/billion-dollar-blunder-on-the-1-year-anniversary-of-a-new-class-of-cholesterol-medicines-study-finds-actual-cost-of-new-drugs-is-billions-less-than-predicted-300311969.html>.

<sup>5</sup> National Institute for Health and Clinical Excellence (NICE). Medical Technologies Evaluation Programme Methods Guide (April 2011), page 8. Available at: <https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-medical-technologies/Medical-technologies-evaluation-programme-methods-guide.pdf>.

### ***The Importance of Evaluating ICER's Impact on Patient Access***

In closing, we ask that ICER consider any changes to the Framework with their potential impact on patient access as a priority consideration. Any “value” framework that garners significant influence in the marketplace will have an impact, for better or worse, on patients’ access to potentially life-saving treatments and technologies and will influence the research and investment decisions that shape the innovation ecosystem, influencing what therapies are pursued by manufacturers and subsequently covered by payers.

We ask that ICER consider evaluating the potential impact of any Framework changes, as well as observing for any real impacts going forward, along two key factors:

- Evaluate the potential for underutilization of innovative therapies, which not only risks appropriate and proper care for patients, but has the effect of undermining investment into the research and development of curative treatments that provide real long-term benefits. Again, we believe ICER’s current Framework is fundamentally biased against innovative therapies and technologies and hope this will be addressed.
- Evaluate the impact any adopted budget impact method, which may prioritize short-term savings over long-term health benefits in healthcare decision-making, on the ability for patients to access innovative technologies or therapies that have been otherwise shown to bring significantly improved clinical outcomes for patients.

### ***Conclusion***

We are hopeful ICER will take the steps necessary to ensure a more equitable and accurate value assessment framework, particularly as it relates to patients, and we thank you for considering our comments. Please contact Brett Johnson ([bjohnson@califesciences.org](mailto:bjohnson@califesciences.org); 916-233-3490) if there is any further information we can provide.

Sincerely,



Todd Gillenwater  
Executive Vice President – Advocacy & External Relations



September 12, 2016

Steven D. Pearson, MD, MSc  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, 9<sup>th</sup> Fl  
Boston, MA 02109

Dear Dr. Pearson:

Through the mandated use of clinical pathways, cancer treatment decisions are increasingly being controlled not by physicians and patients, but by accountants and actuaries. In fact, patients are often not aware that their treatment options have been limited and are dictated by financial concerns.

For those instances when treatment options are being discussed however, cost has joined safety, efficacy and evidence as factors to be considered. New decision frameworks are being developed and implemented in the care setting as tools for oncologists to evaluate treatment options with patients. These so-called 'value frameworks', including ICER's, are shaped through the eyes of payers and providers, without honestly and accurately reflecting the priorities and perspectives of patients and their families.

For people with cancer, the dynamics of treatment decision-making add complexity that exacerbates the already-overwhelming situation of their cancer diagnosis. We know that many patients lack the information they need to make informed treatment choices. We also know that having cancer causes distress in nearly every aspect of patients' lives, and can cause years of financial insecurity. Notwithstanding their confusion and anxiety however, patients are required to make life-defining treatment choices based on criteria they may not understand and which may not reflect their personal goals and values regarding life, quality of life and overall well-being, both short and long term.

The value frameworks are adding to the treatment-decision dilemma for many patients. While these tools have the worthy objective of helping to highlight what is known about the efficacy, toxicity and cost of various cancer treatment options, they measure 'cost' narrowly as the price of drugs and biologics, which is only one element of a true 'value equation'. Moreover, these frameworks overlook the 'value' of a treatment to patients, which may include quality of life measures, total financial exposure, distress, family impact, and longer-term consequences of disease and treatment, among other considerations. For patients, 'value' is about their lives, not just about their disease.

The recently published [2016 CancerCare\\* Patient Access and Engagement Report](#) reflects the findings of 6 surveys based on the input of more than 3000 American adults who were diagnosed with cancer. In one of the survey questions regarding personal priorities, male respondents were





more likely to rate “Caring for the family” as very or extremely important than “living as long as possible”. For this group, the ability to work, earn income, and sustain an acceptable quality of life would likely be preferable to debilitating therapy that inhibited daily activities.

The strong personal preferences of patients and families are critical components of determining the value of a potential treatment regimen. ICER’s value framework needs to incorporate them in a way that figures prominently in the calculation. Furthermore, patients’ should have the opportunity to determine their importance relative to clinical and cost criteria.

We are living in a time of enormous advances in our understanding of cancer as a disease, and of increasing precision in treatment based on each patient’s individual molecular and clinical characteristics. This should be a moment in which it is possible to personalize cancer care in every way, so that individuals are treated in the context of their lives.

Sincerely,

*Ellen Sonet*

Ellen Sonet, JD, MBA  
Chief Strategy and Alliance Officer  
CancerCare

\*CancerCare is the leading national organization dedicated to providing free, professional support services including counseling, support groups, educational workshops, publications and financial assistance to anyone affected by cancer. All CancerCare services are provided by oncology social workers and world-leading cancer experts. For more than 70 years, CancerCare has identified the support needs of patients and served them free of charge.



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September 12, 2016

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

RE: Institute for Clinical and Economic Review Value Assessment Framework

Dear Dr. Pearson,

On behalf of the Cancer Support Community, an international nonprofit organization that provides support, education and hope to over 1 million people affected by cancer each year, we appreciate the opportunity to respond to the request for comments regarding ICER's Value Assessment Framework.

As the largest direct provider of social and emotional support services for people impacted by cancer, and the largest nonprofit employer of psychosocial oncology professionals in the United States, CSC has a unique understanding of the cancer patient experience. Each year, CSC serves more than one million people affected by cancer through its network of 44 licensed affiliates - more than 120 satellite locations, and a vibrant online community- and delivers more than \$40 million in free, personalized services each year.

Additionally, CSC is home to the Research and Training Institute - the only entity of its kind focused solely on the cancer patient experience. The Research and Training Institute has contributed to the evidence base regarding the cancer patient experience through its Cancer Experience Registry®, various publications and peer-reviewed studies on distress screening, and the psychosocial impact of cancer and cancer survivorship, to name a few. This combination of direct services and research uniquely positions CSC to provide organizations like ICER with feedback based on evidence as well as real world impact.

CSC acknowledges ICER's intent to seek multi-stakeholder input as a part of the process involved in assessing the value and effectiveness of different treatment regimes. Both the conversations on value and multi-stakeholder engagement are at the core of CSC's work on access, and we are eager to work with you to move appropriate solutions forward.

However, Dr. Pearson, we remain concerned about several sections of the framework and your engagement requirements.

## **Unrealistic formatting specifications and timeline for response**

On a very basic level, the instructions you give for submitting feedback are limiting in both feedback opportunity and transparency. While encouraging public comment, you specifically limit the length of some submissions to 3 pages and require a font size of 12. Additionally, you require submission in a Word document and indicate that comments **may** be made public.

The two week public comment period does not allow adequate time to review ICER's recommendations and solicit feedback from patients and experts. CSC thanks ICER for extending the time to respond to the non-small cell lung cancer (NSCLC) report and encourages ICER to consider review times that are even more generous in the future.

CSC encourages you to amend these practices to allow the respondent the time and space to provide full and complete feedback on your positions. Additionally, CSC believes you should allow submissions to be in pdf format and that you also make all comments publicly available throughout the entire development and review process.

## **Lack of patient representation**

CSC acknowledges the attempt to include patients on both the Governance Board and also the regional panels.

CSC encourages ICER to consider the following:

1. There should be a sufficient number of patient representatives to allow an equal share of voice when votes are taken.
2. Patient representation on the Governance Board should include expertise and knowledge that represent the full spectrum of wellness, disease understanding and geography. This board should be expanded to include individuals who can represent or who have access to resources which would allow ICER to benefit from a more comprehensive level of information on the patient experience.
3. There should be patient representation as a part of the evidence report development. As an example, the lung cancer evidence report (currently open for public comment) was developed and approved by a panel exclusive of patients. ICER does note that it received input/feedback from patient groups, including CSC, but it should be noted that CSC did not have access to any of the draft reports prior to and including the "final" draft report being made publicly available.

## **Lack of clinical expertise**

In addition to ensuring patients on your panels have the appropriate level of expertise to fully understand complex clinical scenarios, CSC encourages ICER to require health care professionals serving on voting panels to have relevant and deep expertise in caring for patients with the disease condition under review. CSC would like ICER to mandate that physicians serving on the voting panels have board certification in the relevant specialty.

## **Inconsistent methodology**

CSC fully recognizes the importance of evidence in setting policy and when making decisions with patients. CSC encourages ICER to consider the following:

1. ICER must be transparent with all resources used in the development of evidence reports.
2. ICER must include a balance of data derived from controlled clinical trials (including observational trials) and real world evidence.



3. ICER must create principles to ensure that the use of data meets a high level of scientific credibility. For example, the use of cross-trial comparisons should be discouraged.
4. ICER must require peer-review by a panel of experts for all evidence reports.

### **Relevance and timeliness of recommendations**

The plan for ICER to update recommendations as new data becomes available is unclear. For diseases with rapidly changing scientific discoveries, any organization making clinical recommendations must be nimble and responsive to the environment. CSC encourages ICER to implement the following:

1. A transparent timeline for review and update of previously published recommendations.
2. A deadline for decision that does not impact the ability of a patient to access a treatment option determined effective for a particular disease.
3. Expertise on the review and voting panel that mirrors the topic of scientific discovery.
4. Full transparency of the data used for decision making.

### **Lack of patient validated endpoints**

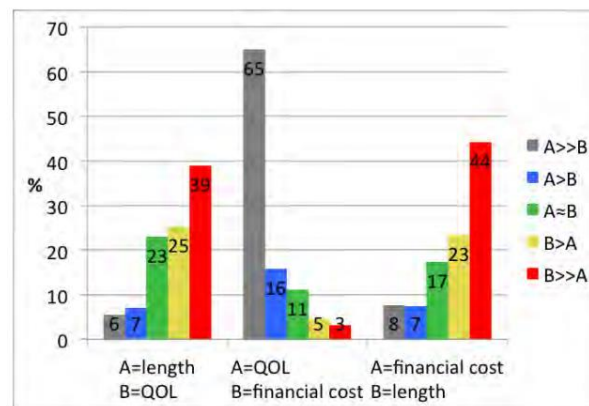
CSC understands your use of quality-adjusted life year (QALY) as an endpoint but does not support this as an endpoint which is meaningful to patients. Multiple studies, including CSC's Registry data, show that for patients with cancer and other long-term debilitating illness, there is a delicate balance between quality and quantity of life. In fact, patients have reported a desire for a shorter overall survival in exchange for quality of life. The QALY framework assigns the exact same score to an individual who lives six months in perfect health and to an individual who lives a full year in a debilitated state. Patients would assign a very different level of value to each of these scenarios. Other value models (American Society of Clinical Oncology and the National Comprehensive Cancer Network) have taken similar approaches to assigning higher levels of value to endpoints such as overall survival without a full appreciation and representation to the value patients assign to shorter, incremental gains. CSC would like ICER to utilize a framework which more closely represents the endpoints that are meaningful to patients.

### **Lack of consideration of the patient definition of value**

As mentioned before, CSC encourages ICER to look beyond their current benchmarks to include outcomes that are important to patients. Data from the Cancer Experience Registry continues to reveal the importance of quality of life as an important indicator of value to patients. This figure, taken from a recent analysis and presentation on patients in the Registry, indicates that quality of life may, in fact, be of greater importance to the majority of patients when making a treatment decision than length of life. Yet framework developers continue to over-value length of life and under-value quality of life.



**Figure 2.** Relative impact of factors A and B when considering a treatment decision



Note: >> much more; > slightly more; ≈ about equal

- 44% indicated LoL had much more of an impact on treatment decision than financial cost
- 65% indicated that QoL had much more of an impact on treatment decision than financial cost
- 39% indicated that QoL had much more of an impact on treatment decision than LoL

Additionally, responses collected directly from cancer survivors in an open-ended question about how they define value in their cancer care show quality of life issues and attention to individual preferences and needs emerging as key factors. For example, one respondent wrote: “Value is most meaningful when it is applied to my individual life, and not to an algorithm or statistical fact.” Another notable trend is time with the health care team to fully understand all available options and the risk and benefit scenarios (including cost) associated with each. A respondent wrote: “A good team of doctors that works with you, not at you.”

Data from CSC’s Cancer Experience Registry demonstrates that in patients with metastatic breast cancer, only 5% of respondents conceived value as having any exchange-based meaning specific to health. As noted in the study, when defining value relative to health care, patients emphasized the importance of their relationship with Health Care Providers (HCPs) rather than the benefit of cost-effective treatment. Although quality, efficiency and cost transparency in value-based care are essential, patients may be more focused on quality care as it relates to the HCP–patient relationship than on value relative to efficiency/cost. While accounting for the clinical merits of a particular therapy is important, the current ICER model represents only a component of the overall care and may overshadow other dimensions of care that are also valuable to patients.

### **Lack of consideration of low-grade chronic side effects**

ICER’s value framework does not include consideration of low-grade, chronic side effects. CSC acknowledges concerns regarding the lack of patient reported outcomes as a part of the formal data collection process, and CSC sincerely looks forward to working with ICER on a plan to remedy future data collection requirements. The reality for patients is that long-term side effects are a significant part of their overall experience, ranging from quality of life, to financial considerations, to work and family challenges. As documented in the 2014 Index, Elevating the Patient Voice, the top concern people want more help managing is long-term side effects. Given the body of evidence currently available on long-term effects of the vast majority of the “prevailing standard of care,” CSC strongly encourages ICER to incorporate that information as an important component in the calculation of clinical-effectiveness.

## **Focus on medications acquisition costs**

The impact on the individual in terms of personal health care spending is increasing and documented in the literature. Indeed, data from CSC's Insight into Patient Access to Care in Cancer report demonstrates that patients are primarily concerned about costs related to insurance premiums, co-pays for services and co-pays for drugs.

We believe the focus solely on sales or acquisition costs to estimate treatment costs minimizes the reality and attention that should be placed on finding solutions that address the multitude of factors impacting elevated spending. Further, this narrow focus can significantly under-weight aspects of the delivery of care that contribute substantially to a patient's calculation. The current evolution of cancer care continues to drive consolidation of care delivery sites, increasing overall costs by shifting patient care to higher cost locations and creating scenarios where patients find themselves outside of their network coverage plans. Aligned with the patient voice, our broader community, including ICER, should focus its attention on creating a system that rewards the provision of comprehensive, quality care inclusive of transparency, shared decision-making and long-term risk/benefit disclosures.

## **Lack of consideration of financial toxicity**

The causes of financial toxicity in patients with cancer are becoming well recognized and the reality of the rising cost of health care is daunting and unsustainable. Patients report financial distress as more severe than other sources of distress associated with physical, social and emotional functioning (e.g., Delgado-Guay et al., 2015).

The current Value Assessment Framework does little to recognize the impact of the comprehensive nature of financial toxicity. In addition to patient cost sharing for medications and services, it is well documented that patients experience additional expenses related to their cancer treatment. Some expenses are more difficult to measure (parking, housing, etc.), but the framework could allow the capture of true out-of-pocket patient costs. In particular, ICER could apply some level of consideration to frequency of treatment as a part of the evaluation. Given the high cost of travel and time off work, a regimen that would be administered once per month may be less financially toxic to a patient than one administered once per week, as one example. Additionally, this framework does not give consideration to the costs associated with interventions required as a comprehensive part of treatment. For example, supportive care agents needed to manage nausea, steroids required as a part of a treatment regimen, etc.

## **Conclusion**

At the Cancer Support Community, we are acutely aware of the rising costs of treating cancer and support efforts that contain costs while ensuring the provision of truly comprehensive care. We believe that patients who have knowledge and experience in the specific topic areas must be fully at the table in discussions about new care models along with providers, payers and other stakeholders. All policy proposals should be evidence-based and promote a rich physician-patient dialogue and care planning that is customized for and with the individual patient. We strongly believe that the process of developing new care models and payment structures and the implementation of those models in practice must be transparent. Patients have the right to know about their full suite of care choices, and the incentives that may influence their providers in terms of treatment recommendations.

In conclusion, CSC sincerely thanks you for the opportunity to comment on ICER's Value Assessment Framework and share the voices of patients living with cancer. We look forward to additional opportunities to contribute to ICER's ongoing work.

Please feel free to contact me at (202) 650-5382 or by email at [linda@cancersupportcommunity.org](mailto:linda@cancersupportcommunity.org) if you have any questions or if we can be of further assistance.

Thank you again for your attention to this very important matter.

Sincerely,

A handwritten signature in blue ink that reads "Linda House". The signature is written in a cursive, flowing style.

Linda House, MSM, BSN, RN  
President  
Cancer Support Community National Headquarters

## References

- Cancer Support Community. (2014). Elevating the patient voice: cancer experience registry index report 2013-2014. Retrieved from:  
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September 13, 2016  
Steven D. Pearson, MD, MSc, FRCP  
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**RE: Call for Proposed Improvements to ICER's Value Assessment Framework**

Submitted electronically via: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

Dear Dr. Pearson,

We appreciate your organization's interest in making the health care system more effective and efficient. While we agree it is imperative to support the achievement of the best patient outcomes in the most efficient way, we believe the Institute for Clinical and Economic Review (ICER) is utilizing an approach and methodology that are not designed to achieve this purpose.

The ICER value assessment framework and its one-size-fits-all approach would not allow for the numerous factors that must be considered for optimal patient access.

1. Each public and private payer in the United States needs to take into account the uniqueness of their individual circumstances when making formulary decisions. Depending on the stakeholders involved and the specificities of the decision-making context they operate within, the elements of value they are considering and the relative importance they attach to each of them are likely to differ. Therefore it is neither possible nor desirable to develop a quantitative algorithm that would be universal and applicable across drugs, diseases (especially in a heterogenic disease like cancer, inflammation and inflammatory conditions), stakeholders and geographies.
2. Cost effectiveness (cost per QALY) analyses, upon which the ICER value assessment algorithm is founded, are not appropriate for assessing either value or price of innovative medicines. Value is a multi-dimensional concept and, therefore, a flexible multi-criteria method for value assessment is required. A cost-effectiveness analysis is not fit to evaluate innovative medicines that address unmet medical needs (e.g., treatments for rare conditions or cancer), as it is rigid and applies a narrow understanding of value.

The specific problems that arise from the use of QALYs in assessing the value of a treatment include:

- QALYs have a variety of known limitations (e.g., discrepant utility scores based upon the methods used to elicit them; patients' perceptions of gains in utility are not the same as their perceptions of loss, assessing the utility of a state before it occurs may differ greatly from its assessment after the fact).
- QALYs are based on the hypothesis that health interventions only affect the health of the individual and not any other aspects of a patient's well-being. The effects of a patient's health on the quality of life of others, such as caregivers or family members, do not figure into the actual QALY calculations but can have wide ranging economic consequences.

- QALYs do not consider the societal costs of disability or disease, nor the benefits to society of reductions in morbidity that allow a return to work/productive pursuits.
  - QALYs do not take into account severity or rarity of the condition. QALYs do not distinguish the aggregation of modest benefits to large numbers of people from a substantial benefit to a few people.
  - ICER's approach to calculation of cost/QALY takes a lifetime approach, but does not consider changes in cost of medications over time, including the introduction of generic alternatives following loss of exclusivity
3. Arbitrarily determined cost-effectiveness ratios limited by an annual budget threshold are not appropriate to determine "Value Base Price Benchmarks". This method does not take into account who is making the decision; what the purpose of the analysis is; how the decision maker and patient value health, money, and risk; and what the available resources are. The value framework assessment sets an annual threshold for the amount a drug could cost to keep overall health expenditures from increasing faster than the Gross Domestic Product (GDP) plus one percent. In our view, this annual budget threshold of \$904 million is an arbitrary cap; we have not seen any scientific rationale to justify it. In addition, it is exclusively focused on cost and not on the net clinical benefit to patients. The threshold prices also do not reflect key economic benefits, such as improvements in worker productivity that are valued by employers, or the savings or reductions in caregiver burdens that are important to patients and their families. The HSV assessment also uses the list price of a drug, which does not consider any actual discounts and negotiations made with public and private payers.
  4. The use of an annual budget impact threshold/cap is counter-intuitive and would prevent patients from having access to many breakthrough, life-saving therapies, (including imatinib, rituximab and bevacizumab). These therapies have provided substantial value to patients, the healthcare system and society. In addition, the framework clearly disincentivizes development of treatments for conditions with broad, unmet medical need, as the method used to determine health system value creates a disincentive for the development of medicines to treat large, unmet disease burdens due to the ensuing budget impact. Because this cap is based upon the number of individuals requiring treatment, drugs that treat conditions with broad, unmet medical need, such as hepatitis C, inadequately controlled high cholesterol, or Alzheimer's, would be viewed as having low health system value merely because of the large treatable population, even though they may be very cost effective for individual patients.

With significantly more new medicines that meet the needs of patients with serious and debilitating diseases being introduced, near-term pressure on healthcare systems' pharmacy budgets is increasing, therefore we agree there is a need for public discussion to understand how best to evaluate the value of innovative therapies. When determining value, Celgene considers the following criteria:

- Patient Benefit: Considers how well the medicine treats disease, patients' quality of life while on treatment, any side effects caused by the medicine, and the convenience of taking the medicine.

- **Benefit to Society:** Considers the positive impact of a medicine on society, such as the benefits to the caregiver and family of the patient; the potential reduction in other healthcare costs; the ability to return patients to work; increases in economic productivity; and the overall positive impact of innovation on social and economic welfare.
- **Benefit of advancing medical progress in a disease:** Considers factors such as the impact a new treatment can have to cure or manage the disease, the severity and rarity of the disease and the availability of other treatments.

Value evolves over time as more evidence is generated via clinical trials and in the real world. Value also varies based on the decision makers' perspective and from stakeholder to stakeholder. In the US, decision-making is increasingly driven by Real World Evidence (RWE). The real world data (RWD) generated by the ecosystem is enabling all stakeholders to make more informed decisions across the continuum of care. RWD (e.g., EMR and claims) is reflective of the vast majority of the population as well as real world outcomes and treatment patterns, whereas trial data reflects only a very small percentage of the patient population (e.g., ~ 4% of the patient population in cancer) and often is constrained due to artificial constructs dictated by the trial.<sup>(1)</sup> Therefore, Celgene is committed to working with healthcare stakeholders to harness RWD and generate data and insights about the value of our products, which are tailored, relevant and meaningful to the individual payers and stakeholders and thus aiming towards making health care more personalized and effective. We are also working to foster a more collaborative environment where the interests of all stakeholders including healthcare professionals and patients are better balanced within pricing and reimbursement decision making systems.

Ensuring patients who need Celgene medicines can receive them is central to our purpose. We are at a time of unrivaled progress in cancer and other life threatening and debilitating diseases and we are committed to continuing our efforts, in collaboration with payers and other stakeholders, to ensure an optimal outcome for patients.

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1. <http://blogs.wsj.com/venturecapital/2014/05/07/google-ventures-leads-130m-round-for-big-data-medical-software-company-flatiron-health/>

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September 12, 2016

To Whom It May Concern:

I have been asked by the Advanced Medical Technology Association (AdvaMed) to provide an assessment of a valuation framework proposed by the Institute for Clinical and Economic Review (ICER).<sup>1</sup> I am a Ph.D. economist who specializes in valuation, and I teach advanced pricing to MBAs at Georgetown's McDonough School of Business.<sup>2</sup> Having carefully reviewed the proposed framework with an economic lens, I conclude that it is inappropriate for application to medical devices.

In particular, I find that there are several problems with the framework that need to be addressed: (1) It relies too heavily on estimating the cost per quality adjusted life year (QALY) gained as a primary basis for establishing a price; (2) Any medical device innovation should be evaluated on a standalone basis, without regard to the growth rate of national gross domestic product or the number of innovations by other medical device makers; (3) Innovations should not be discouraged by virtue of strong uptake percentages; and (4) Annual cost thresholds unfairly penalize medical devices with long lifespans.

In this letter, I briefly describe ICER's proposed framework, and then I explain in detail these four critiques.

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1. ICER, *Evaluating the Value of New Drugs and Devices* (2016) [hereinafter *ICER Framework*].

2. For example, I have served as a valuation expert for Apple regarding the value of songs downloaded on the Internet, and for the Baltimore Orioles regarding the value of its television rights. I have also written about valuation and pricing in medical devices. *See, e.g., Is Greater Price Transparency Needed in the Medical Device Industry?*, HEALTH AFFAIRS (2008), co-authored with Robert Hahn and Keith Klovers. My biography and curriculum vitae are available at <http://www.ei.com/hal-j-singer/>.



## ICER's PROPOSED VALUATION FRAMEWORK

ICER's proposed value framework is meant to address a "need for a more explicit and transparent way for [health technology assessment] groups and payers to analyze and judge value."<sup>3</sup> ICER sought input from participants in the health care industry, including insurers, pharmacy benefit managers, patient organizations, physician specialty societies, and manufacturers.<sup>4</sup>

The framework considers four factors in arriving at what it calls "care value": (1) comparative clinical effectiveness; (2) incremental cost per outcomes achieved; (3) other benefits or disadvantages; and (4) contextual considerations.<sup>5</sup> The first component, comparative clinical effectiveness, estimates the "magnitude of the comparative net health benefit and level of certainty in the evidence on [the] net health benefit."<sup>6</sup> The second component, incremental cost per outcomes achieved, represents the cost per quality adjusted life year (QALY) gained; if each QALY can be achieved for less than \$100,000, then ICER considers the drug/product to be of "high care value;" drugs/products that cost more than \$150,000 per QALY are perceived to be of "low care value."<sup>7</sup> The third component, a catch-all bucket entitled "other benefits or disadvantages," is meant to capture impacts "that would not have been considered as part of the evidence on comparative clinical effectiveness."<sup>8</sup> Included in this list are external benefits ("a public health benefit") or non-market benefits ("reduce disparities across patient groups").<sup>9</sup> The fourth and final component, "contextual considerations," appears to be another catch-all bucket, which includes "ethical, legal or other issues that influence the relative priority of illnesses or interventions."<sup>10</sup> Yet ICER's estimate of the appropriate price for a technology appears to be predominantly based on the incremental cost per QALY achieved.

To derive a "provisional health system value," the net benefits associated with these four components of value are then weighed against the intervention's short-term budget impact over a five-year time horizon.<sup>11</sup> ICER offers the following decision-rule: "If the potential budget impact of a new intervention would contribute to an increase in overall health care costs *at a rate greater than growth in the overall national economy*, health system value would be diminished."<sup>12</sup> Thus, even if the new drug/technology generates benefits in excess of costs (including opportunity costs), the intervention could still be disapproved by ICER's proposed framework so long as it causes health care costs to grow faster than national GDP growth. To estimate an intervention's contribution to

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3. *ICER Framework* at 3.

4. *Id.* at 4.

5. *Id.* at 6.

6. *Id.* at 7.

7. *Id.* at 8.

8. *Id.* at 9.

9. *Id.*

10. *Id.* at 10.

11. *Id.* at 13 ("Estimated *net* change in *total* health care costs over an initial 5-year time-frame") (emphasis in original); *id.* at 14 ("*Unmanaged* cumulative 5-year uptake patterns") (emphasis in original).

12. *Id.* at 12 (emphasis added); *id.* at 19 ("5-year potential uptake if not strictly controlled").

health care costs, ICER places the new drug or device into one of four “uptake patterns”<sup>13</sup>—ranging from 10 percent (“low uptake”) to 75 percent (“high uptake”)—to gauge the percentage of eligible patients assumed to use the intervention. Interventions that cause health costs to grow by one percentage point faster than GDP “serves as an ‘alarm bell’ for greater scrutiny.”<sup>14</sup>

ICER provides an illustrative example of how devices would be considered under its proposed framework. Given an expected growth in U.S. GDP of 3.75 percent, and given aggregate expenditures on medical devices of approximately \$185 billion in 2014, incremental expenditures across all new medical devices in 2015 would be limited to \$6.9 billion (equal to 3.75 percent of \$185 billion).<sup>15</sup> With an average of 23 new medical devices expected in a given year, the incremental expenditures per new medical device should not exceed \$301 million (equal to \$6.9 billion divided by 23).<sup>16</sup> Any new device that generates more than \$603 million in annual expenditures would set off an “affordability ‘alarm bell.’”<sup>17</sup> Recognizing that its value metric links the fate of all new devices introduced in the same year, ICER suggests that a “low-value” intervention can be remedied by, among other things, “seek[ing] savings in other areas to optimize the entire portfolio of services”<sup>18</sup> or by seeking price reductions.

#### **EVALUATION OF ICER’S PROPOSED FRAMEWORK**

ICER’s proposed value framework presents several problems, many of which are particularly acute when applied to medical technologies.

##### **ICER’s Framework Relies Too Heavily on Estimating the Cost Per Quality Adjusted Life Year Gained**

Cost per QALY is a widely used tool for evaluating the value of many medical interventions. Special characteristics of medical devices, however, imply that ICER’s heavy reliance on cost per QALY as the fundamental basis for evaluating prices is inappropriate. ICER’s QALY-derived “bright line rule” would generate substantial error costs.

Any QALY-based decision rule rests on strong assumptions, because QALY itself relies on a highly simplified and stylized model of the preferences of healthcare consumers. Weinstein, Torrance and McGuire (2009) identify “identify nine assumptions that underlie the conventional QALY approach as used in societal resource allocation decisions.”<sup>19</sup> Among the more restrictive is that individuals are risk neutral with respect

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13. *Id.* at 13.

14. *Id.* at 15.

15. *Id.* at 16.

16. *Id.*

17. *Id.* at 19.

18. *Id.* at 17.

19. Milton Weinstein, George Torrance & Alistair McGuire, *QALYs: The Basics*, 12(1) VALUE IN HEALTH 5-9, 8 (2009).

to longevity, and that individuals have utility that is additive over time. As the authors observe:

These are very strong assumptions about preference that undoubtedly simplify reality, but they are necessary in order for QALYs to represent an individual's utility function for health over time. To say that the empirical evidence is mixed as to whether those assumptions provide a serviceable approximation to reality is probably generous for QALYs. For the most part, the evidence is that most people are probably risk averse with respect to their own longevity (although as societal agents, they may be less so), and there is substantial evidence that additivity over time may or may not hold.<sup>20</sup>

While QALYs are often viewed as an important conceptual tool,<sup>21</sup> a QALY-based “bright line rule” such as that proposed by ICER is likely to impose substantial error costs. The cost per QALY thresholds that ICER selects are not specific to medical devices; they are simply “commonly cited cost/QALY thresholds.”<sup>22</sup> ICER makes no attempt to determine the extent to which the assumptions underlying QALYs are appropriate for medical devices—many of which are valuable precisely because they reduce certain health risks to risk-averse patients. For example, artificial hips or knees reduce the risk of debilitating falls; intra-uterine devices (IUDs) reduce the risk of unplanned parenthood, giving parents control over the timing of childbirth.

Noting that “no threshold that is appropriate in all decision contexts,”<sup>23</sup> a 2014 article in the *New England Journal of Medicine* recommends adopting thresholds “based on the available resources for the relevant decision maker and possible alternative uses of those resources.”<sup>24</sup> The authors propose thresholds as high as \$200,000.<sup>25</sup> Because the ICER proposal does not take the available resources or opportunity costs of its audience into account, its “one size fits all” solution is likely to be a poor fit.

Given significant economies of learning in the device industry, an early snapshot of a device's QALY-derived value can be quite misleading. Medical devices undergo a rapid series of incremental improvements once they are introduced; an improved model typically replaces a device within 18 to 24 months. Thus, the performance of many devices generally improves over time. In a classic study of the sensitivity of cost-effectiveness to changes over time as measured by QALYs, David Cutler and Robert Huckman found that the cost-effectiveness of angioplasty in New York State changed

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20. *Id.* at S9.

21. *Id.*

22. *ICER Framework* at 8.

23. Peter Neumann, Joshua Cohen & Milton C. Weinstein, *Updating Cost-Effectiveness—The Curious Resilience of the \$50,000-per-QALY Threshold*, 371 *NEW ENGLAND JOURNAL OF MEDICINE* 796-797 (2014).

24. *Id.*

25. *Id.*

from a *net cost* in each of the first three years 1982-1983 to a *net benefit* of \$18,000 per patient per year by 2000.<sup>26</sup>

Moreover, many medical devices interact with other procedures or health care providers, further complicating the estimation of incremental benefits of a medical technology in terms of QALY. Unlike the case of a new drug, device makers must educate and train physicians on how to use the new medical technology. Spinal screws and rods are used for spinal fusion surgeries to address back problems; they necessarily involve the delivery by a skilled physician. Whenever two treatments are administered in combination—here, the spinal screws and the surgery—attributing the incremental benefit of one (the screws) is a daunting empirical task. Another example of complex interaction effects involves screening and diagnostic medical devices; for example, a scanner might detect cancer earlier than otherwise, but the treatment that follows the early detection will impact the QALY in ways that are arguably more profound than the medical device. A metal screw used to treat a bone fracture is clearly vital to the patient’s quality of life, but ascertaining the incremental benefit in QALY would turn on post-operation treatments, including the patient’s level of exercise and diet.

Finally, many medical devices provide benefits that are important to practitioners and patients, but are not well measured by a QALY approach. For example, a technology that allows discharge of a patient from a hospital two weeks early and reduces the pain associated with the procedure would be unlikely to generate a high QALY score, since it would not be associated with an extension of life and the benefits are of relatively short duration; yet the value to patients and hospitals would be considerable.

**Any Medical Device Innovation Should Be Evaluated on a Standalone Basis Without Regard to the Growth Rate Of National Gross Domestic Product or the Number of Other Device Innovations**

Setting aside the problem of characterizing a medical device in terms of cost per QALY, the second stage of ICER’s proposed framework could deny funding for a new device for arbitrary reasons. Pegging medical device budgets to GDP growth and the number of new devices results in inefficient outcomes. Using the example provided by ICER above, spending on all new medical devices cannot exceed \$6.9 billion under normal GDP growth conditions (3.75 percent), assuming generously that spending on existing medical devices stays constant from one year to the next; any inflation in existing medical devices would crowd out opportunities for entry under the ICER framework. If GDP growth slows to say one percent per year, then the aggregate budget for new devices under the ICER framework falls from \$6.9 billion to \$1.5 billion.

ICER’s valuation framework also penalizes medical devices during times of peak innovation. If entry among device makers is robust in a given year, then the per-device budget falls. For example, while 23 new device makers would have a budget of \$301

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26. David M. Cutler & Robert S. Huckman, “Technological Development and Medical Productivity: Diffusion of Angioplasty in New York State,” Working Paper 9311, National Bureau of Economic Research (October 2002).

million each (under normal GDP growth), 46 new device makers would have to make do with \$151 million apiece. With GDP growth of one percent and 46 new entrants, expenditures on any new device in excess of a mere \$80 million would set off ICER's "alarm bells." It bears noting that new medical devices must be approved or, in the case of a new iteration of a device already approved, be "cleared." When a cleared device replaces an older version, it is not obvious whether, under ICER's framework, it would be entitled to the budget of the former device or the incremental cap space for the new version.

The mechanical nature of the formula also means that the cap for any given device will actually be lower than should be allowed under the total cap concept. The cap is based on an assumed average cost for all devices. But if devices are all capped at the projected average, the result will be a true average that is lower than the average used to establish the cap. This is so because no device's price can exceed the assumed average, but some devices will have prices lower than the assumed average.

Moreover, relative to new drugs, new medical devices are penalized under ICER's framework purely based on devices' smaller share of health care expenditures. To make this concrete, assume that device spending and drug spending each contributed 13.3 percent to total health care spending (rather than 13.3 percent for drugs versus 6.0 percent for devices). Now aggregate spending on new devices could be \$15.4 billion under ICER's framework, and the budget per new device assuming 23 new devices would be \$668 million (as opposed to \$301 million).

For devices, imposition of an arbitrary price cap may also actually increase prices over the long run. Prices for medical technology have been falling in real terms for the last two decades.<sup>27</sup> For the most common implantable devices, prices have been falling sharply in both real and nominal terms.<sup>28</sup> This is the case because a new device's ability to capture the monopoly rents associated with innovation only lasts for a few years, until competing products enter the market. By artificially suppressing initial prices, application of the ICER model would substantially reduce the incentive for new entrants and thus potentially result in higher prices in the long term.

The funding (and hence fate) of an upstart device maker should not be tethered to GDP growth or the number of new entrants in that year. There is no economic reason that links expenditures for a given device to these extraneous factors. Instead, the demand for a given device should be based purely on the benefits—and not just those benefits that can be expressed in terms of QALY—the device generates. So long as benefits exceed the seller's asking price for the device, the buyer enjoys what economists call "consumer surplus." No new device should set off an "alarm bell" simply by virtue of its price

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27. Gerald Donahoe & Guy King, "Estimates of Medical Device Spending in the United States" (October 2015), *available at* <http://advameddx.org/resource-center/estimates-medical-device-spending-united-states-3>.

28. Genia Long, et al., "Recent Average Price Trends for Medical Devices, 2007-2011" (February 2013), *available at* <http://advamed.org/resource-center/recent-average-price-trends-implantable-medical-devices-2007-2011>.

exceeding some arbitrary cutoff based on GDP growth and the number of new devices introduced that year.

### **Innovations Should Not Be Discouraged By Virtue of Strong Uptake Percentages**

As explained above, a health care consumer (for example, a hospital or patient-insurer combination) will purchase a device so long as the private benefits exceed the price. Demand and thus uptake will be especially strong for innovative devices that generate significant consumer surplus. Yet ICER's valuation framework perversely discourages funding of such innovative devices by imposing a lower price as the percentage of eligible patients treated rises. The framework fails to appreciate that the private benefits attached to a device do not depend in any way on the (social) uptake percentage. Harry's hip replacement generates value to Harry regardless of how many other patients receive the same hip that year. The device maker might enjoy economies of scale with greater uptake, potentially leading to lower prices for hip replacements, but Harry's willingness to pay for the new hip is unfazed.

ICER reveals how its framework could be used to put downward pressure on PCSK9 drugs. The drug is originally priced at \$14,350.<sup>29</sup> To achieve ICER's threshold \$150,000 cost per QALY, the price would have to fall to \$7,735.<sup>30</sup> But even at that price the drug would set off ICER's "alarm bells" because it would exhaust its (arbitrary) \$904 million allotment under the GDP-growth threshold. According to ICER, at a price of \$14,340, the demand for the drug was 2.6 million units.<sup>31</sup> Figure 1 illustrates the impact of ICER's valuation framework on consumer welfare.

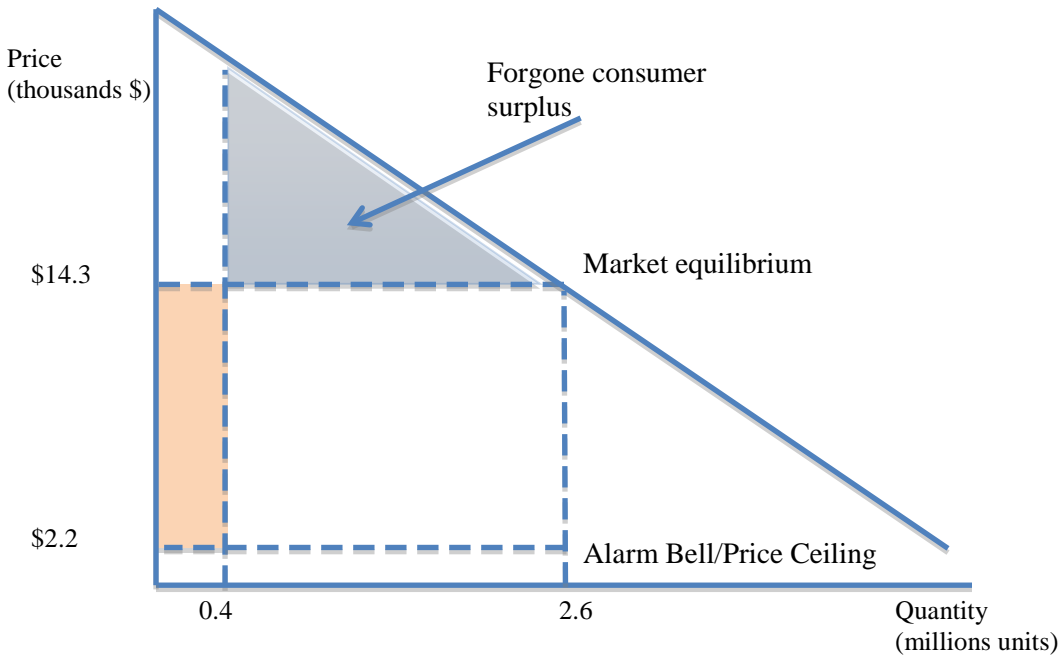
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29. *Id.* at 20.

30. *Id.*

31. *Id.*

FIGURE 1: ICER'S VALUATION FRAMEWORK SERVES AS A PRICE CEILING



To fit under its arbitrary maximum budget for a new drug of \$904 million, the price of PCSK9 drugs would have to fall to \$2,177, yielding just over 400,000 units. The (original) consumer surplus associated with the market-determined equilibrium is the area under the demand curve bounded from below by the price of \$14,350 per unit. The forgone consumer surplus resulting from ICER's framework is depicted as a light blue triangle, depicting the reduction in consumer welfare associated with a market contraction from 2.6 to 0.4 million prescriptions. At the lower price, some additional surplus is obtained on the smaller base of prescriptions (shown in orange), but consumer welfare will be lowered on net to the extent that the blue triangle exceeds the orange rectangle. To keep the figure simple, I omit the forgone producer surplus (also recognized as a deadweight loss) associated with the compulsory reduction in output. The example makes clear that any new drug (or device) that enjoys high uptake will be forced to incur a sizable haircut; the bigger the uptake, the greater the consumer surplus, the bigger the haircut.

### ICER's Yearly Analysis Creates Timing Issues and Disproportionately Penalizes Medical Devices with Long Lifespans

The effective life of many medical technologies—for example, scanning devices and surgical units—is often much longer than that of a particular drug.<sup>32</sup> Furthermore, as

32. Medical device effective life declarations suggest that the majority of devices have effective lives of seven years or more. *See, e.g., Commonwealth of Australia's Effective Life Declaration, Health and Community Services, Table A, available at <http://law.ato.gov.au/atolaw/view.htm?docid=ITD/DEP20032/00001>* (accessed Sept. 8, 2016).



noted above, the efficient and efficacious use of such technologies depends upon training medical staff and doctors in their proper use, as well as “learning-by-doing” know-how acquired only through extended use and experience.<sup>33</sup>

Consequently, the cost of a medical device is often front-heavy, where significant fixed costs must be incurred in installing, training, and creating the necessary infrastructure to properly apply such devices. While variable costs may decrease over the long term (such that marginal costs may fall beneath the QALY threshold as determined by GDP growth and uptake levels), any implementation of new medical technologies may set off the “alarm bells” due to short-run outlays, while not accurately reflecting the overall cost structure and value of such devices.

An especially serious problem with use of the five-year window is that both the value and the cost-reductions due to medical technologies may accrue over a very long time period. For example, artificial hips and knees have a useful life that can exceed twenty years. The vast majority of the costs associated with the device occur in the first year from implantation and rehabilitation. The cost reductions due to reduced dependency and nursing home use, as well as reduced comorbidities from such illnesses as diabetes and heart disease because the patient can maintain a greater degree of activity, by contrast, will accrue over the lifespan of the device.

In sum, any attempt to value medical technologies with a rigid five-year window will confront serious timing issues. To quote Buxton’s Law, “It is always too early until, unfortunately, it’s suddenly too late.” ICER’s framework would likely overestimate the costs, by not amortizing them over the relevant lifespan of medical device. Put differently, the five-year window currently proposed does not match the value of the device to the costs incurred over the relevant timeframe.

## CONCLUSION

For the forgoing reasons, ICER’s proposed framework should not be used to guide purchase decisions relating to medical technologies. ICER purports to consider other amorphous factors that are not captured by QALY, but at the end of day, cost per QALY is paramount. It is not clear whether ICER’s framework would account for device-related savings from outside the health system, such as increased productivity, labor force participation, and reduced dependency. An acceptable price under the ICER framework must not exceed \$150,000 per QALY, and further price reductions can be justified based on factors—such as GDP growth and the number of new devices introduced in a given year—unrelated the net benefits of the device in question. The ICER framework appears to be nothing more than a crude mechanism to put downward pressure on the price of medical devices.

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33. Indeed, NSF International offers certification courses for medical device usage offering learning-by-doing opportunities beside experienced experts. *See* NSF-DBA, Medical Device Diploma, *available at* [https://www.nsf.org/newsroom\\_pdf/110719\\_Medical-Devices-Diploma-Program.pdf](https://www.nsf.org/newsroom_pdf/110719_Medical-Devices-Diploma-Program.pdf) (accessed Sept. 8, 2016).



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September 12, 2016

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**RE: Lilly Response to the ICER Methodology Review**

Submitted electronically via: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

The following comments are submitted on behalf of Eli Lilly and Company (Lilly) to the Institute for Clinical and Economic Review (ICER) Value Framework Methodology Review. Lilly is one of the country's leading innovation-driven, research-based, pharmaceutical and biotechnology corporations. The company is devoted to seeking answers for some of the world's most urgent medical needs through discovery and development of breakthrough medicines and technologies and through the health information we offer. Ultimately, the company's goal is to develop products that save and improve patients' lives. Lilly appreciates the opportunity to be able to respond to ICER's request on their Value Framework methods. We have significant concerns and specific suggestions to improve the ICER Value Framework Methodology that we have detailed in the points below.

Lilly is committed to meeting the diverse needs of people by offering a comprehensive and complementary portfolio of innovative solutions. As Lilly develops new products to address significant unmet clinical needs, we are concerned that the current state of the ICER Value Framework will not recognize the true value of these interventions. In disease states where treatment options are few and the healthcare system provides a very limited structure for care management of these patients and their unduly burdened families, the current ICER framework would seemingly dis-incentivize any innovations aimed at changing the care paradigm for complex and devastating diseases. For example, new treatments are expected to come into the market in Alzheimer's disease. The complexity of Alzheimer's disease and its relatively high prevalence rates will engender debate around how to assess the value and affordability of these emerging therapies. The current ICER methods are inadequate to appropriately recognize the value of these new treatments to the patients who anxiously await an effective treatment for this devastating disease.

The same is true for oncology where a medicine's clinical value is not static and evolves significantly over time.<sup>1 2</sup> For example, a newly approved medicine may realize additional value from the accumulation of new evidence, both through clinical trials and real-world evidence. Current ICER methods and evaluations may become quickly outdated and fail to represent the emerging evidence and value without modifications to their current methods to include frequent updates of previous evaluations. In oncology specifically, changes in drug sequencing, changes in drug combinations and additional indications can lead to new valuations of the drug in a different context.<sup>2</sup> The methodology currently employed by ICER may only determine a drug's value for a particular place in therapy at the time of regulatory approval and not the value to patients and society for evolving therapeutic uses.

## I. Care Value

### I.A. Integrating "Additional Benefits or Disadvantages" and "Contextual Considerations"

*ICER seeks "Methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value intended to fall in the current value framework within "additional benefits or disadvantages" and "contextual considerations."*

There are several elements needing change within the current ICER methods in order to achieve this goal:

- greater use of quantitative vs. qualitative data
- the choice of the most appropriate measure of benefit or effectiveness
- appropriate use and transparency on the use of qualitative data by the ICER committees

#### **1.A.1 We recommend that ICER formally incorporate quantitative measures from the "Additional Benefits" and "Clinical Contextual Considerations" domains into their measure of "Comparative Clinical Effectiveness."**

ICER addresses qualitatively necessary evidence that would be more accurately addressed quantitatively. The following are all examples presented by ICER as valid measures under the "Additional Benefits" and "Clinical Contextual Consideration"

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<sup>1</sup> Towse A, Barnsley P. **Approaches to identifying, measuring, and aggregating elements of value.** *International Journal of Technology Assessment in Health Care* 2013. 29:4(360-4).

<sup>2</sup> Sweeny N, Goss TF. **"The Value of Innovation in Oncology: Recognizing Emerging Benefits Over Time."** May 2015.

dimensions which are currently assessed in a qualitative and opaque manner by ICER's Value Framework methods:<sup>3</sup>

#### Additional Benefits

- *Are there benefits of treatment that extend beyond patient-specific health improvement?*
  - *reduction in care needed from friends and family,*
  - *ability to return to work sooner.*
- *Will the treatment expand the population that will benefit from treatment?*
  - *Removes or reduces barriers to treatment through new route or delivery mechanism.*
  - *Allows sicker patients or those with comorbidities to be treated.*
- *Does the treatment offer a new or different mechanism of action when significant variation of treatment effect suggests that many patients who do not achieve adequate outcomes on other treatments may benefit?*

#### Contextual Consideration

- *no other acceptable treatments exist*
- *high severity and/or priority condition*
- *vulnerable population (e.g., children) (NOTE: this would apply to the elderly as well.)*

ICER acknowledges that part of a product's value is expanding the population that will benefit from treatment. ICER should also note and acknowledge that the success of a treatment on this important objective of reaching an expanded population will exacerbate the current affordability construct used by ICER. This is a clear example of the lack of internal consistency in the ICER framework that needs to change.

These and many other measures are essential to validly assess emerging treatments in many therapeutic areas with significant unmet clinical need. In addition to the ICER examples, there are many excellent measures of patient- and caregiver-reported outcomes that too often go unused or are not given the full credit they deserve. This is critical in areas such as rheumatoid arthritis, Alzheimer's disease, and oncology. We propose that a valid, reliable, and fair assessment of value needs to use quantifiable measures within the "Additional Benefits" and "Clinical Contextual Consideration" domains. All quantifiable measures would be aggregated and reported at the level of each domain. Most importantly, they all must be incorporated into an overall composite measure of "Clinical Care Value" and "Comparative Clinical Effectiveness" results.

The current ICER methods need to be specific on what measures are included within the "Additional Benefits" or "Clinical Contextual Considerations" domains. For example,

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<sup>3</sup> Pearson, S. "Best Practices for Assessing the Value of Drugs for Formulary Decisions" AMCP Nexus 2015, Boston, MA. October 8, 2014

ICER should adopt measures for the “Value of Innovation”<sup>4 5</sup> and the “Enduring Value of Pharmaceuticals”<sup>6 7</sup> within these domains. All ICER measures must be specified well in advance so that manufacturers developing new products can prepare and provide the necessary evidence to ICER for a full and fair evaluation of their products.<sup>8</sup>

### **I.A.2 ICER Needs To Have Greater Transparency about Its Methods**

ICER reaches out proactively to manufacturers and provides high-level information about assessment models, underlying assumptions, and evidence base. However, this level of information is not sufficient to enable reviewers to reproduce the results and provide meaningful, real-time input. Full transparency—down to the equation level—is needed to enable reproducible results and support fully informed stakeholder collaboration. We recommend that ICER make their methods or models available to all stakeholders along with the draft report, perhaps on a protected web-based platform, to enable understanding and validation of the results by the relevant stakeholders.

### **I.A.3. Qualitative Evidence Is Necessary and Needs To Be Evaluated and Reported In A Transparent Manner**

ICER relies significantly on its evaluation committees (i.e., NECEPAC, Midwest CEPAC and CTAF) to assess the qualitative evidence in a “deliberative appraisal” manner. Qualitative data and assessment of it by experts is necessary for a complete and valid assessment of value. However, ICER needs to make it clear how this evidence is

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<sup>4</sup> **Innovation:** New products often bring benefit beyond the specific value of treating the targeted condition. ICER currently fails to specifically credit the value of Innovation within their assessments. There are many options to quantify innovation. For example, innovation could be defined and quantitatively measured as novel mechanisms of action for indications with significant unmet clinical need or qualitatively as the potential of a new treatment for its “Scientific Spillover” or the “Value of Hope” it provides (i.e., the potential of a treatment that offers an incremental benefit in survival until a newer more effective treatment is introduced).

<sup>5</sup> Paddock, S., Brum, L., Sorrow, K., et. al **PACE Continuous Innovation Indicators—a novel tool to measure progress in cancer treatments**. Ecancer Medical Science. ecancer 9 498 / DOI: 10.3332/ecancer.2015.498. <http://ecancer.org/journal/9/full/498-pace-continuous-innovation-indicators-a-novel-tool-to-measure-progress-in-cancer-treatments.php> Accessed on September 8. 2016

<sup>6</sup> **Enduring value:** This is the enduring value that pharmaceuticals bring beyond their patent life or even the lifetimes of the patients that are treated. Many products bring health benefit for longer time frames than currently considered by ICER (i.e., far beyond the life expectancy of the individuals that benefit from the treatment). In addition, ICER needs to consider that many products are far less expensive over the lifetime of the product than the cost estimates that are considered by ICER.

<sup>7</sup> Dylst P., Vulto, A., and Simeons, S., **Societal value of generic medicines beyond cost-saving through reduced prices**. Expert Review of Pharmacoeconomics & Outcomes Research. Volume 15, 2015 - Issue 4 <http://www.tandfonline.com/doi/pdf/10.1586/14737167.2015.1017565?needAccess=true>. Accessed on September 8. 2016

<sup>8</sup> Tunis, SR. Clarke, M., Gorst, SL., et. al. **Improving the relevance and consistency of outcomes in comparative effectiveness research**. Journal of Comparative Effectiveness Research. March 2016 ,Vol. 5, No. 2, Pages 193-205

considered and used in decision-making by the committees. ICER's process and subsequent conclusions should be well structured and documented according to a pre-defined rubric. The EMA and FDA offer examples of transparent methods of structuring qualitative assessments and decision-making in their benefit-risk assessments.<sup>9 10</sup> ICER committees should use structured and transparent methods for its deliberations and reporting their assessments and decisions.

#### **I.A.4. Achieving a Strong Emphasis on Having Patient Perspective and Greater Patient Involvement**

Although a variety of perspectives are represented at ICER meetings, comments made by panel participants during meetings indicate they are approaching value assessment through a cost-containment lens. Panel members must have a broader view of value beyond cost-containment. In recent years, significant amounts of research have been published that gives guidance on best practices for engaging different stakeholders,<sup>11</sup> to include patients, in the value assessment process (e.g., HTAi Value and Standards,<sup>12</sup> etc.). Providing a mechanism for stakeholder representatives (e.g., consumer, industry) to receive nominations for inclusion on a panel which would be reviewed by a separate committee could bring this broader perspective to the panels. It also is important for voting panel members to have expertise in the disease under discussion.

More specifically, ICER evaluations should always take a societal perspective and not a payer perspective. The societal perspective can allow the use of many additional constructs within the "Additional Benefits" and "Clinical Contextual Considerations" domains. Examples are "Value of Innovation" and "Value of Scientific Spillover." A societal perspective will ensure that appropriate cost-offsets are included and not just those that will be accrued by the payer. This is all necessary but perhaps not sufficient. An even better approach would be to take the emerging importance of a patient perspective, which allows for societal values and constructs that matter significantly to patients (e.g., caregiver burden of those caring for Alzheimer disease patients, the utility of 100% skin clearance to psoriasis patients, the "value of hope" for more effective

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<sup>9</sup> <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm>

<sup>10</sup> Mt-Isa, S., Ouwens, M., Robert, V., Gebel, M., Schacht, A., and Hirsch, I. (2016) **Structured Benefit-risk assessment: a review of key publications and initiatives on frameworks and methodologies**. *Pharmaceut. Statist.*, 15: 324–332. doi: [10.1002/pst.1690](https://doi.org/10.1002/pst.1690).

<sup>11</sup> Henshall C, Schuller T; HTAi Policy Forum. **Health technology assessment, value-based decision making, and innovation**. *Int J Technol Assess Health Care*. 2013 Oct;29(4):353-9. doi: 10.1017/S0266462313000378. Epub 2013 Jul 11 Accessed September 8, 2016

<sup>12</sup> [http://www.htai.org/fileadmin/HTAi\\_Files/ISG/PatientInvolvement/v2\\_files/Info/PCISG-Info-ValuesandStandards-30-Jun14.pdf](http://www.htai.org/fileadmin/HTAi_Files/ISG/PatientInvolvement/v2_files/Info/PCISG-Info-ValuesandStandards-30-Jun14.pdf) Accessed September 8, 2016

cures, etc.) to be considered. Finally, ICER should clearly state the perspective it takes and be ready to address issues of inclusion and exclusion in both its assessment of benefit and cost. This could be achieved by incorporating a “Cost-Consequence Analysis” into the ICER Value Framework methods.<sup>13</sup>

**I.B ICER Needs To Modify their Value Framework Methods to Select and Use the Most Optimal Measures of Effectiveness Within Individual Evaluations.**

*ICER seeks input on Incremental Cost-Effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures*

**I.B.1 ICER Needs to Change their Methods to Select the Most Appropriate and Valid Measure of Effectiveness Within their Individual Evaluations.**

ICER has exclusively adopted the QALY as the sole measure of effectiveness. This decision results in suboptimal assessments of effectiveness and value in many therapeutic areas (e.g., oncology, Alzheimer’s disease). ICER itself has acknowledged the limits of the QALY:

*Whereas many international payer agencies have adopted the QALY as a universal metric of health outcomes by which to analyze comparative net health benefit across different types of medical interventions, very few payers in the US use the QALY in a systematic way. In part, this is because of methodological concerns about whether the QALY adequately reflects the preferences of patients for different types of health outcomes. There are long-standing concerns that QALYs fail to capture important societal values favoring health benefits for patients with the most severe illnesses. And QALYs usually must be estimated from published literature through analyses that can be complex, time consuming, and ultimately lacking in the degree of transparency that is one of the most important goals of a value framework. The methodological concerns are most relevant when QALYs are used as part of analyses comparing the incremental cost-effectiveness of treatments for different conditions<sup>14</sup>....*

ICER concludes that the QALY is the best measure despite these limitations. However, the use of cost-effectiveness does not require the QALY. Given that the QALY is often not a good fit for some evaluations, it should be replaced with the most suitable alternative for the therapeutic area being evaluated rather than relying on a metric that tries to force comparison between disease states that may be at very different stages in

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<sup>13</sup> Mauskop JA, Paul JE, Grant DM, et.al, **The Role of Cost-Consequence Analysis in Healthcare Decision-Making**. Pharmacoeconomics 1998 Mar; 13 (3): 277-288

<sup>14</sup> Steven D. Pearson, M.D., M.Sc. “A Framework to Guide Payer Assessment of the Value of Medical Treatments” ICER White Paper, published June 12, 2014.



scientific understanding, diagnostic advances, and care management pathways. This would be another rationale for incorporating a “Cost-Consequence Analysis” into the ICER methods<sup>13</sup>. However, a valid assessment still requires the use of a composite measure of effectiveness. There are many good examples of “Comparative Clinical Effectiveness” assessments in health care that use composite measures other than the QALY.<sup>15 16 17</sup> Composite measures can be developed and implemented via the use of multi-criteria decision analysis methods.<sup>18</sup>

Others that have developed their own value assessments and frameworks have explicitly rejected the use of the QALY due to its limitations for their value assessments (e.g., IQWiG).<sup>19</sup> In 2014, the IMS Institute released a report on the impact of cost per QALY (CPQ) criteria for reimbursement regarding access to cancer medicines. They compared 5 CPQ countries to 5 non-CPQ countries and determined that those countries using the CPQ reimbursed fewer cancer drugs, took longer to come to a reimbursement decision, had lower and slower adoption rates of new cancer medicines, and had lower overall survival. In short, they concluded that CPQ methods achieve less for cancer patients.<sup>20</sup> We consider that these are signals of a failure of the methodology and that the sole use of the CPQ as a measure is suboptimal within a value assessment framework.

Alternative approaches to CPQ currently used by HTA bodies to value oncology products involve flexible ICER thresholds, special end-of-life criteria, and pragmatic decision-making and patient-access schemes.<sup>21</sup> The commonality of alternative approaches to CPQ suggests the method is insufficient for determining value in oncology. As already noted, there are additional methods that may provide a sufficient

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<sup>15</sup> Drummond, O’Brien, B., Stoddart, GL., Torrance, GW. “Methods for the Economic Evaluation of Healthcare Programmes, Second Edition”, Oxford University Press, 1997

<sup>16</sup> Banta, D. et.al. The Implications of Cost-Effectiveness Analysis of Medical Technology August 1980 NTIS order #PB80-216864 <https://www.princeton.edu/~ota/disk3/1980/8011/8011.PDF>

<sup>17</sup> The Office of Technology Assessment (OTA) provided Congressional members and committees with objective and authoritative analysis of the complex scientific and technical issues of the late 20th century, (i.e. technology assessment). This website lists many individual OTA reports of health technologies and interventions. Many reports define and use individual and composite measures in order to use the most valid and appropriate measure of effectiveness for that specific evaluation. <http://ota.fas.org/otareports/topic/ghtopics>. Accessed August 26, 2016.

<sup>18</sup> Thokala P, Duenas A. **Multiple Criteria Decision Analysis for Health Technology Assessment**. *Value in Health* 2012;15;1172-81.

<sup>19</sup> Mark V. Pauly, Thomas G. McGuire, Pedro Pita Barros. **Handbook of Health Economics, Volume 2**. Elsevier, 2012. Pg. 487

<sup>20</sup> **“Impact of cost-per-QALY reimbursement criteria on access to cancer drugs”** *IMS Institute for Healthcare Informatics*. Dec. 2014.

<sup>21</sup> **International comparisons of Health Technology Assessment”** A report from *Breast Cancer Now and Prostate Cancer UK*. 2016.

determination of value that include Cost-Consequence Analysis (CCA), and Multi-Criteria Decision Analysis (MCDA).<sup>13, 18</sup>

**ICER's ultimate conclusion to use the QALY as the sole measure of effectiveness for all of their evaluations penalizes the products they evaluate by using a sub-optimal measure. If ICER wants to use the QALY as a complementary measure of effectiveness in order to provide a comparator across therapeutic areas then it needs to acknowledge the limitations of the measure for this purpose. In conclusion, the QALY should rarely be used as the sole measure of effectiveness given its known limitations.**

#### **I.B.2 Decision-Criteria (e.g., Cost Thresholds) Must Be Allowed To Vary across Diseases and Populations**

Transparent and valid decision criteria are necessary based on what is most appropriate for the indication or condition under evaluation. ICER currently uses a single cost-effectiveness threshold as its criteria for determining value. There is no single measure or set of measures that will be optimal across evaluations. The use of optimal criteria for assessing value must be applied as well to the ICER decision criteria for evaluating what is or is not “good value.” The current ICER method of setting and using a single threshold is inadequate since it is arbitrary in nature and does not take into account all relevant criteria in setting the threshold (e.g., differential willingness to pay in areas of high-unmet clinical need, evidence from the “Other Benefits” and “Clinical Contextual” domains).

Valid decision criteria require a variety of relevant, appropriate, and necessary factors (e.g., the current state of investments in a therapeutic area, disease priority, opportunity to address unmet clinical need and willingness to pay, etc.) While ICER may resist the notion that differential criteria and investments are viable constructs for value-based decision making, real world practice shows it to be quite viable and often used (e.g., a significant willingness to pay existed for treatments for AIDs and other conditions with significant unmet clinical need).

#### **I.B.3 Forthcoming Treatment Innovations Will Be Penalized Without Adopting a Broader Set of Measures and Decision Criteria That Address the Challenges That These New Products Will Offer In Assessing Their Value**

As we stated previously, the value of innovations currently in development and preparing to enter the market place will not be recognized and rewarded by the current ICER Value Framework Methodology. As an example, listed below are a few of the challenges presented by Alzheimer's disease that will not be adequately addressed in the current ICER value framework:

- As previously noted, the QALY will be woefully insufficient. While survival and Quality of Life are essential, they are not adequate alone to assess the benefit of new treatments. Measures of caregiver burden, indirect costs, (e.g., longer term institutional care, impacts on productivity of caregivers etc.) will require the use of a dedicated individual and composite measure of effectiveness in order to recognize and reward the value of the forthcoming interventions in areas of high-unmet need and high biological complexity like for Alzheimer's disease.
- As previously noted, adopting a patient perspective, and valuing measures of benefit and effectiveness is essential. The Patient Perspective must include the burden and impact placed on caregivers. Alzheimer's Disease presents unique measurement issues where patients cannot always accurately respond for themselves but valid and reliable measures can be obtained from caregivers. This evidence needs to be formally incorporated in any assessment of value by ICER.
- ICER's methods should define the role and acceptability of surrogate endpoints when long-term outcomes are not yet available. As an example, multiple treatment options are being studied in individuals who have evidence of beta amyloid accumulation but who have not experienced cognitive nor functional decline. Assessment of these treatments will likely require a more long-term view with ongoing monitoring of both surrogate and long-term outcomes. There are emerging methods for how this can be achieved.<sup>22</sup> ICER must address how surrogates will be incorporated within the ICER methodology beyond the uncertainty they inherently have.
- ICER methods do not specify how the integration of new diagnostics (e.g., amyloid imaging or Cerebrospinal Fluid for identifying appropriate candidates in conjunction with the introduction of new and effective treatments will be evaluated, reimbursed, and adopted into clinical practice.

In summary, ICER needs to modify its framework accordingly to use the most valid and fit-for-purpose measures and decision criteria within their evaluation framework. The current ICER approach to measuring effectiveness and setting decision-criteria is inadequate. Both composite quantitative and qualitative measures are required in a valid, reliable, and transparent manner. There needs to be more transparency by ICER on the nature of its process and models employed in its evaluations.

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<sup>22</sup> Bognar K., Bae J., Murray J., et. al. *An Economic Model of Surrogate Endpoints*. ASHEcon Conference 20166, Philadelphia, PA, June 13, 2016

## 2. Health System Value

*ICER seeks input on the following issues:*

- *Methods to estimate the market uptake and “potential” short-term budget impact of new interventions as part of judging whether the introduction of a new intervention may raise affordability concerns without heightened medical management, lower prices, or other measures.*
- *Methods to set a threshold for potential short-term budget impact that can serve as a useful “alarm bell” for policymakers to signal consideration of whether affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.*

We encourage ICER to rename its “Health System Value” as “Short-Term Budget Impact.” The name “Health System Value” is misleading and suggests that the assessment is representative of health system benefit relative to health system cost. In fact, ICER’s assessment is simply an estimate of budget impact and should be referred to as such.

## 3. Market Uptake and “Potential” Short-term Budget Impact

*ICER seeks “Methods to estimate the market uptake and “potential” short-term budget impact of new interventions as part of judging whether the introduction of a new intervention may raise affordability concerns without heightened medical management, lower prices, or other measures.”*

We encourage ICER to use realistic estimates of utilization and include sensitivity analysis that looks at a range of possible costs. More realistic utilization estimates would: (1) be based on the typical medication management that payers would use to impact utilization in the clinical area of interest, (2) incorporate uptake predictions from manufacturers and clinical experts, and (3) use sensitivity analysis to capture uncertainty and the range of possible uptake rates. In addition, ICER needs to **use a more realistic estimate of price**. The “list price” that ICER assessments currently use does not represent the actual discounted price that is relevant to, and negotiated by payers. Using third-party data to obtain an industry-wide discount rate estimate and conducting sensitivity analysis around this rate (using a range of discount assumptions) would provide a more realistic price estimate.

## 4. Affordability

*ICER seeks: Methods to set a threshold for potential short-term budget impact that can serve as a useful “alarm bell” for policymakers to signal consideration of whether affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.*

#### 4. A. Separate Budget Impact from Affordability

“Affordability” is an important concept. Evaluating it involves making assessments and trade-offs at an overall health system level (i.e., a broad assessment of all investments in a healthcare system and spending on healthcare vs. other societal considerations such as education, police, etc.). In addition, there are various mechanisms at a local level that can address affordability for the specific payer involved (e.g., discounts, rebates, etc.). Most mature HTA and decision-making processes within a single jurisdiction are careful to separate assessment from appraisal and appraisal from budgetary decision-making in order to minimize conflicts of interest.<sup>23</sup>

An estimate of budget impact is a necessary but an insufficient part of evaluating affordability. If ICER is to address Affordability then a separate framework, distinct from value, is required. Short-term budget impact is a measure of resource use and does not adequately represent the construct of “Affordability” rendering the current ICER approach as woefully inadequate. A comprehensive approach to affordability requires considerations of concepts such as disinvestment and willingness-to-pay, needs to be informed by cultural and societal values and by both health and non-health needs, and requires broad stakeholder involvement. ICER’s current approach to assessing affordability, (i.e., setting an “alarm bell” threshold), is not a comprehensive consideration of the healthcare system, does not consider societal values, and does not adequately measure affordability.

Not only would an affordability assessment require decisions about health care spending vs. non-health care spending, it would also require societal decisions about intra-health care spending—tradeoffs regarding spending on the elderly vs. the young, rare disease vs. common ones, curative therapies vs. life prolonging vs. quality-of-life enhancing, as well as allocations between medications, surgery, hospital care, and physician services. We recommend ICER separate its “Affordability” assessments from its “Value” assessments

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<sup>23</sup> For example: In Germany IQWiG assesses clinical added value, the G-BA makes the appraisal and the GKV-Spitzenverband negotiates price. In the UK, the ERGs assess the manufacturers submission while independent appraisal committees within NICE make the reimbursement decision. Currently, ICER’s approach combines the assessment, appraisal, budget impact elements and a final recommendation all within the same organization. We would consider this to be poor practice as it is open to conflict of interest. An added complication is that ICER’s deliberations are meant to serve multiple, diverse payers. A far more satisfactory option for ICER from a governance perspective would be for them to undertake an assessment of the added clinical value and potentially comparative costs and cost offsets, however rather than roll these up into a single output, instead provide a factual report that presents the different elements of care value (e.g. comparative *efficacy* per comparator, comparative safety, costs and offsets) and then provide that data for the individual payers to use when they make their deliberations. There is a precedent for this, which is the developing pan-European HTA process – the so-called Relative Effectiveness Assessment (REA) -, which seeks to remove the duplication of assessment at the national level. In developing this assessment, it was recognized that different health systems had different comparators, differences in health provision processes, differences in populations and budgets and as such it was not possible to come to a single cost-effectiveness assessment or even a single estimate of comparative *effectiveness*. Therefore, the REA does not include a single recommendation but rather it is a factual assessment of added clinical value only.

and develop methods, which would appropriately and validly address all the necessary elements to validly assess the issue of affordability.

## **5. Administrative Issues and the ICER Assessment Process**

### **5.A. Extend Length of Time for Review and Feedback**

ICER needs to allow a more conducive open comment period by relevant experts and stakeholders. Timelines are too short and may not reach all relevant parties. ICER has extended the time for stakeholders to submit comments on scoping documents and reports, but the amount of time is still too short. Stakeholders recognize the review time is limited because ICER is trying to get reviews out quickly, but form should follow function and sufficient time is required for meaningful review and feedback by all interested stakeholders.

### **5.B. Review Assessments Regularly**

ICER currently has no plans to revisit and revise any assessments. The shelf life for ICER assessments is short and some are already out of date as new evidence has become available and new treatments are approved. Assessments should be revisited on a regular basis and revised when they are out of date.

### **5.C. Greater Transparency on ICER's Criteria for selecting Evaluation topics**

ICER should be more transparent regarding their criteria for selecting topics for evaluation. This selection process should include multiple stakeholders with a significant representation by patients in the topics for their evaluations

### **5.D. Greater Transparency on Comments received by ICER**

ICER is currently selective in its disclosure of comments and concerns raised to them. We feel that all comments and their disposition should be publically available. Ideally, ICER should report should give their rationale for issues that they have chosen not to address.

### **5.E. Greater Transparency on the ICER Board and Committee Member Selection Criteria and Process**

ICER should be more transparent regarding their criteria for selecting review board members, particularly in the area of patient advocacy and representation.

### **5.F. Products without Regulatory Approval should not be included within an ICER Evaluation.**

ICER should not assess a product prior to its receiving regulatory approval as necessary information and evidence is not available to be able to conduct a valid assessment. This includes but is not restricted to the following necessary information: (1) all evidence submitted in support of the regulatory approval, (2) an approved indication and target

population, (3) final label language, and (4) a market price for the product.

We appreciate the opportunity to raise these issues and offer these suggestions to ICER. We welcome the chance to explore these in more detail should you wish.

Sincerely,

A handwritten signature in black ink, appearing to read 'Mark J. Nagy', written in a cursive style.

Mark J. Nagy  
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September 12, 2016

Institute for Clinical and Economic Review

Steven D. Pearson, MD, MSc, President

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Re: ICER's National Call for Proposed Improvements to its Value Assessment Framework

Dear Dr. Pearson,

The FH Foundation welcomes to opportunity to offer input regarding ICER's value assessment framework process and scientific accuracy based on our experience with ICER's *PCSK9 Inhibitors for Treatment of High Cholesterol: Effectiveness, Value, and Value-Based Price Benchmarks* and related publications.

The Familial Hypercholesterolemia Foundation is a patient-centered, non-profit, research and advocacy organization – a collaboration of individuals with FH and medical experts from across the United States and around the world.

Our comments focus on the opportunity and the responsibility ICER has to improve the accuracy of its analyses with the input of disease-specific experts and most current data. Erroneous assumptions were made for the model analyzing PCSK9 inhibitors as well as the voting questions for the CEPAC event. These assumptions misrepresent the FH population and underestimate the risk in the patient population, for which PCSK9 inhibitors were approved. The likely uptake for PCSK9 inhibitors in the given timeframe was also overestimated, given that upwards of 90% of those living with FH have not been properly diagnosed. The result has contributed to increased barriers to care for an already highly undertreated population.

We recommend the following to ICER for improving the analyses and accurate representation of any disease that is under review:

- Proactively contact experts, including advocacy groups, clinicians and researchers. Meaningful input can help inform the scoping document and the development of the voting questions, as well as the assumptions going into the analyses and the report itself. Experts, including non-profit disease specific groups with national registries, can provide relevant data about prevalence, risk, and gaps in care that can inform the analyses.
- Allow sufficient time for outside organizations to comment, including time at the CEPAC/CTAF meetings. Include experts in the CEPAC/CTAF councils. Incorporate expert perspectives in the discussion before the CEPAC/CTAF vote.



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- Ensure that the disease is accurately reflected in published reports by including data from real world clinical understanding that informs diagnosis and treatment. Assumptions about diagnostic criteria or treatment thresholds made for an economic analysis do not always give the accurate depiction. However, most readers cannot be expected to know the difference and ICER's publications must make that difference clear.
- Use assumptions that are more in line with the likely real-world use of the drugs under review, based on some of the following:
  - FDA indication
  - Prevalence
  - Diagnosis rates
  - Current understanding of risk
  - Patient subgroups
  - Likely uptake
  - Other treatment alternatives.

When these are reflected in a scenario analysis, highlight that in the conclusions, in the voting questions, and in the press.

People affected by the diseases under review, such as Familial Hypercholesterolemia (FH), as well as the clinicians who treat them, are interested in understanding the comparative effectiveness and “value” of any given treatment or combination of treatments. We recognize the important role that ICER seeks to play in informing that understanding. The FH Foundation is deeply committed to improving the understanding of FH in order to improve diagnosis and optimize treatment for individuals with FH. We know that there are many who are unable to achieve their treatment goals on previously existing therapies and we hope that those who need new and promising treatments will have access to them. Still, the biggest barrier to treatment for FH remains the fact that 90% are undiagnosed and therefore not even optimized on first-line statin treatment.

We hope that ICER and others who play a key role in our healthcare system will work with us to highlight the opportunity to prevent heart disease. We can achieve this by ensuring that FH is diagnosed proactively and appropriately. We want to ensure that potentially affected families are screened for this inherited genetic condition and individuals have the chance to decide with their healthcare provider what the best treatment plan is for them.

Thank you for the opportunity to comment.

Sincerely,

*Cat Davis Ahmed*

Cat Davis Ahmed  
Director of Outreach



September 12, 2016

Steven D. Pearson, MD, MSc  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

Dear Mr. Pearson:

## **INTRODUCTION**

*FasterCures*, a center of the Milken Institute, is a non-profit, non-partisan action tank driven by a singular goal -- to save lives by speeding up and improving the medical research system. We appreciate the opportunity to share this input, prepared and authored by *FasterCures*, in response to ICER's National Call for Proposed Improvements to its Value Assessment Framework.

At *FasterCures*, we believe it is critical for stakeholders to develop more systematic ways of capturing and integrating patient perspectives into all aspects of medical product development and delivery. Since its inception in 2003, *FasterCures* has been working to put patients forward as partners in the biomedical research enterprise. To that end, through our [Patients Count](#) program, we are focused on expanding opportunities for patients' perspectives to shape the processes by which new therapies are discovered, developed and delivered. This includes ensuring that patient perspectives, including patients' real-world experience living with -- and undergoing treatment for -- their conditions are considered when assessing the value of a therapy and how specific patient populations will be able to access these treatments.

There has been growing concern, expressed by a variety of different stakeholders, about increased health care spending. These concerns have spurred several different initiatives and activities to explore appropriate ways to assess the value of treatment options. ICER's ongoing work to assess the value of medical treatments using its value assessment framework has been a significant part of this discussion. We believe it is important to undertake these inquiries and take a critical look at how we pay for value in our healthcare system. However when assessing value, it must be informed by criteria that matter to patients.

ICER has identified four priority areas for potential revision. Our comments are focused on addressing ICER's specific request for input regarding: "methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature...."

- We encourage ICER to create more meaningful opportunities through which patients and the organizations that represent them can submit data – both qualitative and quantitative – to be formally, and transparently, integrated into its Value Assessment Framework. Early and ongoing engagement with those directly impacted by the specific therapy or treatment under consideration will provide considerable benefit to the assessment

process. To that end, stakeholders representing patients should be involved and integrated into the discussion as soon as a specific treatment area is under consideration. Patients can provide valuable input about available treatment options and outcomes that are meaningful to them. Patients and organizations who represent them can also help ensure that the appropriate populations are identified to ensure that different perspectives are taken into account. Many of these organizations also have access to unique sources of real-world evidence in the form of patient registries, biorepositories, social networks, and mobile health initiatives that can help define key subpopulations and quantify patient preferences. Moreover, these organizations are often the most trusted intermediaries for and stewards of patients' data. Some have been involved in the development of validated patient-reported outcome measures and patient-relevant endpoints in their disease areas, as well as other efforts to capture the priorities of those most impacted by the clinical development process.

- While we commend ICER for taking a more proactive approach to engaging patients and patient organizations in recent months, we encourage ICER to look for ways it can act on the input received through that outreach and improve the quality of its engagement with patients. Meaningful engagement requires more than passively receiving input.

Last fall, we partnered with Avalere Health, to host a workshop at Partnering for Cures to discuss the existing value frameworks and identify gaps where additional work is needed. In March 2016 we published a [report](#) describing the workshop and laying out our plan to develop a value framework that incorporates patients' perspective on value. In collaboration with Avalere Health we launched the Patient-Perspective Value Framework (PPVF) initiative this summer. The framework's design will include a number of technically specified criteria, measures, and data sources that can be used to measure value from patients' perspective. A draft version of the PPVF will be shared during our 2016 [Partnering for Cures](#) meeting. We look forward to continued engagement with ICER and other value framework developers to explore whether and how the PPVF can help existing frameworks better address value from the patients' perspective.

At *FasterCures*, we believe patient-relevant outcomes drive value. To pay for value, payers and other stakeholders need to understand how care is impacting patients' functioning in the real world. Evaluating value from the perspective of the patient in this way can have substantial benefit for all stakeholders.

We appreciate your consideration of these comments and look forward to continued engagement and ongoing dialogue with ICER as it revises and improves its value framework in the coming months.

Sincerely,



Margaret Anderson  
Executive Director  
*FasterCures*, a Center of the Milken Institute



GlaxoSmithKline

**Martin D. Marciniak, Ph.D.**  
**Vice President**  
**US Health Outcomes &**  
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Date September 12, 2016

Steven D. Pearson, MD, MSc  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, 9th floor  
Boston, MA 02109  
301-435-8717

Via electronic submission: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

**Re: Recommendations for enhancing the ICER value framework**

Dear Dr. Pearson:

I am pleased to respond on behalf of GlaxoSmithKline (GSK) to your national call for suggestions on how to improve The Institute for Clinical and Economic Review (ICER) value assessment framework.

GSK is a science-led global biopharmaceutical company dedicated to improving the quality of human life by enabling people to do more, feel better and live longer. As an industry leader, GSK develops a broad range of innovative products in Pharmaceuticals, Vaccines and Consumer Healthcare. In the context of value assessment, we work with like-minded companies, value assessment organizations (VAOs), stakeholder groups and individual patients to improve the dialog around assessing the value of pharmaceuticals.

GSK envisions an environment where VAOs, with representation from a broad number of stakeholders, develop assessments that are comprehensive, transparent and trustworthy. These assessments both facilitate improved health outcomes for individual patients and work toward a sustainable health care system that ensures patient affordability, rewarding innovations and allowing free flow of scientific dialogue. Specifically, value assessments must be designed and executed to be patient-centered, transparent in process, robust in methodology and dynamic in approach, all of which contribute to quantifying a healthcare intervention's value over its entire life cycle. Further, VAOs should strive to achieve significant and meaningful representation across stakeholder groups to inform how value frameworks are built and implemented and to inform specific assessments. Trusted value assessments can benefit decisions that support high quality patient care.

Our comments are informed by GSK's years of commitment to strengthening methodological approaches that support high quality value assessments and our engagement with key stakeholders including academia, ICER, The International Society for Pharmacoeconomics and Outcomes Research, The Patient Centered Outcomes Research Institute, and payers. GSK desires to be seen as "partner of choice" by all parties intending to improve the quality of care through high quality assessment of the clinical and economic benefits of medicines and vaccines.

To realize GSK's vision and in response to your request for input, we provide recommendations for methodological advancements that are rooted in principles of health technology assessments that are published and recognized by stakeholder groups including PhRMA<sup>1</sup> and ISPOR<sup>2</sup>. We also make recommendations to strengthen the transparency of ICER's process and the public discourse around ICER's work.

**ICER Topic category 1. Methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value intended to fall in the current value framework within "additional benefits or disadvantages" and "contextual considerations"**

ICER must take a broader approach to what constitutes relevant evidence. This includes adequately representing and weighting the perspectives of patients. ICER's value assessment approach should generally align with considerations articulated in the Patient-Centered Value Model Rubric (The Rubric) recently published by the National Health Council<sup>3</sup>. The purpose of the Rubric is to provide a tool that the patient community, physicians, health systems, and payers can use to evaluate the patient centeredness of value models and to guide value model developers on the meaningful incorporation of patient engagement throughout their processes. The Rubric offers important examples of meaningful patient engagement. For example, "Processes are in place for identifying and incorporating emerging information on outcomes of importance to patients." Such outcomes can include functional status (mental/physical/societal), well-being and productivity. The example continues by describing that high engagement could be that "A clear link was described between the outcomes incorporated into the model and their importance to patients." Our comments, below, concerning "real endpoints" offer a strong example of quantifying and incorporating more patient centered-evidence to inform the estimate of value of a medical intervention.

- **Recommendation:** ICER should redouble its efforts to engage with patients, patient groups and other stakeholders to strengthen its use of "Outcomes Patients Care About" **as described in the Rubric.**

ICER's Value Assessment Framework process factors in other benefits or disadvantages of a therapy under evaluation. However, the cost-effectiveness and short-term budget impact analysis results tend to be cited most prominently in your press releases and thus in subsequent media coverage.

Often, these other benefits may be difficult to measure in a short-term experimental setting such a blinded, randomized, controlled clinical trial (RCT) and it is unclear



whether these limitations are acknowledged in your economic considerations. For example, in infectious conditions that have public health implications, patient adherence to a therapy may be a critical component to ensuring acute and enduring disease control, minimization of the risk for developing treatment resistance thereby preserving treatment options, reducing healthcare resource use and hospitalizations, and for preventing further disease transmission. Adherence in experimental settings such as RCTs is often artificially optimized and may not be generalizable to real-world settings. As a result, the benefit of newer regimens with the potential to positively impact treatment adherence and outcomes as a result of improved tolerability, administration simplicity or frequency may be underestimated. These types of data are rarely available at the time of initial therapy approval. The concern is that, under your current framework, recommendations regarding the value, or lack thereof, of a new therapeutic option may be made prematurely on the basis of incomplete short-term experimental data alone. Another example from the infectious disease perspective is the importance of maintaining therapeutic options in the face of evolving treatment resistance which results in fewer effective options.

- Recommendation: ICER's formal communications on any specific assessment, including press releases, should clearly and prominently describe the impact of other benefits or disadvantages /contextual consideration on ICER's final estimate of value.

## **ICER Topic category 2. Incremental cost-effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures**

There is an urgent need to redefine value as a composite of specific, agreed, quantifiable components that represent the interests and needs of patients, payers, providers and manufacturers. From a methodology view, a quality-adjusted life year (QALY) is only one measure of value and does not consider additional important aspects of a more holistic measure of value. ICER should incorporate "real endpoints" by co-reporting an endpoint incremental cost effectiveness ratio as a supplement to the cost per QALY assessment. Results that incorporate a cost per endpoint avoided or reduced (e.g. COPD exacerbation or myocardial infarction) provide a defined measure of expected efficacy and a value that can be directly translated in the context of a budget or medical practice. Real endpoint selection should be driven by expert stakeholder input and available data to essentially tailor an assessment to the disease state and therapy under review. These experts should be, at a minimum, a clinician or health economics modeler with deep clinical knowledge of the disease area. Their views may also be supplemented by a payer with deep clinical knowledge of the disease area. Thus the cost per real endpoint will be treatment- and disease state-specific and will vary across medical interventions. Further, these value components should quantify and weight the value of measured endpoints using standard, validated methods and must provide agreed ways to isolate and quantify these perspectives.

Recommendation: ICER should report a "real endpoint" incremental cost effectiveness ratio as a supplement to the cost per QALY assessment. Real endpoint selections should

be driven by clinicians or health economics modelers having deep clinical knowledge of the disease area.

Value encompasses the balance of benefits and costs experienced by patients and society over time. A value assessment performed at product launch will be driven by factors including the competitive environment, comparative clinical effectiveness, the particular indication and the assumed market uptake of the drug. However, the components of value evolve over the life cycle of a drug until its patent or marketing exclusivity expires. In order to better understand the use of a therapy in real life clinical practice across a heterogeneous group of patients, the consideration of Real World Evidence (RWE) is an important complement, over time, to the data that is available at product launch.

In its full holistic form, value assessments would consider long-term benefits, medical cost offsets and improvements in total cost of care with a new therapy. Indeed, The Rubric cites the potential need to update value models by putting processes in place for identifying and incorporating new knowledge and emerging information.<sup>3</sup> Completing multiple value assessments over time is essential to informing stakeholder decisions that ultimately impact patient access and longer term health outcomes. In contrast, a single assessment performed only at launch does not serve the longer term interest of the patient. Therefore ICER should perform value assessments after product launch and at intervals that are driven by important, evidence-driven changes to the value including line extensions, new indications, and important safety developments. This calls for a flexible approach to scheduling follow-up assessments but at a minimum occurring at perhaps 2, 5 and 10 years post-launch. Follow-up assessments, like initial ones, should use standard, validated methods.

- Recommendation: ICER should partner with manufacturers and other stakeholders to agree threshold criteria and processes for conducting follow-up value assessments of medical interventions.

### **Aligning ICER's communications policies with its mission**

ICER's mission is to help provide an independent source of analysis of evidence on effectiveness and value to improve the quality of care that patients receive while supporting a broader dialogue on value in which all stakeholders can participate fully<sup>4</sup>. ICER's call for stakeholder input to improve its value framework, while focused on methods, must not overlook opportunities to strengthen this broader dialog.

ICER publishes its evidence reviews with the explicit intention of triggering pricing discussions between manufacturers and payers at product launch. As detailed above, new evidence accumulated over the life cycle of the drug justifies periodic reassessment of the value of a drug product. In fact, ICER has publicly stated that "ICER is committed to looking at drugs again as our resources allow, and as new data become available..."<sup>5</sup>

We are therefore surprised that ICER has recently published in a peer reviewed journal an evidence report already made public in 2015.<sup>6</sup> This publication reinforces the assessment

results calculated at launch while diminishing the potential value of an updated assessment that would incorporate more accurate estimates of uptake, cost, durability of effect and safety plus any new indications, line extensions or other improvements that could materially benefit patients. We urge ICER to consider how their publication strategy may negatively impact subsequent value assessments of drugs. This is especially timely as ICER is now also considering how to assess gene therapies and other “cures” whose value may change significantly after launch and require repeated assessments.


- Recommendation: ICER-should share with the public their publication strategy (i.e. specific evidence reports selected, the intended journal and the expected publication timeframe) in the same spirit they publish the categories of drugs they intend to review. In the full spirit of improving the public conversation around value, ICER should also encourage the relevant manufacturers, patient advocacy groups and other stakeholders to submit letters to the editor to create a fuller public discussion of their article(s).

ICER’s evidence reports are scientific documents, written to document a blend of methods, analysis and interpretations. Although ICER’s principle audiences for these reports are payers and manufacturers, ICER has demonstrated a limited effort to disseminate their findings to the broader stakeholder audience, including patients (e.g. Proven Best Choices), consistent with their mission. However, is this effort sufficient to prevent patients and providers from making misinformed treatment decisions as a result of lay press accounts of ICER’s evidence reports? ICER’s value assessments should be translated and communicated for use by stakeholders having varying abilities to appreciate the technical content and its implications.

- Recommendation: ICER should redouble its efforts to create and disseminate versions of their economic assessments in plain, non-scientific language to enable users to understand the analysis and to think through how the assessments are likely to impact their decisions (e.g. for payer: book of business, for employer: group satisfaction, for provider: likely treatment risks, for patients: out-of-pocket costs, desired clinical endpoints and quality of life tradeoffs).

These recommendations are not exhaustive and GSK appreciates the opportunity to provide input as the ICER value framework evolves. We look forward to exploring these and other related issues in greater depth in the future with you. Please feel free to contact me should you wish to discuss these recommendations in further detail.

Sincerely,



**Martin D. Marciniak, Ph.D.**  
**Vice President**  
**US Health Outcomes & Medical Policy**

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September 12, 2016

Steven D. Pearson, MD, MSc  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

**Re: National Call for Proposed Improvements to Value Assessment Framework**

Dear Dr. Pearson:

On behalf of the Hematology/Oncology Pharmacy Association (HOPA), I would like to thank you for the opportunity to submit comments on ICER's Value Assessment Framework. HOPA is a nonprofit professional organization launched in 2004 to help hematology and oncology pharmacy practitioners and their associates provide the best possible cancer care. HOPA's membership includes not just oncology pharmacists, but also pharmacy interns, residents, technicians, researchers, and administrators specializing in hematology/oncology practice. The roles of our membership span from direct patient care, to education, to research. HOPA represents more than 2,500 members working in hundreds of hospitals, clinics, physician offices, community pharmacies, home health practices, and other healthcare settings.

Hematology/oncology pharmacists play an important role in the delivery of care for individuals living with cancer—they are involved with the care of cancer patients at all phases of their treatment; from assessment and diagnosis, to treatment decisions, medication management, symptom management and supportive care, and finally with survivorship programs at the completion of their treatment. Additionally, oncology pharmacists work closely with patients and their families to ensure access to the medications that are part of a patient's treatment plan. As part of this work, oncology pharmacists are often faced with the challenge of helping patients overcome the high cost of many cancer therapies and other medications that are needed for quality cancer care.

This Framework is an important and needed first step in considering the balance of clinical benefit and financial toxicity when making treatment decisions. HOPA supports the need for improved transparency and consistency of value determinations in order to improve patient care and control costs. We would like to offer the following recommendations to the ICER Framework:

- 1. Methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value**

**intended to fall in the current value framework within “additional benefits or disadvantages” and “contextual considerations.”**

- HOPA is involved with The Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) which is promoting the development and use of standards for biosimilar drugs that is "value" oriented. In order to ensure consistency we believe that the BBCIC should be included in the Framework.
- The Academy of Managed Care Pharmacy (AMCP) is leading an effort to promote the use of SNOMED CT codes for documenting therapy management services which adds value for patients. We recommend that this effort be acknowledged and included within the Framework.

**2. Incremental cost-effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the Quality-Adjusted Life Years (QALY) or other measures.**

- There is a need for new metrics that measure outcomes and are transparent to all stakeholders. QALY, while an acceptable pharmacoeconomic concept, may not have enough literature support in cancer care to provide an adequate assessment of cost-utility without making assumptions. Drug development should include more quality of life information so that QALYs can be adequately determined.
- An analysis of the statistical methodology used to compute the value determinations should be completed in order to address areas of concern.
- Much of the criticism surrounding the Framework involves the concept of "fail first" before a drug can be used. By developing better predictive diagnostics, and requiring companion diagnostics, personalized care can be provided that works as first line therapy.

**3. Methods to set a threshold for potential short-term budget impact that can serve as a useful “alarm bell” for policymakers to signal consideration of whether affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.**

- The cost-effectiveness threshold commonly used in pharmacoeconomics may not apply to cancer care. More research is required to determine the “acceptable” threshold for determining cost-effectiveness in the oncology population.
- Once the model is complete, an independent disease specialty advisory group (including physicians, pharmacists, nurses and other healthcare providers) should be convened to review the model before completing all of the calculations.

Cancer drugs are reaching new heights in cost, and reforms that will establish the least expensive, most effective therapy should be implemented. However, these reforms should not lead to barriers in patient access and choice. We hope that the recommendations above will



# HOPA

Hematology/Oncology Pharmacy Association

improve the Framework's utility in clinical practice, and we would welcome the opportunity to collaborate with you and other stakeholders to revise, implement, evaluate, and/or promote the Framework. We truly support the initiative by ICER to begin this important conversation to improve cancer patient care. Thank you very much for your consideration of our comments. If HOPA can be of any assistance to you, please do not hesitate to contact me or HOPA's Health Policy Associate, Jeremy Scott (202/230-5197, [jeremy.scott@dbi.com](mailto:jeremy.scott@dbi.com)).

Sincerely,

Sarah Scarpace Peters, PharmD, MPH, BCOP  
President





## APPRAISAL OF ICER'S VALUE ASSESSMENT FRAMEWORK: PROPOSAL FOR IMPROVEMENTS

The Institute for Clinical and Economic Review (ICER) announced an update to the methods used in its evidence reports on new drugs and other health care interventions in 2017 and is soliciting input on its value framework from all interested parties. This report covers aspects of the framework that could be improved and provides 12 specific recommendations, focusing on the topic of integration of patient and clinician perspectives on the value of interventions and on the topics of incremental cost-effectiveness ratios and thresholds.

The recommendations are to:

- 1. Formally and transparently involve patients and clinician stakeholders throughout the valuation process.**
- 2. Incorporate patient reported outcomes in the comparative assessment of clinical effectiveness.**
- 3. Consider benefits and disadvantages other than the clinical effectiveness and adverse effects of new treatments.**
- 4. Explicitly incorporate contextual factors into the valuation process.**
- 5. Clearly describe the methods used for achieving consensus on care value.**
- 6. Use multi-criteria decision analysis more formally to assess care value.**
- 7. Replace the general efficiency threshold with therapeutic-area specific ones.**
- 8. Derive specific thresholds by constructing efficiency frontiers in each area.**
- 9. Increase transparency by making models available to reviewers.**
- 10. Report expected budget impact but don't use it to derive acceptable price.**
- 11. Involve patients and clinicians in deliberations regarding the budget impact ("health system value").**
- 12. Provide formal methodological guidelines or citations to existing ones for every aspect.**

## INTRODUCTION

The Institute for Clinical and Economic Review (ICER) announced that it will update the methods used in its evidence reports on new drugs and other health care interventions in 2017. The organization is soliciting input on its value framework from all interested parties. In the call for feedback, ICER seeks comments on the value framework, highlighting elements that are perceived to work well and others that need to be re-examined. Where change is recommended, ICER welcomes specific proposals presenting alternative methods.

This report is written in response to this call for feedback. It focuses on two topics that ICER has labeled as high priority: (1) Incremental cost-effectiveness ratios and thresholds and (2) Integration of patient and clinician perspectives on the value of interventions, but also touches on other aspects.

The first section of the report specifies the recommendations. This is followed by a more detailed exposition of the background and rationale for these recommended improvements.

## RECOMMENDATIONS

The 12 recommendations are described in this section.

### 1. Formally and transparently involve patients and clinician stakeholders throughout the valuation process

Patient and clinician stakeholder engagement is necessary throughout the ICER valuation process, and needs to be more formally and transparently described in the valuation framework. ICER should consider reviewing the research and findings supported by PCORI in the US and active patient engagement strategies currently implemented in Australia, Canada and the UK [1, 2] for examples of effective engagement methods that meaningfully involve patients in the valuation process. PCORI has been working on the development and

evaluation of various methodologies for actively involving patients throughout the research and health policy development enterprise [3]. At the University of Leeds, UK, patients are directly involved in all elements of clinical research including the study design (including identification of outcomes and comparators groups), development of protocols, study implementation and dissemination of the findings of clinical studies [4].

In addition to the areas previously identified by ICER, engaging patients and clinicians may also be useful during: (1) Construction of the overall model; (2) Review and evaluation of evidence; (3) Determination of the quality of life inputs; (4) Estimation of care value; (5) Assessment of other aspects related to the treatment; and (6) Rating care value. The experience in Leeds [4] demonstrates that patient engagement during the research process can be effectively implemented and results in improvements in clinical studies.

To meaningfully engage patients and clinicians in the valuation framework and process, ICER needs to further develop existing methodologies and invest in developing new strategies for implementing them. This would involve explicitly involving patients and clinicians as part of the intervention valuation exercise. It would extend confidence that a comprehensive range of relevant outcomes and factors are being considered as part of the value assessment process for a new intervention.

### 2. Incorporate patient reported outcomes in the comparative assessment of clinical effectiveness

In the ICER framework, it is uncertain how and, in some cases, even whether patient-reported outcomes (PRO) are incorporated into the value assessment. PROs provide direct assessments of treatment outcomes from patients' perspectives. They also reveal both the benefits and disadvantages of treatment, helping to demonstrate the value of new interventions.

Patients should participate in identifying which outcomes are to be used to evaluate the

effectiveness of a new treatment compared with existing treatment options [4, 5, 6, 7].

Methods other than quality-adjusted life years are needed to evaluate treatments for particular diseases so that they incorporate effectiveness, adverse effects and survival. For example, the Q-TWiST (quality-adjusted time without symptoms or toxicity) approach [8, 9, 10] may be effectively applied to evaluate the overall effectiveness of treatments for cancer, where apart from progression-free survival and overall survival, there may be treatment-related toxicity of varying severity that should also be evaluated. The Q-TWiST method may not be applicable, however, to the evaluation of all disease conditions and treatments.

More comprehensive approaches to evaluating treatment effectiveness should be identified and assessed. All of the outcomes that are relevant to patients may not be included in the available evidence at the time of the valuation assessment, but understanding which ones are absent and their importance will may provide for a more complete evaluation of the targeted intervention in comparison with the alternatives. This will be most challenging for rare disorders, where there may be few or no alternative treatments, and where only limited effectiveness evidence may be available.

The clinician perspective is also important in understanding and incorporating clinical experience across multiple patient-related health states and trajectories for the target medical condition.

The involvement of patients and clinicians needs to be more formal and transparent, and methods for ensuring equal input and representation need to be put in place.

### **3. Consider benefits and disadvantages other than the clinical effectiveness and adverse effects of new treatments**

Patient and community groups should be asked about intervention-related benefits and

disadvantages that may be less directly related to the clinical effectiveness of the intervention. Issues to be considered include route of treatment administration (i.e., oral, subcutaneous injection, infusion, etc.); aspects of the treatment that may reduce or improve adherence; other treatment-administration related characteristics; and other benefits and disadvantages to the broader community (e.g., herd immunity conveyed by vaccination, other interventions aimed at reducing transmission of infection). These factors can be considered at the treatment and care level, and may be directed at the broader community level and improvement in public health.

Clearly, engagement of patients and their clinicians in understanding the advantages and disadvantages of new treatments is necessary as part of the valuation process. The methods for identifying and assessing these benefits and disadvantages must be clearly described and supported in written methodological guidelines [3].

### **4. Explicitly incorporate contextual factors into the valuation process**

The ICER process does not formally incorporate the contextual factors into the valuation process. Possible contextual factors are examined by the independent public appraisal committee, but little detail is provided on the methods used to incorporate them in the care value rating. In reports on specific topics, little information is included on the deliberations of these committees and how contextual factors were considered in the valuation process.

Contextual considerations may include legal, ethical, and other aspects that influence the priority of an illness or treatment. For example, for a particular disease, are alternative treatments available or is there an under-served need for interventions for the targeted condition? Issues related to the prevalence and severity of the illness may make the intervention a priority for the

community. Are there ethical considerations related to the intervention?

Patients, their clinicians, and perhaps the general public should be involved in discussing these more intangible issues associated with new interventions, working toward consensus on the valuation of an effective, targeted intervention.

#### 5. Clearly describe the methods used for achieving consensus on care value

Based on the ICER webinar and slides describing its methods, the elements of care value are publically discussed and then treatments are rated as low, intermediate or high value. The methods employed in arriving at these recommendations are not well articulated. While it may not be possible to provide exact details, the approach for achieving consensus on care value, taking into consideration existing clinical evidence on effectiveness and adverse effects, other factors, and contextual issues need to be described fully. These methods must ensure that patient and clinician stakeholders are well represented and are formally involved in this process of review, evaluation, and discussion, leading to the eventual consensus on level of care value.

Methods for ensuring equal input and representation of patients and clinicians in the evaluation of care value exist and can be applied in a more formalized and transparent process [11,12,13]. For example, many organizations developing clinical guidelines now follow explicit formal methods [14, 15, 16].

#### 6. Use multi-criteria decision analysis more formally to assess care value

ICER evaluates the care value of products using four types of criteria: the strength of the evidence, the efficiency, the existence of other benefits and “contextual” factors such as ethical or legal aspects [see The ICER Process on page 8]. Each product is rated in each category and this information is presented to an appraisal committee for discussion and voting on the overall rating (low, intermediate

or high value). This process constitutes an informal multi-criteria decision analysis (MCDA) [17].

Following a more formal MCDA process would offer some benefits, chief among them the increased rigor involved. In addition, the emerging guidelines for good practices can be leveraged to further substantiate the recommendations that are made. A formal process will help members of the appraisal committee understand each other’s position, assist in resolving discrepancies, and, in any case, it will increase transparency and facilitate reporting.

The first step in a formal MCDA is to delineate the criteria to be used. ICER already specifies these in broad categories which can be made more specific for particular therapeutic areas. This approach should be maintained: general criteria “buckets”, with more detailed specification of what is in each bucket for each assessment.

Although there is some controversy about this, efficiency (i.e., “cost-effectiveness” or “long-term value”) should be removed as a criterion because it is used later in the derivation of the value-based price. There is no need—indeed it is counterproductive methodologically—to include it twice. In its stead, it would be beneficial to add a category having to do with unmet need. It has been shown that the degree of unmet need in a therapeutic area is an important consideration for most people [18]: adding say, yet another antihypertensive agent, even at a very reasonable price, does not have as much value as providing a first treatment in a heretofore orphan disease.

In a formal MCDA, the importance of each criterion relative to the others is established and used to aggregate the ratings into an overall rating. The current ICER approach does not use formal weighting. Instead, the efficiency aspect is given most importance while the other criteria act as modifiers [see The ICER Process on page 8 and Figure 1]. A formal weighting of the criteria will take some effort and will open the door to disagreements about the appropriate values, but it

provides greater transparency and consistency across assessments, at least within a therapeutic area.

As there is no formal weighting or aggregation of ratings in the current ICER process and the overall assessment is obtained by voting, there is no need to consider whether the same benefits obtained on different portions of a scale are valued equivalently. For example, is an improvement of 10 points in a symptom score when the symptom is severe of equal value to a 10 point improvement when the symptom is only moderate to begin with. This aspect can be considered by incorporating non-linear value functions. As with weighting of criteria, the development of formal value functions can require significant effort and provide additional fodder for controversy but it may enable more realistic valuations, and increase transparency of the process.

If a formal MCDA is carried out, then a summary score will be produced as an end result. This score will reflect the value of the product in comparison with other products available in the therapeutic area. This, the score can form the basis for the benefit axis on the efficiency frontier, allowing direct computation of the costs per unit of benefit at different points on the scale. The absolute score can be converted to a proportionate one by dividing the value obtained by the maximum possible score. This yields a percentage of maximum, ranging naturally from 0 to 100%, in a more meaningful and relevant manner than the QALY-based scoring.

## 7. Replace the general efficiency threshold with therapeutic-area specific ones

ICER uses an efficiency (“cost-effectiveness”) threshold to derive a possible “value-based” price [see The ICER Process on page 8]. A single threshold (in the range of USD \$100,000-\$150,000) is used for all products across therapeutic areas [see Use of Threshold “Cost-effectiveness” Ratios on page 10]. No rationale is given for this methodological choice but neither the US context

nor the purpose of ICER assessments support, much less require, a single threshold [see Rationale for Setting a Single System-wide Threshold on page 11].

Using a single threshold is problematic. It imposes the idea that all products must abide by the same efficiency requirement, regardless of the severity of the illness, the unmet need or ICER’s own rating of value. It has been repeatedly shown that most citizens do not agree with this [19]. Moreover, a single threshold is impossible to support empirically—the UK researchers who spent an enormous amount of time and money trying to establish an empirical basis found, instead, an enormous range of actual efficiencies in the health care system [20] and resorted to recommending an unsupported mean [see Basis for the Single Threshold on page 11].

Instead of a general efficiency threshold, ICER should switch to therapeutic area-specific thresholds. This would accord much better with reality, where efficiency differs substantially across therapeutic areas. In the UK, for example, the cost-effectiveness ratios obtained in the study [21] were well below £10,000 per QALY in some areas like circulatory and respiratory diseases, but far above £100,000 per QALY in others. It is not sensible to allow efficiency to deteriorate in some areas by setting an average threshold, while at the same time making entry of new products nearly impossible in areas that struggle to be efficient.

By using therapeutic-area specific thresholds, the assessments can also take into account differences in the difficulty of developing new products in a given area and allow for public preferences such as providing treatments in rare diseases that are otherwise underserved. It should be noted that in other areas of the economy, efficiency thresholds are specific. The EPA and NHTSA, for example, do not mandate that all vehicles, regardless of their purpose, meet the same efficiency standards—as one would expect, there are separate efficiency thresholds for passenger cars, light trucks, medium



and heavy duty vehicles, and so on [22]. Most people would consider it illogical to take the average of the existing efficiency across all vehicle types and set that as the threshold for everyone, regardless of purpose.

A major benefit of supplanting the single threshold is that it permits the efficiency standards to be evidence-based and, thus, addresses a major weakness in ICER's approach [see Basis for the Single Threshold on page 11]. Countries with a long experience in trying to stick to a single threshold have found it increasingly difficult to defend the use of an arbitrary value. Stakeholders quite rightly demand to know why that particular value is appropriate and alluding to others' use of a similar arbitrary value does little to alleviate the outrage.

#### 8. Derive specific thresholds by constructing efficiency frontiers in each area

Deriving an efficiency threshold is difficult in the absence of a legitimate market because it requires establishing what is reasonable to pay for a given benefit and there is no good way to do that. An approach that circumvents this conundrum is to rely on the actual market: what are we paying for benefits in a given area? This value provides the area-specific threshold assuming that one should be reluctant to accept a product with lower efficiency.

These area-specific thresholds can be easily obtained by deriving the efficiency frontier in each area [23]. The frontier reflects the best extant efficiency at particular levels of benefit. Typically, the efficiency declines as the benefit nears its maximum possible value. Interpretation and use of the efficiency frontier is facilitated by a graphical display where each product is plotted according to its benefit and costs (Figure 1). This graph readily demonstrates the existing efficiency in the actual market in that area and provides an evidence-based threshold (the slope of the last segment) for new entrants. A value-based price for a new product can be derived easily based on that threshold.

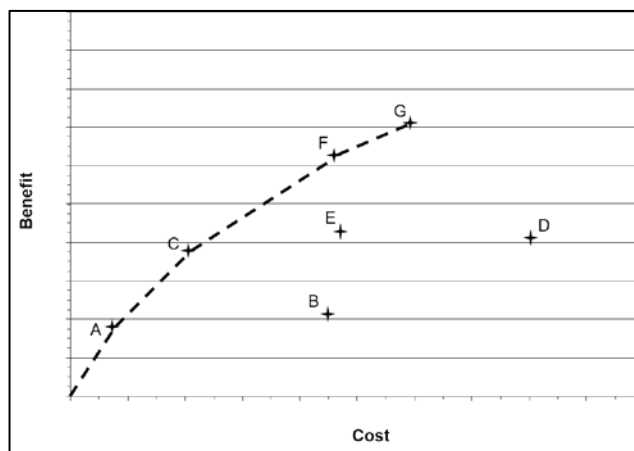
Arguments can still be made for accepting a price

that implies lower efficiency (e.g., a massive increase in benefit not otherwise available) but on a foundation for the discussion that is explicit, transparent and driven by evidence.

The efficiency frontier approach provides additional gains. One is that it reveals which products are inefficient (i.e., to the right and below the frontier) and can provide a basis for discussions with their manufacturers regarding efficient prices, which in turn might yield savings that can help fund newer entrants that provide greater benefits.

The frontier approach also enables an ongoing assessment of products. New entrants may redefine the frontier by selecting a price that increases efficiency. As data accumulate on new (and existing) products, the frontier can be revisited. Perhaps effectiveness turns out to be different than was expected or a new side-effect emerges. These circumstances can be addressed by modifying the plot accordingly and refreshing the conclusions in line with the evolving implications.

**Figure 1. Graphical representation of the efficiency frontier for a therapeutic area with 7 options on the market.**

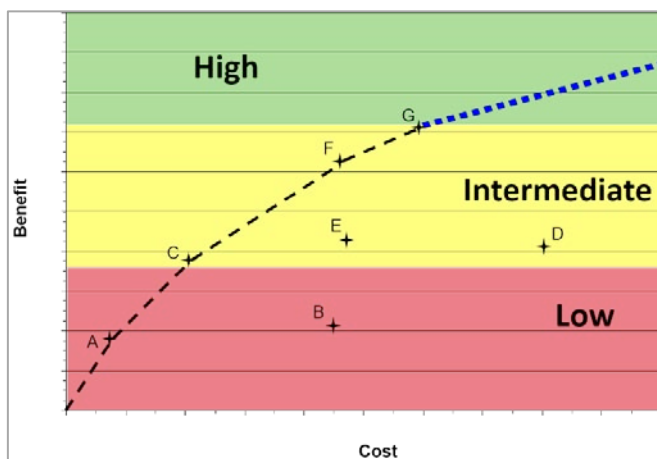


*The products on the frontier (A, C, F, G) provide the best efficiency at their respective benefit levels while B, D and E are priced too high as they are to the right and below the frontier.*

Another advantage is that the measure of benefit can be tailored to the therapeutic area, increasing its relevance and allowing it to accord best with patient preferences. Although the QALY can be used as the

measure, it doesn't have to be, and this opens up the assessment to fully consider care value without requiring dubious extrapolations of short-term clinical trial results to the full lifetime of patients. For example, if the goal is to use an anticoagulant to reduce the risk of stroke in atrial fibrillation, the focus can be on the balance of strokes and serious bleeds without having to extrapolate their consequences long-term. This will also help simplify the required economic models.

**Figure 2. Superimposition of Care Value Bands on the Efficiency Frontier Plot**



*Products in the Low and intermediate bands would need to meet the existing efficiency in those zones (higher standard to meet for lower value products) while a product rated as providing a high value might be allowed the somewhat lower efficiency threshold given by the blue extrapolation.*

Finally, use of the efficiency frontier would allow ICER to take into account its rating of care value, something which is currently left dangling [see The ICER Process on page 8]. The benefit axis could be cut into three (or more) segments to reflect the value ratings. Products that are rated as providing low value would have to achieve the higher efficiencies that are typical on the initial part of the frontier curve. Products rated as yielding intermediate value would have to meet the efficiency in the upper part of the frontier; while products rated at high value might be allowed to “curve” the frontier further and come in at a somewhat lower efficiency. This would eliminate the disconnect between the care value rating and the

use of cost-effectiveness to derive one of the value-based benchmark prices.

## 9. Increase transparency by making models available to reviewers

Although ICER has formally expressed a commitment to transparency, the economic models that underlie much of the work are not open and available for review. This is unacceptable and contrary to the guidelines on good modeling practices [24]. In line with those guidelines, any intellectual property rights claimed by the developers of the models can be protected via appropriate non-disclosure agreements that must be signed before access is provided. Failure to do this will render all of the estimates suspect and raise questions about the commitment to transparency.

## 10. Report expected budget impact but don't use it to derive acceptable price

Affordability of new products is an important consideration but at present, ICER addresses this by deriving a maximum budget impact in an arbitrary manner, using various unsupported assumptions, and applying it to every product regardless of its rated value or any other consideration. This crude approach does not support credible budget impact deliberations and should be abandoned.

There is no basis for constraining every product to the same amount. A major breakthrough should not be held to the same standard as a product that provides little advantage. There needs to be flexibility in the amount of budget allowed to be consumed by a new product. Moreover, an overall budget impact threshold is an unsound idea in the context of a health care system like the American one, which does not have anything like a global budget. Budget impact is a difficult aspect to assess in an overall manner without a specific payer in mind. Each budget holder must be able to address in its own context the strain a new product may apply.

The impact of a new product on a payer's budget is difficult to forecast because it depends on the

frequency with which candidates for treatment appear in that jurisdiction, and the rate at which they are prescribed the new product; neither quantity being readily estimated, particularly for the entire health care system. Instead of deriving an “alert” price, the ICER evaluation should facilitate the budget holder’s deliberations by providing a tool for estimating the impact to their budget under assumptions that make sense for them, including coverage modalities and other aspects that affect the budget impact. This is in line with the most recent recommendations of the task force on good practices for budget impact analysis [25].

In addition to the budget impact calculation tool, ICER can carry out some illustrative analyses that provide a range for the budget impact under a variety of plausible assumptions about uptake. These assumptions need to be more sophisticated than linear and need to consider various distributions for existing products and patterns of displacement.

#### 11. Involve patients and clinicians in deliberations regarding the budget impact (“health system value”)

Patients and clinicians should be directly involved in determining the health system value of new treatments and interventions. Methods are available for involving patients and other stakeholders in the design and implementation of clinical studies [4, 6, 7]. These methods are directly generalizable to engaging patients (and others) in determining value to the health care system. While this may be challenging, meaningful engagement of patients and clinicians in the process of valuing these new interventions ensures that assessments are transparent and that they consider comprehensively the range of interested stakeholders and perspectives. This involvement also ensures that all relevant and important outcomes are at least considered in the valuation process.

#### 12. Provide formal methodological guidelines or citations to existing ones for every aspect

The work that ICER does is exposed by its very nature to review and critique by many different stakeholders. In this context, it is extremely important that every step of the process be conducted following solid methodological guidelines. For many aspects, guidelines that have been developed and vetted by experts already exist and can be cited. Where there are gaps in the guidelines, or in places where ICER wishes to introduce its own approach, this needs to be carefully documented. As some of the work is performed on behalf of ICER by other institutions, they should also be held to strict standards. At the very minimum, they should be required to provide detailed technical documentation of what they do, and this information should be provided to all stakeholders upon request.

## BACKGROUND AND RATIONALE

### THE ICER PROCESS

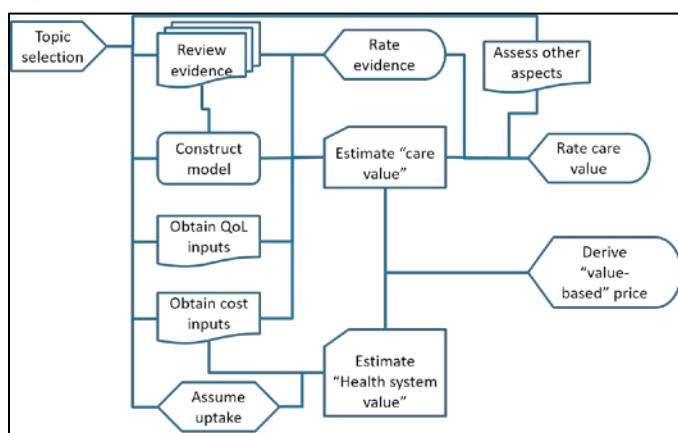
ICER assesses health care interventions with a view to providing stakeholders what it calls “value-based price benchmarks” [26]. The suggested price for an intervention is derived via a combined assessment of the longer-term “care value” and the shorter-term “health-system value”—whichever results in a lower price dictates the recommendation. The only description of the process (Figure 3) is provided in a webinar [27] and accompanying set of slides—there appears to be no formal written guide to the methods used.

The longer-term care value is driven by an analysis of the efficiency with which an intervention yields health benefits, measured in quality-adjusted life years (QALYs). This efficiency is characterized using incremental cost-effectiveness ratios which produce an estimate of the additional cost required to yield one QALY. The efficiency estimated at the intervention’s actual price also enters into a summary judgement of the care value, which is



arrived at via a discussion and vote by an appraisal committee. One of three levels of value—high, intermediate, low—is assigned, presumably by simple majority. Although the judgement is largely driven by the estimate of efficiency, other aspects may be considered in the voting (Figure 1). These pertain to the strength of the clinical evidence, to the existence of other effects not considered in the efficiency calculation and to additional aspects such as ethical or social issues that are particularly relevant in the therapeutic area.

Figure 3. Schematic of the ICER Process



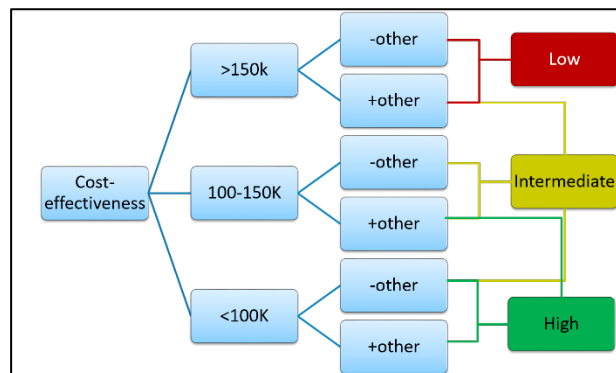
*Process culminates in two ratings (of the evidence of clinical value and of the care value) and a derivation of a “value-based” price driven by the lower of either the longer-term cost-effective (“care value”) price or the shorter-term affordable price (“health system value”)*

The analysis of efficiency is based on an economic model of the intervention and its effects. It appears that, when possible, the analyses use existing models but, if needed, a new model is commissioned from an academic institution. It appears that the methods to be used in the modeling are left up to the institution building it and, despite a written commitment to transparency [28], the models are not made available for review.

The sources of inputs to the economic models vary according to the topic of the assessment. Although there does not seem to be a formal written guide, it appears that systematic reviews are sought, or carried out when none exist, to assess the clinical

evidence. Although clinical trials are preferred, data obtained via other means can be considered, as is information available only in the “grey” literature [29]. The strength of the clinical evidence is rated using a process guided by a formal written method [30].

Figure 4 Use of Cost-effectiveness Ratio and Other Considerations to Rate “Care Value”



The model used to provide an input to the longer-term care value rating is also employed in deriving the prices required to meet pre-specified levels of efficiency. The two main efficiency levels targeted are USD \$100,000 per QALY and \$150,000 per QALY; but often other levels, such as \$50,000 per QALY are also pursued. There does not appear to be any attention given to the datum of the targets’ currency.

Another “value-based” price is computed by supposing a maximum amount that ought to be spent on a new product. This limit is derived by assigning a portion of the estimated growth in gross domestic product (GDP) inflated by one percentage point. The augmented GDP growth is applied to the total health care spend due to drugs (separately calculated for devices). This yields a presumption of the permissible budget impact of new products, which is then doubled (no basis given) and allocated equally to the postulated number of such new products approved in the year (based on previous years). The allocation is used to derive the desired ceiling price for a product by imagining various linear rates of uptake. The lower of this ceiling price

or the efficiency-based one is used in the appraisal to arrive at a recommended price.

### **POSITIVE ASPECTS**

- The call for suggestions itself
- The ICER rating of care value considers aspects other than purely monetary
- Commitment to transparency

### **ASPECTS THAT CAN IMPROVE**

- All new products are treated the same, regardless of their features, the degree of unmet need they address, the therapeutic area involved, or any other aspects.
- After deliberating on and rating the care value, the rating appears to have no impact on the recommended price. A product rated highly is treated no different than one rated low. In other words, no real value is accorded to the care value—only efficiency and budget impact are considered in the price recommendation.
- Reviewers cannot assess the model at the core of the estimates. Intellectual property protection is not a valid reason. The Modeling Good Practices Task Force recommendations explicitly deal with this.
- No methodological guidelines for much of the process
- Use of arbitrary thresholds and key inputs (e.g., uptake)
- Despite stating that “patient groups inform what outcomes are important”, the endpoints actually considered are those studied in pivotal clinical trials.

## **USE OF THRESHOLD “COST-EFFECTIVENESS” RATIOS**

The threshold ratio represents the minimum efficiency that a product needs to meet in order to

be acceptable for reimbursement. In our field the reciprocal of efficiency is used, so the threshold is treated as a maximum level: a product’s ratio must be below the threshold to be tolerable.

There are two types of threshold, depending on what motivates the value chosen. One type [31], driven by a commitment to utilitarianism, is based on the idea of opportunity cost: the benefit obtained by spending resources on a new product should not be inferior to that foregone when those resources are no longer spent on something else. Since it is impossible to determine what is foregone—at least at the system-wide level—it is presumed that that “something else” is the least efficient use of resources extant at the time the new product begins consuming resources [32]. In principle, this ensures that efficiency is not diminished by a new entrant, but it does not help the system abide by a budget [33]. The other major type of threshold is based on the amount that someone is prepared to pay for a particular benefit [34]. This type of threshold also fails to adhere to a budget and, further, does not ensure the system retains efficiency. Moreover, it raises thorny questions about who the “someone” is supposed to be, and whether the limit is about what one should be willing to pay or what one is actually prepared to spend [35].

The ICER process uses a threshold range of USD \$100,000-150,000 without clarifying whether this is meant to be an opportunity cost or a willingness-to-pay threshold, or something else.

### **How is the Ratio Used?**

An efficiency threshold can be used in several ways. By analogy with vehicular efficiency standards [36], it could be set as an official limit that new products must meet to be allowed on the market or be subject to fines or other penalties. This is how it is used in various countries [37]. Another approach is to use the threshold as the basis for deriving a maximum reimbursable price. Since price is the most easily varied determinant of efficiency, it is natural to work backwards to the

price that yields the threshold efficiency. This is how ICER employs the threshold.

### **Rationale for Setting a Single System-wide Threshold**

ICER chooses to apply a common threshold across all products evaluated. No rationale is provided for this decision.

In jurisdictions where a single threshold is used, the formal rationale typically has to do with the opportunity cost idea. Since the benefits to be obtained cannot be directly compared with those to be foregone because the latter are unknown, the threshold serves as the intermediate means of assessing the trade-off. It is presumed that the displacement may occur in therapeutic areas different from that of the new product and, therefore, that a single threshold applicable across the system is required. This is not universally accepted. In the transportation system, for example, it is recognized that efficiency standards necessarily differ by the type of vehicle [38]. By the same token, in some countries such as Germany and France, it is understood that insisting on the same efficiency across therapeutic areas is neither required nor sensible, and the thresholds, to the extent they exist, are specific to a therapeutic area.

In places following the willingness-to-pay approach, the rationale for a single threshold is less clear. It appears to be based on a sense that all products should be treated equally, without a clear reason for why this should be so. In all other areas of the economy, it is well accepted that willingness to pay varies according to the type of benefit at issue, the context of the decision, what is affected, and many other considerations. In the military, for example, there is no requirement that all purchases—be they fighter jets, tanks, guns, uniforms or other—adhere to a general willingness to pay for some common unit of military benefit.

### **Basis for the Single Threshold**

In establishing its threshold, ICER alludes to the levels used in other jurisdictions, but provides no basis for its choice, which does not correspond exactly to any of the

cited ones. This is not surprising since the other jurisdictions provide very little basis either. The suggestion of the World Health Organization (WHO) that societies ought to be willing to spend three times the per capita GDP on a health benefit unit [39], but no less than one GDP is one of the sources cited. The WHO based their recommendation [40] on the supposition made in a report arguing for greater investment in health in poor countries—values entirely based on conjecture that were not even pertinent to this topic [41].

The other levels alluded to are even more nebulous and, in at least one case, incorrect. The UK is said to use one per capita GDP for its threshold but that is not the case. The current threshold is arbitrary but there is a push to change it to the value estimated in a study carried out to try to provide an empirical basis for the limit [42]. That study attempted to assess the actual efficiency across 23 budget categories (roughly corresponding to broad ICD-10 therapeutic classes). They found, not unexpectedly, an enormous variation in efficiency and, contrary to all theory, opted not for the lowest but for the mean efficiency as the suggested threshold.

### ***POSITIVE ASPECTS***

- None

### ***ASPECTS THAT CAN IMPROVE***

- Clarity as to whether the threshold is meant to reflect opportunity cost or WTP
- Rationale for using a single threshold in the American context
- Greater rigor in citing other jurisdictions
- Providing a formal basis for setting the threshold

## **USE OF THE QALY AS THE MEASURE OF BENEFIT**

The quality-adjusted life year (QALY) is a construct proposed as an index of health status that incorporates two dimensions: duration and quality of life [43]. The idea was that a universal measure

of health status was needed so that comparisons could be made across therapeutic areas. By making three highly restrictive assumptions (all subsequently shown to not hold [44]), the QALY can serve as this measure.

### **Rationale for the QALY**

The main rationale for using the QALY is tied to the determination to restrict all appraisals to a single threshold: a common measure is needed if this is to be the case. Moreover, under the three restrictive assumptions, this index maps linearly to “utility” (a highly technical type of valuation). This, in turn, allows use of the QALY as a “currency” of value with the highly desirable property that a given change in QALYs has the same value anywhere along the scale. Any incremental ratio using the QALY as a measure of health benefit can be compared directly with the threshold, regardless of the therapeutic area in question or what the background quality of life or life expectancy might be.

ICER uses the QALY as the measure of health benefit but provides no rationale for this choice beyond labeling it the “standard”.

### **Essential Assumptions**

As the original proponents stated, “the use of quality-adjusted life expectancy as a decision criterion can only be justified if three main assumptions hold”; and then emphasized “quality-adjusted life years is valid... *if and only if* [emphasis theirs] ... (the assumptions)... all hold” [43]. It has been repeatedly shown that these assumptions don’t hold in reality and it is easy for anyone to ascertain this by simply asking their peers.

One assumption requires that people have a neutral attitude to risk. In other words, they have to consider an alternative that promises five more years of life to be of equivalent value to one that promises a 50% chance of 10 years but a 50% chance of immediate death. Few people are neutral

to this kind of gamble. In addition, people have to equate one year of life at full quality with two years at half quality. Most people do not adhere to this constant proportional trade-off. The third key assumption is that the value of a gain does not depend on the underlying quality of life. This utility independence is more difficult to test but has not held in the extensive work done to value EQ5D states [45].

The validity of using a measure that requires these assumptions is not addressed by ICER. One possibility would be that although people do not adhere them, societal decisions ought to do so, for some reason. This prescriptive approach is not adduced by ICER, however.

### **Estimation**

To estimate the QALY gains that a product yields, the analyst needs to forecast the health gains (ideally over a long enough time that they are fully counted) and apply to these benefits an appropriate quality adjustment. ICER appears to leave the methods for doing this entirely up to the analysts involved and no guidelines or rationale are provided. The health gains appear to be typically estimated by reviewing relevant literature and carrying out some sort of meta-analysis but there is no reference to any standards that are followed. The quality weighting is even less well documented and appears usually to be drawn from other publications.

#### ***POSITIVE ASPECTS***

- None

#### ***ASPECTS THAT CAN IMPROVE***

- Rationale for using the QALY as the measure of health benefit
- Methodological guidelines for estimating QALYs

## INTEGRATION OF PATIENT AND CLINICIAN PERSPECTIVES ON THE VALUE OF INTERVENTIONS

Based on the limited detailed information available on the methods used by ICER to assign value to health care interventions, it is difficult to completely understand where and how patients impacted by the targeted medical disorder, their clinicians and the general public participate in the value assessment exercise. Clearly, the more recent emphasis on patient engagement in research, policy discussions, and medical decision-making makes the participation of patients and their clinicians essential to the valuation framework [1,46,47,48,49]. Based on the available information, there are several identified stages in the ICER value assessment where patients, clinicians and the public may have inputs, including (1) comparative clinical effectiveness; (2) understanding other factors, benefits or disadvantages; (3) contextual considerations; (4) examination of care value; and (5) evaluation of health system value (ICER, July 2016). Based on documents presented and distributed by ICER, terminology, full definitions and explication of the meaning of “care value” and “provisional health care value” may require further development (ICER, July 2016).

Patient and clinician stakeholder engagement is necessary throughout the ICER valuation process, and needs to be more formally and transparently explicated in the ICER valuation framework. ICER may want to consider reviewing the research and findings supported by PCORI in the US [1, 2] and active patient engagement strategies currently implemented in Australia, Canada and the UK [50] for examples of engagement methods that may be effective in the meaningful involvement of patients in the valuation process. For example, PCORI has been actively involved in the development and evaluation of various methodologies for actively involving patients throughout the research and health policy development enterprise (see

www.pcori.org). In addition to the areas previously identified by ICER for patient and clinician involvement, engagement in the following ICER process steps may be advisable: (1) Construction of the overall model; (2) Review and evaluation of evidence; (3) Quality of life inputs; (4) Estimation of care value; (5) Assessment of other aspects related to the treatment; and (6) Rating care value (see Figure 3).

ICER may need to further develop methodologies for meaningfully engaging patients and clinicians in the valuation framework and process. Basically, this would represent a specific application of patient and clinician engagement as part of the intervention valuation exercise, and would extend confidence that a comprehensive range of relevant outcomes and factors were considered as part of the value assessment process for a new treatment or intervention. The patient and clinician engagement and perspective may provide qualitative context to formal methods of value assessment.

### COMPARATIVE CLINICAL EFFECTIVENESS

Clinical trials comparing interventions provide the evidence supporting the clinical effectiveness and adverse effects of new treatments. As part of these clinical trials, various types of patient-reported outcomes (PROs; i.e., disease-related symptoms, health-related quality of life, functioning and well-being, treatment satisfaction, etc.) may be included to evaluate the new treatments from the patient’s perspective. In the ICER framework, it is uncertain how and in some cases whether these outcome data will be incorporated into the value assessment for new health interventions. PROs provide direct assessments of the outcomes of treatment from the perspective of patients and evaluate both the benefits and disadvantages of treatment.

There are challenges related to incorporating these outcomes into the value assessment process, since there may be few comparative studies including PRO endpoints, incorporation of different generic and disease-specific health-related quality of life instruments in clinical trials, and various statistical



method issues (i.e., missing data, different statistical analysis models, etc.). The PROs provide a valuable and useful component to understanding the value of new treatments.

Patients and clinicians should be involved in identifying the relevant and important outcomes associated with the evaluation of the effectiveness of a new treatment compared with existing treatment options in the health care system. The clinician perspective is important in understanding and incorporating clinical experience across multiple patient-related health states and trajectories for the target medical condition. Identified outcomes relate to patient-reported and clinician-reported, as well as, other relevant clinical outcomes. Methods, other than quality-adjusted life years may be needed to evaluate treatments for specific diseases that incorporate the effectiveness, adverse effects and survival. For example, the Q-TWiST (quality-adjusted time without symptoms or toxicity) approach [51,52,53] may be effectively applied for the evaluation of effectiveness of oncology treatments, where there may be varying severity of treatment-related toxicity, progression-free survival and overall survival that may need to be evaluated. However, Q-TWiST methods may not be applicable in the evaluation of all disease conditions and treatments.

More comprehensive approaches to evaluating treatment effectiveness should be identified and assessed, if possible. We recognize that not all relevant outcomes may be included in the available evidence at the time of the valuation assessment, but understanding what important outcomes are absent may assist in the more complete evaluation of the targeted treatment compared with other treatment for the target medical condition. This may be most challenging for rare disorders, where alternative treatments may be unavailable and where only limited effectiveness evidence may be available.

The involvement of patients and clinicians need to be more formalized and transparent, and methods

for ensuring equal input and representation needs to be ensured. Methods are currently available, and advances are being made, for active patient engagement.

### **POSITIVE ASPECTS**

- None

### **ASPECTS THAT CAN IMPROVE**

- Clarity on how PRO data will be incorporated into the value assessment for new health interventions.
- Patients and clinicians involvement in identifying the relevant and important PRO related domains.
- Comprehensive approaches to evaluating treatment effectiveness, by understanding what important outcomes are present and absent.
- Formalized and transparent involvement of patients and clinicians, including incorporation of currently available methods for ensuring equal input and representation.

## **UNDERSTANDING OTHER FACTORS, BENEFITS AND DISADVANTAGES**

Factors, other than the clinical effectiveness and adverse effects of new treatments, need to be considered when valuing the broader outcomes of new treatments. Patient and community groups can be asked about intervention-related benefits and disadvantages that may be considered that may be less directly related to the clinical effectiveness of the intervention. Issues to be considered include route of treatment administration (i.e., oral, subcutaneous injection, infusion, etc.), aspects of the treatment that may impact adherence, and other treatment-administration related characteristics, and other broader benefits and disadvantages to the community (e.g., reduced transmission of infection, etc.). These factors can be considered at the treatment and care level, and may be directed at the broader community level and public health.

Clearly, engagement of patients and their clinicians in understanding the advantages and disadvantages of new treatments as part of the valuation process is necessary. Further explication of the methods for accomplishing the identification and assessment of these treatment-related benefits and disadvantages are needed.

#### **POSITIVE ASPECTS**

- None

#### **ASPECTS THAT CAN IMPROVE**

- Factors, other than the clinical effectiveness and adverse effects of new treatments should be considered when valuing the broader outcomes of new treatments, such as route of treatment administration, aspects of the treatment that may impact adherence, other treatment-administration related characteristics, and other broader benefits and disadvantages to the community (e.g., reduced transmission of infection, etc.).
- Patients and clinicians engagement in understanding the advantages and disadvantages of new treatments as part of the valuation process.

### **CONTEXTUAL CONSIDERATIONS**

Contextual considerations may be legal, ethical, and other issues that influence the priority of an illness or treatment. For example, for any given disease, are there alternative treatments available or is there an under-served need for interventions for the targeted condition? Issues related to the prevalence and severity of the illness may impact a priority for the intervention in the community or health care system. Are there ethical considerations related to the intervention? Patients, their clinicians and perhaps the general public should be involved in discussing these more intangible issues associated with new interventions, and to come to some consensus on the potential valuation of an effective, targeted intervention.

Currently, the ICER approach does not formally incorporate considerations of contextual factors into the valuation process. Contextual considerations are examined through the independent public appraisal committees, but little detail is provided as to the methods and outputs of these committees and how contextual factors are incorporated into the treatment valuation process.

#### **POSITIVE ASPECTS**

- Some level of considerations of contextual factors examined through the independent public appraisal committees.

#### **ASPECTS THAT CAN IMPROVE**

- Involvement of patients, their clinicians and perhaps the general public in discussing these more intangible issues associated with new interventions, and to come to some consensus on the potential valuation of an effective, targeted intervention.
- Clarity on methods and outputs of the independent public appraisal committees involved in examining the contextual considerations and how these are incorporated into the treatment valuation process.

### **EXAMINATION OF CARE VALUE**

Based on the ICER documents, care value is publically discussed and then treatments are assigned a “care value” of low, intermediate or high, but the exact methods for making these recommendations are not very well articulated. While it may not be possible to provide exact details, the methods for achieving consensus on “care value” by taking into consideration existing clinical evidence on effectiveness and adverse effects, other factors, and contextual issues need to be further described. These methods must ensure that patient and clinician stakeholders are well represented and are formally involved in this process of review, evaluation, and discussion, with the eventual consensus on level of “care value”.

The involvement of patients and clinicians in the evaluation of “care value” needs to be more formalized and transparent, and methods for ensuring equal input and representation needs to be ensured. Methods are currently available, and advances are being made, for active patient engagement (see [www.pcori.org](http://www.pcori.org)). Furthermore, the methods for evaluating and developing clinical and treatment guidelines for different diseases may be potentially generalizable to examining “care value”.

#### **POSITIVE ASPECTS**

- Broad discussion on care value among concerned stakeholders.

#### **ASPECTS THAT CAN IMPROVE**

- Clear description on implemented methods for achieving consensus on “care value”.
- Involvement of patients and clinicians in the evaluation of “care value” in more formalized and transparent manner.

### **EVALUATION OF HEALTH SYSTEM VALUE**

Patients and clinicians should be involved in deliberations regarding the health system value of new treatments and interventions. While this may be challenging, meaningful engagement of patients and clinicians in the process of valuing these new interventions ensures that assessments are transparent and that they consider comprehensively the range of interested stakeholders and perspectives. This involvement also ensures that all relevant and important outcomes are at least considered in the valuation process.

#### **POSITIVE ASPECTS**

- None

#### **ASPECTS THAT CAN IMPROVE**

- Need for patients and clinicians involvement in deliberations regarding the health system value of new treatments and interventions.

### **ABOUT THE AUTHORS AND THE INSTITUTE FOR PATIENT ACCESS**

*The Institute for Patient Access is a physician-led nonprofit 501(c)(3) research organization promoting the benefits of the physician-patient relationship in the provision of quality healthcare. To learn more visit [www.AllianceforPatientAccess.org](http://www.AllianceforPatientAccess.org).*

*This report was prepared with the assistance of researchers from Evidera, Inc. (Sandra Milev, MSc; Dennis Revicki, PhD; and J. Jaime Caro MDCM, FRCPC, FACP).*



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September 12, 2016

***Submitted electronically to:*** [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

Steven D. Pearson, MD, MSc  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

***Re: Feedback on ICER's Value Framework***

Dear Dr. Pearson:

On behalf of the Institute for Patient Access, I thank you for the opportunity to provide feedback on the Institute for Clinical and Economic Review's value framework.

The Institute for Patient Access (IfPA) is a physician-led policy research organization dedicated to maintaining the primacy of the physician-patient relationship in the provision of quality healthcare. To further that mission, IfPA produces educational materials and programming designed to promote informed discussion about patient access to approved therapies and appropriate clinical care. IfPA was established in 2012 by the leadership of the Alliance for Patient Access, a national network of nearly 800 physician advocates committed to patient access. IfPA is a 501(c)(3) public charity non-profit organization.

Matters of patient access are increasingly influenced by third-party evaluations of what medications, diagnostics and devices are worth for patients and the overall health care system. Far from an end unto itself, a calculation such as ICER's value-based price benchmark goes on to inform crucial health plan features such as formulary design, cost-sharing ratios and the use of utilization management tools such as prior authorization and step therapy. These factors often determine whether a patient can access the treatment prescribed by his or her physician, and whether a physician can direct patient care as needed.

In light of the ICER value framework's impact on health care, patients and physicians across the United States, we offer the following 12 suggestions for the updated framework to be implemented in 2017. These suggestions focus primarily on two areas for which ICER requested feedback: 1) Integration of patient and clinician perspectives on the value of interventions, and 2) Incremental cost-effectiveness ratios and thresholds.

Please see the attached report for a full description of these recommendations and related background.

**1. Formally and transparently involve patients and clinician stakeholders throughout the valuation process.**

Patient and clinician stakeholder engagement is necessary throughout the ICER valuation process, and needs to be more formally and transparently described in the valuation framework. ICER should consider reviewing the research and findings supported by PCORI in the US and active patient engagement strategies currently implemented in Australia, Canada and the UK [i, ii] for examples of effective engagement methods that meaningfully involve patients in the valuation process. At the University of Leeds, UK, patients are directly involved in all elements of clinical research including the study design (including identification of outcomes and comparators groups), development of protocols, study implementation and dissemination of the findings of clinical studies [iii].

In addition to the areas previously identified by ICER, engaging patients and clinicians may also be useful during: (1) Construction of the overall model; (2) Review and evaluation of evidence; (3) Determination of the quality of life inputs; (4) Estimation of care value; (5) Assessment of other aspects related to the treatment; and (6) Rating care value. The experience in Leeds [iii] demonstrates that patient engagement during the research process can be effectively implemented and results in improvements in clinical studies.

**2. Incorporate patient reported outcomes in the comparative assessment of clinical effectiveness.**

In the ICER framework, it is uncertain how and, in some cases, even whether patient-reported outcomes (PRO) are incorporated into the value assessment. Patients should participate in identifying which outcomes are to be used to evaluate the effectiveness of a new treatment compared with existing treatment options [iii, iv, v, vi].

In addition, methods other than quality-adjusted life years are needed to evaluate treatments for particular diseases so that they incorporate effectiveness, adverse effects and survival. For example, the Q-TWiST (quality-adjusted time without symptoms or toxicity) approach [vii, viii, ix] may be effectively applied to evaluate the overall effectiveness of treatments for cancer, where apart from progression-free survival and overall survival, there may be treatment-related toxicity of varying severity that should also be evaluated.

More comprehensive approaches to evaluating treatment effectiveness should be identified and assessed. The clinician perspective is also important in understanding and incorporating clinical experience across multiple patient-related health states and trajectories for the target medical condition.

**3. Consider benefits and disadvantages other than the clinical effectiveness and adverse effects of new treatments.**

Patient and community groups should be asked about intervention-related benefits and disadvantages that may be less directly related to the clinical effectiveness of the intervention. Issues to be considered include route of treatment administration (i.e., oral, subcutaneous injection, infusion, etc.); aspects of the treatment that may reduce or improve adherence; other treatment-administration related characteristics; and other benefits and disadvantages to the broader community (e.g., herd immunity conveyed by vaccination, other interventions aimed at reducing transmission of infection).

These factors can be considered at the treatment and care level, and may be directed at the broader community level and improvement in public health.

**4. Explicitly incorporate contextual factors into the valuation process.**

The ICER process does not formally incorporate the contextual factors into the valuation process. Possible contextual factors are examined by the independent public appraisal committee, but little detail is provided on the methods used to incorporate them in the care value rating. In reports on specific topics, little information is included on the deliberations of these committees and how contextual factors were considered in the valuation process.

Contextual considerations may include legal, ethical, and other aspects that influence the priority of an illness or treatment. For example, for a particular disease, are alternative treatments available or is there an under-served need for interventions for the targeted condition? Issues related to the prevalence and severity of the illness may make the intervention a priority for the community. Are there ethical considerations related to the intervention?

Patients, their clinicians, and perhaps the general public should be involved in discussing these more intangible issues associated with new interventions, working toward consensus on the valuation of an effective, targeted intervention.

**5. Clearly describe the methods used for achieving consensus on care value.**

Based on the ICER webinar and slides describing its methods, the elements of care value are publically discussed and then treatments are rated as low, intermediate or high value. The methods employed in arriving at these recommendations are not well articulated. While it may not be possible to provide exact details, the approach for achieving consensus on care value, taking into consideration existing clinical evidence on effectiveness and adverse effects, other factors, and contextual issues need to be

described fully. These methods must ensure that patient and clinician stakeholders are well represented and are formally involved in this process of review, evaluation, and discussion, leading to the eventual consensus on level of care value.

#### **6. Use multi-criteria decision analysis more formally to assess care value.**

ICER evaluates the care value of products using four types of criteria: the strength of the evidence, the efficiency, the existence of other benefits and “contextual” factors such as ethical or legal aspects. Each product is rated in each category and this information is presented to an appraisal committee for discussion and voting on the overall rating (low, intermediate or high value). This process constitutes an informal multi-criteria decision analysis (MCDA) [x].

Following a more formal MCDA process would offer some benefits, chief among them the increased rigor involved. In addition, the emerging guidelines for good practices can be leveraged to further substantiate the recommendations that are made. A formal process will help members of the appraisal committee understand each other’s position, assist in resolving discrepancies, and, in any case, it will increase transparency and facilitate reporting.

#### **7. Replace the general efficiency threshold with therapeutic-area specific ones.**

Using a single threshold is problematic. It imposes the idea that all products must abide by the same efficiency requirement, regardless of the severity of the illness, the unmet need or ICER’s own rating of value. It has been repeatedly shown that most citizens do not agree with this [xi]. Moreover, a single threshold is impossible to support empirically—the UK researchers who spent an enormous amount of time and money trying to establish an empirical basis found, instead, an enormous range of actual efficiencies in the health care system [xii] and resorted to recommending an unsupported mean.

Instead of a general efficiency threshold, ICER should switch to therapeutic area-specific thresholds. This would accord much better with reality, where efficiency differs substantially across therapeutic areas.

#### **8. Derive specific thresholds by constructing efficiency frontiers in each area.**

Deriving an efficiency threshold is difficult in the absence of a legitimate market because it requires establishing what is reasonable to pay for a given benefit and there is no good way to do that. An approach that circumvents this conundrum is to rely on the actual market: what are we paying for benefits in a given area? This value provides the area-



specific threshold assuming that one should be reluctant to accept a product with lower efficiency.

These area-specific thresholds can be easily obtained by deriving the efficiency frontier in each area [xiii]. The frontier reflects the best extant efficiency at particular levels of benefit.

#### **9. Increase transparency by making models available to reviewers.**

Although ICER has formally expressed a commitment to transparency, the economic models that underlie much of the work are not open and available for review. This is unacceptable and contrary to the guidelines on good modeling practices [xiv]. In line with those guidelines, any intellectual property rights claimed by the developers of the models can be protected via appropriate non-disclosure agreements that must be signed before access is provided. Failure to do this will render all of the estimates suspect and raise questions about the commitment to transparency.

#### **10. Report expected budget impact but don't use it to derive acceptable price.**

There is no basis for constraining every product to the same amount. A major breakthrough should not be held to the same standard as a product that provides little advantage. There needs to be flexibility in the amount of budget allowed to be consumed by a new product. Moreover, an overall budget impact threshold is an unsound idea in the context of a health care system like the American one, which does not have anything like a global budget. Budget impact is a difficult aspect to assess in an overall manner without a specific payer in mind. Each budget holder must be able to address in its own context the strain a new product may apply.

The impact of a new product on a payer's budget is difficult to forecast because it depends on the frequency with which candidates for treatment appear in that jurisdiction, and the rate at which they are prescribed the new product; neither quantity being readily estimated, particularly for the entire health care system. Instead of deriving an "alert" price, the ICER evaluation should facilitate the budget holder's deliberations by providing a tool for estimating the impact to their budget under assumptions that make sense for them, including coverage modalities and other aspects that affect the budget impact.

#### **11. Involve patients and clinicians in deliberations regarding the budget impact ("health system value").**

Patients and clinicians should be directly involved in determining the health system value of new treatments and interventions. Methods are available for involving patients and

other stakeholders in the design and implementation of clinical studies [iv, vi, vii]. These methods are directly generalizable to engaging patients (and others) in determining value to the health care system. While this may be challenging, meaningful engagement of patients and clinicians in the process of valuing these new interventions ensures that assessments are transparent and that they consider comprehensively the range of interested stakeholders and perspectives. This involvement also ensures that all relevant and important outcomes are at least considered in the valuation process.

**12. Provide formal methodological guidelines or citations to existing ones for every aspect.**

The work that ICER does is exposed by its very nature to review and critique by many different stakeholders. In this context, it is extremely important that every step of the process be conducted following solid methodological guidelines. For many aspects, guidelines that have been developed and vetted by experts already exist and can be cited. Where there are gaps in the guidelines, or in places where ICER wishes to introduce its own approach, this needs to be carefully documented. As some of the work is performed on behalf of ICER by other institutions, they should also be held to strict standards. At the very minimum, they should be required to provide detailed technical documentation of what they do, and this information should be provided to all stakeholders upon request.

In conclusion, the Institute for Patient Access appreciates your consideration of the 12 recommendations listed above and detailed in the attached report. If we may provide further detail or aid the Institute for Clinical and Economic Review in incorporating any of the above recommendations, please contact us at 202-499-4114.

Sincerely,



Brian Kennedy  
Executive Director

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September 12, 2016

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

RE: Call for Proposed Improvements to ICER's Value Assessment Framework

Submitted electronically via: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

Dear Dr. Pearson:

Janssen, the pharmaceutical companies of Johnson & Johnson, appreciates the opportunity to comment on the ICER Value Assessment Framework, as stakeholder feedback is a critical component in evaluating evidence, judging value, and supporting innovation. Janssen is a leading global developer and manufacturer of transformational medicines, with significant interests in the health of the American public and the future of the U.S. health care system. As a member of the National Pharmaceutical Council (NPC), the Pharmaceutical Research and Manufacturers Association (PhRMA), and Biotechnology Innovation Organization (BIO), we understand these organizations will also be providing comments on ICER's Value Assessment Framework.

We have additionally outlined below our key suggestions for improving ICER's Value Assessment Framework methodology and review process. These suggestions include:

1. The ICER Framework should take a societal perspective
2. The ICER Framework should reconsider the short-term budget impact methodology ('alarm bell')
3. Potential flaws of the QALY approach for the US healthcare system, and its resulting public acceptability or unacceptability, should be taken into consideration
4. If ICER does determine that a QALY approach is appropriate despite its flaws, cost per QALY thresholds should be a range that varies by disease state, not a fixed set of numbers, and guided by societal values when utilized by decision makers who determine access to treatments
5. Estimated net drug prices should be used in the Framework
6. Comparability of trial designs and breakthrough designations should be taken into consideration in indirect treatment comparisons
7. Real world evidence should be included and considered where appropriate

8. ICER must meaningfully include a broad range of stakeholders for input in the value assessment process
9. ICER should have staff with deeper expertise and allow adequate time for stakeholder feedback

## **1. The ICER Framework should take a societal perspective**

Beyond clinical comparative effectiveness, ICER's approach to "other benefits or disadvantages, or contextual considerations," while important, is neither well defined nor characterized, nor is there broad societal agreement as to how these considerations should be quantified or addressed. Janssen supports using a societal perspective for ICER's Value Assessment Framework, as it is the only perspective that provides a full accounting of the value of an intervention or set of interventions. Any other perspective will risk taking a partial view of value by excluding some aspects of the benefits or disadvantages of available treatment choices. In taking a societal perspective, ICER needs to include not just drug effects and costs, but also cost offsets in the health care ecosystem as well as indirect costs related to productivity (absenteeism, presenteeism, and disability), caregiver or family burden, reduced educational attainment due to impaired health, or increased interactions with the criminal justice system due to serious mental illness. Concerns about potential discrimination against those not actively employed can be alleviated through appropriate methodology adjustments. Given ICER's contention that health care costs crowd out spending on other social goods, like education or infrastructure or policing, a societal perspective to any analysis of value in health care would be most appropriate.

## **2. The ICER Framework should reconsider the short-term budget impact methodology ('alarm bell')**

Janssen is concerned by the budget impact analysis methodology of ICER's Value Assessment Framework and the attention this section receives compared to the rest of the report. The budget impact section noticeably detracts from the larger conversation on value. This short-term approach, with its "alarm bell," is inconsistent with value maximization from the societal perspective in the long term, essentially ignoring the long-term value of innovation to society. Statins and HIV drugs are excellent examples of treatments that were widely criticized for their supposed lack of cost-effectiveness early in their product life cycle, but as evidence accumulated regarding their effectiveness and net costs declined due to competition, value increased over time. Eventual generic availability and pricing further enhanced their overall value to society. Using a 5-year time horizon and focusing on short term budget impact, rather than using the 25- or 30-year time horizon needed to fully appreciate the value that technological innovation in the health sciences brings, has the potential to harm today's patients through reduced access, and harm tomorrow's patients through negatively impacting investment in technology that addresses unmet needs and brings high societal value in the long run. Restraining the drug component of health care spending to the anticipated growth in national GDP + 1% is an artificial and unhelpful construct, and can interfere with efficient allocation of

resources over time. It also has no scientific basis, can have unintended consequences, and does not have broad public support.

ICER's budget impact uptake assumptions have been largely inaccurate to date and do not take into account payer restrictions, the time it takes to change treatment practices, or patient behaviors involved in adopting new technology. The uptake assumptions also appear to be significantly biased, so as to present a far more aggressive scenario than actually plausible, ring the "alarm bell" and unduly pressure manufacturers. If uptake assumptions remain a part of the budget impact assessment, we would recommend ICER seek more expert input from those entities known to have strong experience in forecasting, such as stock analysts or consultants familiar with modeling and the use of analogues. It would not be appropriate for manufacturers to share their own forecasts, which are proprietary, and could also be material from an investor relations perspective.

### **3. Potential flaws of the QALY approach for the US healthcare system, and its public acceptability or unacceptability, should be taken into consideration**

Janssen is concerned about ICER's unqualified embrace of the QALY concept as the metric for value assessment. It should be noted that the QALY methodology is not used in many countries, including France, Japan, and Germany. Even in countries where the QALY methodology is used by national governments for their socialized health care systems, such as the UK, Canada, Australia, and Sweden, it has been recognized as having serious flaws, and those flaws may not be acceptable to the US public.<sup>1</sup> Of significant interest is the recent ECHOUTCOME project, in which six European universities and research agencies invalidated four key QALY assumptions:<sup>2</sup>

- Time and quality of life can be measured in consistent intervals
- Life years and quality of life are linked
- People are neutral about risk
- Willingness to sacrifice life years is constant over time

If the assumptions underlying the QALY approach are indeed invalid, then its use in decisions that can negatively affect access to treatments is questionable.

If ICER insists upon continued use of the QALY approach, it should recognize that the utility measures inherent in QALYs are culturally sensitive, hence should be derived from the US population.<sup>3,4</sup> It is not always clear or transparent that the utilities being applied in ICER value assessments are representative of what Americans value with regard to improvements or tradeoffs in health status. Utilities are also experientially sensitive, as patients who have experience with a certain disease will have different utilities than persons with no experience with the disease. Reconciling the differences or justifying the choice between using general population utilities and patient-specific utilities deserves further attention.

**4. If ICER does determine that a QALY approach is appropriate despite its flaws, cost per QALY thresholds should be a range that varies by disease state, not a fixed set of numbers, and guided by societal values when utilized by decision makers who determine access to treatments**

Using a fixed set of cost per QALY thresholds for all therapies could reduce patient access for innovative therapies in special circumstances (e.g. orphan drugs, cancer), where the public feels differently. In other countries using QALYs, different cost per QALY thresholds are increasingly being applied for different diseases.<sup>5</sup> For instance, UK's NICE (The National Institute for Health and Care Excellence) has recently had to introduce two modifiers to its QALY calculations, as its standard methodology was not supporting access decisions that society valued. The first modification was an "End of Life" adjustment to utility weights for life limiting conditions when the innovation offered a demonstrable survival gain.<sup>6</sup> The second modification was an adjustment to how discounting methodologies were applied when treatment costs are incurred today, but survival benefits are well into the future, as in pediatric oncology. A key issue in both cases was that the "established" threshold did not support what British society valued, making workarounds necessary.

Of important note is that the academics computing the cost per QALY estimates within the UK NICE system are answerable to the National Health Service and the public, and as it became clear the existing methodology was at odds with societal expectations, changes could be, and were, made.<sup>6</sup> Another key distinction is that thresholds in the UK are not set by those who calculate the incremental cost-effectiveness ratios (also known as ICERs), but by those who have to answer to the decisions made using them.

If cost per QALY is used for value assessment in the US, we suggest using a range of thresholds that reflect societal values instead of a fixed set of point estimates.<sup>7</sup> The American public has not yet substantially weighed in on what it would regard as acceptable thresholds for resource allocation decisions in health care, and understandably resists attempts by a few experts to do so. Indeed, even the heralded 'no lifetime limits' requirement for health care insurance brought about by the Patient Protection and Affordable Care Act speaks to our societal reluctance to use costs as a sole basis for decision-making in health care.

Placing a universal cost threshold on a life year, quality adjusted or not, is widely recognized to be fraught with ethical and logistical challenges. Alternatively, non-QALY related cost-effectiveness measures may be a more acceptable approach, such as costs per response or number needed to treat.

**5. Estimated net drug prices should be used in the Framework**

It is widely acknowledged that drug Wholesale Acquisition Costs, or WAC, do not represent actual net prices to the health care delivery system or payers. Market competition as well as statutory discounts are known to reduce prices, substantially in

many cases. Other factors such as rebates and patient assistance programs further reduce drug prices. Using estimated net drug prices, as well as sensitivity analyses to reflect uncertainty by varying price to approximate a range of net prices that are realistically present in the marketplace, would provide a better approach to understanding actual costs and, therefore value. For example, for treatments paid through a medical benefit, average sales price (ASP) could be used. The ASP calculation captures the list prices and the non-statutory discounts provided for all manufacturers. ASP is published quarterly and is available on the CMS website, but lags in time by approximately 2 quarters. For other medications delivered through a commercial pharmacy benefit or through Medicare Part D, ICER could use publicly available claims datasets which contain actual payer paid costs or alternatively could use Medicaid's statutory discount level and/or solicit information from analysts who cover the pharmaceutical industry to develop a range of discounts that are used in general practice, applying sensitivity analysis using that range, in order to get a more realistic assessment of costs for use in value assessment.

#### **6. Comparability of trial designs and breakthrough designations should be taken into consideration in indirect treatment comparisons**

ICER utilizes statistical methods such as network meta-analysis of clinical trials to develop its comparative effectiveness data. However, ICER needs to incorporate in its reviews an evaluation of the scope and comparability of trial designs in order to fully characterize and qualify its findings. Significant differences in the selection of clinical trials for inclusion in network meta-analysis, as well as variations in trial design features such as patient populations, endpoints, comparators, timeframes, statistical analyses and reporting, will produce variable and potentially biased results. Readers of ICER reviews would benefit from a better understanding of such differences, and the potential role they may play in any final analysis.

There are also a number of unique circumstances that cannot conform with ICER's approach to evidence. In ICER's quest to include products in its evaluations that have not yet received FDA approval, manufacturers may be unable to share all their relevant data, as these data may not yet be published or publically available. Moreover, such details may be material to a company's stock price, and cannot be selectively shared. This will lead to incomplete evidence resulting in a premature and potentially biased assessment, as well as one which may become quickly outdated.

Regarding treatments that have received FDA's "Breakthrough Designation," comparative data are often lacking due to the fact that there may not have been any acceptable treatment options for patients, yet these new treatments by definition address high unmet need.<sup>8</sup> Breakthrough designation, originating from the 2012 the Food and Drug Administration Safety and Innovation Act, defines a therapy "to treat a serious or life threatening disease or condition" where "preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints."<sup>9</sup> Characterizing such treatments as having "insufficient" data is therefore misleading. Again, the risk is premature assessment, with



consequences that include reduced patient access to drugs to treat serious or life-threatening diseases.

**7. Real world evidence should be included and considered where appropriate**

In further pursuit of relevant and reliable data that informs decision-making, Janssen supports the use of real world evidence in the ICER value assessment framework, where appropriate and of sufficient quality. Real world experience can generate valid scientific evidence of both comparative treatment safety and effectiveness, and is of keen interest to those closest to treatment decision-making, including physicians and patients, as well as those who control access to innovation, such as insurers. Requiring or including only randomized clinical trials to address all the questions that relate to comparative value is not practical, timely or efficient, and may not be possible in all circumstances due to ethical issues.

**8. ICER must meaningfully include a broad range of stakeholders for input in the value assessment process**

Outreach that results in broad and representative patient input into an evaluation of value is of utmost importance. Patient-focused drug development and patient-centric outcomes research, both major initiatives of the Department of Health and Human Services, are leading the way in ensuring that patient perspectives are incorporated into drug approval and technology assessment. ICER would be well served by incorporating meaningful, not token, patient input into its review process. An additional voice that bears amplifying is that of professional medical society members who will be at the front line of patient care. While there is variation in the extent and sophistication of those organizations in the field of value assessment, it is incumbent upon any technology review organization to seek their input. As a practical matter, not adequately considering the input from a key stakeholder whose alignment with review findings is necessary for recommendations to affect treatment practices reduces the impact any such a review will have.

**9. ICER should have staff with deeper expertise and allow adequate time for stakeholder feedback**

We recognize and appreciate that ICER has provided multiple opportunities for stakeholder feedback during its Value Framework Assessment process, and the organization is continuously open to feedback from stakeholders. In that spirit, we have noted that on occasion ICER appears to lack the deep disease-state knowledge and modeling expertise necessary to carry out its mission and would benefit from more expert input. Also, manufacturers, especially smaller companies with fewer resources, may have difficulty meeting the very aggressive timelines of ICER reviews, and this could impact the assessment of their innovation.

We trust that all our feedback will prove useful, and look forward to continued engagement.

Thank you for your consideration,



Anastasia G. Daifotis, MD  
Chief Scientific Officer  
Janssen Scientific Affairs, LLC



Catherine Tak Piech  
Vice President  
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September 12, 2016

Steven Pearson, MD  
President  
Institute for Clinical and Economic Review  
Boston, MA 02109

**RE: National Call for Input on Value Framework**

Dear Dr. Pearson:

JDRF, the leading global and largest charitable organization funding type 1 diabetes (T1D) research, appreciates the opportunity to provide input on the Institute for Clinical and Economic Review's (ICER) value assessment framework. JDRF's research mission is to discover, develop, and deliver advances that cure, better treat, and prevent T1D. Since our founding in 1970 by parents of children with T1D, JDRF has awarded more than \$2 billion to diabetes research. In 2015, JDRF directly funded \$72.4 million in T1D research, including research in 18 countries and more than 50 human clinical trials.

JDRF commends ICER's effort to understand and to better integrate the patient perspective within its current value framework by seeking comments. JDRF believes that the patient should be the focus of any framework that aims to evaluate the value of drugs and other medical technologies. As such, it is essential that value determinations are conducted from the perspective of the patient and are based on criteria and outcomes that are important to individual patients. Further, it is essential that framework developers actively engage with patients and patient advocacy groups throughout the development and refinement of the frameworks and ensure that input from these groups are incorporated in a meaningful way. Finally, the output of the framework should be understandable to patients and useful in helping patients and clinicians evaluate treatment options.

***Limitations of ICER's Current Value Framework***

JDRF believes that ICER's current value assessment framework is limited with respect to patient-centricity. In addition, we believe improvements can be made in consulting with clinical experts and increasing transparency. Below we outline limitations of the current framework and offer approaches to address the limitations.

***Insufficient consultation with patients and patient advocacy groups***

The current value framework is limited in the degree to which ICER consults with and engages patient advocacy groups. In the public comments on the multiple myeloma draft report, the Cancer Support Community encouraged ICER to seek input earlier in the process and in a more comprehensive way.<sup>1</sup> Further, in reference to the draft report on obeticholic acid, seven patient

advocacy groups stated that ICER's process of public and patient engagement is contrary to the concepts of a patient-centered value framework.<sup>2</sup>

***Recommendations:***

- Consult with and incorporate input from relevant patient advocacy groups and patients throughout the assessment process beginning with the development of the draft scoping document.
- To ensure transparency, the draft scoping document should include the names of the patient groups who provide input.

***Inadequate consideration of criteria and outcomes important to patients***

ICER's current value framework does not adequately consider outcomes that are important to patients. In a comment letter, the Multiple Myeloma Research Foundation (MMRF) noted that "absent in the draft report are considerations around ease-of-use as well as management of toxicities and side effects so patients can enjoy an improved quality of life."<sup>3</sup> While ICER's framework purportedly considers "additional benefits or disadvantages" and "contextual considerations", it is not clear how these components are factored into the determination of care value.

***Recommendations:***

- Incorporate a transparent approach to integrating "benefits and disadvantages" and "contextual considerations" into the determination of care value.
- Ensure that criteria and outcomes that are important to patients, e.g., route of administration, caregiver burden, etc. are transparently integrated into the determination of value.

***Insufficient consultation with disease-specific clinical experts***

It is essential that ICER consult with disease-specific clinical experts throughout the assessment process. It is concerning that the American Society of Hematology commented that the drug combinations and regimens in the multiple myeloma assessment did not reflect current clinical practice.<sup>4</sup> In addition, patient advocacy groups representing patients with primary biliary cholangitis noted a lack of patient and clinical subject matter experts on the voting panel for obeticholic acid.<sup>5</sup>

***Recommendations:***

- Consult with and incorporate input from disease-specific clinical experts throughout the assessment process including the development of the draft scoping document.
- List the names, titles and affiliations of the clinical experts who provided input into the draft scoping document and subsequent evidence reports.
- Seek out and incorporate feedback from therapeutic area experts, both clinical and economic, to inform the design, assumptions and inputs in the economic models.

- Include disease-specific clinical experts and patient advocates on the panel that votes at the public meetings.

### ***Lack of transparency***

ICER's current value framework lacks transparency in several important areas. The first, as mentioned previously, is how patient-relevant outcomes, e.g., ease of use, etc. are factored into the determination of value. Second, while ICER posts public comments on the draft reports to its website, comments on the draft scoping document do not appear to be publicly available. Finally, there is a lack of transparency in how ICER addresses public comments on the draft scoping document and the draft report. While ICER produces a document that summarizes public comment on the draft report, more detail is required for stakeholders to understand how concerns are addressed and the rationale for incorporating or not incorporating public feedback.

### ***Recommendations:***

- Post public comments on the draft scoping document to ICER's website when the revised scoping document is released. Provide a detailed explanation for how each issue is addressed.
- Provide a detailed account for how ICER addresses each issue raised during the public comment period for the draft report.

JDRF appreciates ICER's consideration of our recommendations and would be pleased to collaborate with ICER to implement improvements to its value framework.

Sincerely,

/s/

Cynthia Rice  
Senior Vice President, Advocacy & Policy  
JDRF

### **References:**

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Karbowicz

In most pharmacoeconomic analyses, the clinical assessment really drives the assumptions and ultimately the results. If the clinical assessment is off a little, the economic assumptions are further exaggerated / amplified and can get farther off base. So, my comments are primarily focused here.

Comparative clinical effectiveness:

- 1) Completely agree with need for additional patient input to frame relative value of specific endpoints / outcomes on net health benefit in the overall context of a disease. Visually, think of it as a Trivial Pursuit game piece.

For example, for diabetes (whole pie) – outcomes are varied (cardiovascular outcomes, nephropathy, neuropathy, retinopathy, etc, are pie pieces). If a drug “only” completely prevented retinopathy but improved no other aspect of the diabetes, how would that stack up in the context of the overall disease burden? This is important to consider.

When we take this global view of a disease and the limited potential benefit of many treatments, the incremental value (in terms of “net health benefit) can be relatively small...especially when considering poly-pharmacy from using multiple therapies to achieve an overall impact on the disease. I would love to see how this can be considered in a reproducible way that can develop over time – especially as new evidence is generated for a disease.

- 2) Would like to see additional definition / detail / standards / examples of “low” “intermediate” or “high” clinical value. Trying to avoid the appearance of a “cookbook” might be a detriment to the process. The more subjectivity that goes into a process means less reproducibility, and the more likely it will be influenced by a skilled orator. For this reason, a firmer benchmark here can be useful to take out the wiggle room, and drive towards an even more systematic approach.

Incremental cost-effectiveness ratios

- 3) It’s not enough to describe “relative” benefit of a new treatment over an old treatment. It matters what the “absolute” benefit might be of the original treatment, as well – otherwise it begs the question, is the original treatment worth it? That must be answered first. I’d like to see the value framework call that out. For example, what if a new drug was twice as expensive as hyaluronic acid injections for osteoarthritis of the knee... well, now effective is hyaluronic acid injections? Both are needed for an accurate assessment. Another example, I just went back and looked at the Multiple Myeloma review, and I’m not easily finding what the “net health benefit” is of lenalidomide and dexamethasone. How much better is it than no treatment? (because that’s also an option). While I understand we may not necessarily need a description of the “absolute benefit” when relying on QALYs, it seems to me that it’s a very valuable piece of contextual

information that needs to be considered nonetheless. For MedSavvy's use, and I suppose other P&Ts and health plans, having each therapy's NHB grade would be very useful.

I'm comfortable so far with the "alarm bell" principles and methodology. I'm interested to hear about criticisms. As far as the methodology pertaining to "affordability" or "value" – my suggestion is to go back and run the model through a few therapies that have been on the market for some time and see how the predictive model might have performed. For example, asthma or COPD medications have been on the market for years





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September 12, 2016

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Dear Dr. Pearson,

The Massachusetts Biotechnology Council (MassBio) appreciates this opportunity to comment on the Institute for Clinical and Economic Review (ICER) current Value Assessment Framework (the “Framework”). MassBio represents more than 750 life sciences companies, academic institutions, service providers and patient organizations, the majority of which are directly engaged in the research, development and manufacturing of innovative products that solve unmet medical needs for patients around the world. MassBio is committed to advancing Massachusetts' leadership in the life sciences to add value to the healthcare system and improve patient lives.

MassBio supports efforts that bring the benefits of our members' innovative products and treatments for patients and the healthcare system. We recognize that the current healthcare system has problems that need to be fixed, including health plans' increasingly frequent tactic of shifting the cost of innovative medicines onto the sickest patients. We are also mindful of the fiscal impacts of new and innovative medicines on strained budgets. As a result, we take very seriously the emerging frameworks and methodologies currently under development to assess the cost and comparative effectiveness of new medicines. We know, however, that in many cases such reviews can generate policy initiatives primarily designed to achieve upfront cost savings rather than ensuring access for patients or encouraging more rapid development of badly needed cures. We continue to urge ICER to recognize its role—intended or not—in fueling those misguided policy initiatives.

We continue to take the strong view that long-term policy goals for our industry cannot be achieved when they are based solely on snapshots of upfront drug costs. This approach risks upsetting the delicate balance of incentives and regulation in our current system that has allowed the U.S. to lead the world in the development of new and innovative treatments, as well as providing patients with the most rapid access to those medicines. True cost, value and outcomes can only be measured with a longer time horizon perspective on quality, access, and the health of patients. Many of our member companies are working to do just that—proactively exploring reforms to regulatory and legal barriers to value-based pricing models and pay-per-performance agreements that both address cost, but also ensure patients

receive the treatments they need and that will work for them. We must encourage all stakeholders to explore more creative solutions rather than revisit failed approaches and policies of the past.

It is with this mindset that we have reviewed the Framework, and offer the following comments.

## 1. Short Term Perspective / Affordability

An integral component of the Framework is the assessment of short term budget impacts of the utilization of a newly launched medicine, described as the “Provisional Health System Value” component. According to ICER’s recent webinar on the Framework, the stated purpose of this objective is to assess “short term affordability” and to provide “a reasonable alarm bell for consideration by all stakeholders of whether there are mechanisms that are needed around utilization management, lower prices, reallocation of resources or other means.”

As an overall threshold matter, we do not support calculating short-term budget impacts as bearing any meaningful connection to a particular therapy’s overall cost effectiveness or true value to patients or the healthcare system, even if such an impact could reliably be determined based on available data. This is because estimating the short-term impact of a particular therapy on public coffers and payer profits is entirely unrelated to its comparative clinical effectiveness over prior treatments on either a population-wide or a patient-by-patient basis. Instead, generalized conclusions about budgetary impacts - particularly when conducted as budget siloed analyses - promote access restrictions and price control policies that are ultimately harmful to individual patients, as was seen in price-per-pill cost-based formulary initiatives in the Medicaid and the Veterans’ Health Administration programs in the 1990s and earlier. Such outcomes tend to undermine clinical decision making as a primary driver of clinical value, therapy utilization, and patient care, and can also deter future innovation in drug development through the implementation of price controls or dramatic utilization management mechanisms. These approaches also risk removing from individual clinicians and patients the ultimate decision on the appropriate use of a particular therapy, and instead drive those decisions based primarily upon the payer’s perspective.

Aside from this general concern about the role of “provisional value” in any discussion of cost effectiveness, we have more specific concerns about ICER’s provisional value methodology used to gauge “uptake” of new therapies upon launch. First, ICER’s reliance on WAC to calculate short term budgetary impacts risks greatly overstating true costs. Unfortunately, this in turn risks overreactions by payers and policymakers in connection with the perceived cost impact of new drugs. As you know, WAC pricing does not incorporate rebates, discounts and other price concessions that are commonly applied to drug purchases in the commercial market, and is in fact required in connection with certain federal health care programs. The use of WAC pricing generally to project overall drug spending can mislead payers and the public about the actual impact of drug spending, and promote overreaching public policies such as onerous disclosure requirements and even price caps. In fact, in Massachusetts, legislation was passed just this year requiring the Center for Health Information Analysis (CHIA) to incorporate some aggregate measure of rebates and discounts when calculating the drug spend component of annual health care cost increases. We understand that in many cases the precise amount of a rebate or discount is protected, confidential information. That said, and particularly given the generalities utilized in other aspects of the Framework, the unavailability of the precise data should not deter ICER from arriving at more reliable spend figures through rebate estimates as Massachusetts law now requires CHIA to do.

Moreover, we submit that ICER’s approach for determining potential uptake patterns for new therapies also overstates initial utilization patterns by ignoring the impact of approval restrictions, real world access restrictions, doctor guidelines, impediments to care and other factors that can serve to limit utilization

levels. Because the calculation of “percentage of eligible patients treated” can essentially dictate whether a drug’s cost should sound the hypothetical “alarm bell” under the Framework, we would urge for a more consistent, more transparent and more realistic approach to calculating the uptake. The apparent lack of consideration of real world access restrictions particularly penalizes drugs treating wider patient populations with more prevalent diseases and, like the utilization of WAC pricing, risks greatly overstating budget impacts and deterring innovation in areas of high unmet need. At the very least, ICER should consider a more realistic “uptake” that more accurately reflects the very real fact that payers often impose utilization restrictions on new therapies and, further, the calculation of “eligible patients” should consider such factors as clinical treatment guidelines and the portion of the patient population for a particular disease is linked to, or even will likely seek, immediate treatment. To paint a more accurate utilization picture, ICER should examine real world claims data on the initial utilization of prior therapies targeted at the same patient populations as the particular drug under review, or other real world evidence bearing on initial uptake patterns. Therefore, we recommend that to capture a more realistic perspective of new therapies, ICER’s reviews should be timed to enable it to use more robust and substantive data available from actual usage based upon claims data, extended clinical trials, or expanded access programs. The importance of this type of data was noted in a recent Health Affairs article that pointed out how the clinical benefits of new medications for cancer can differ from what is seen in registration trials because with experience physicians learn how to better manage side effects allowing patients to remain on medications longer, and because new medicines may also be used in patients excluded from clinical trials.<sup>1</sup>

As a final comment in this area, with respect to ICER’s budgetary impact calculations, we are also concerned that ICER’s utilization of a five year time frame does not capture cost savings to the health care system that can be realized during longer periods of time. This can especially be the case for therapies that treat chronic, rare diseases over more extensive timeframes. Some of these therapies may have high up-front costs but save health care expenditures and improve patient outcomes in the longer term, and a five year cost projection can greatly overstate the actual cost impacts of the utilization of those medicines. As the Health Affairs study referenced above noted, “The introduction of costly new therapies increases [total costs in the year after diagnosis], but by prolonging survival, the drugs push the high costs associated with end-of-life care further into the future. As survival improves, costs incurred in the year after diagnosis for end-of-life care decrease. For this reason, it is important to examine lifetime medical costs instead of costs in the first year or two after diagnosis.” Therefore, we recommend that ICER’s analyses both recognize this temporal shifting of costs and include extended time projections for costs and savings that are inclusive of all direct and indirect costs, i.e. the total costs of care.

## 2. Care Value Framework

ICER’s Care Value framework as applied to individual drug reviews relies on comparative clinical effectiveness data available at - or even before - a drug’s launch. We understand that ICER takes this approach to ensure that its conclusions are available to payers as soon as possible. However, the approach necessarily limits the range of meaningful data available for each drug review. As noted above, in almost all cases, data available at or before launch is not nearly as robust as real world evidence of a therapy’s use in the longer term. At the very least, in order to balance its desire for expediency with the importance of real world evidence of value, we suggest that ICER provide meaningful, if not formal, opportunities for the submission of data suggesting that certain of its drug review conclusions should be corrected or updated given the emergence of new evidence of value.

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<sup>1</sup> “New Anticancer Drugs Associated With Large Increases In Costs And Life Expectancy”, *HEALTH AFFAIRS* 35, NO. 9 (2016): 1581–1587  
B4593510.1

Because of the early timing of ICER's reviews, they are conducted with a limited data set. ICER's exclusion criteria for selecting data results in ICER's meta-analyses being conducted on only a few trials, typically largely the same ones the FDA uses for approval of new medicines. This was seen in the August 19, 2016 Draft Evidence Report about non-small cell lung cancer (NSCLC). This use of limited data - and particularly the use of data about compounds not approved as medicines by FDA - adds a significant amount of data uncertainty to ICER's already uncertainly-laden drug review methodology. For example, the NSCLC Draft Evidence Review includes many stated assumptions and areas of uncertainty in both the data and ICER's methodologies. Drawing conclusions around a care value that raise "alarm bells" with assumptions and uncertainties at every step of the analysis raises concerns about the validity of the entire process. We suggest that ICER expand its discussion with appropriate clinical experts and patient stakeholders about the extent of available data, the appropriate use and limitations of data selected by ICER for its reviews, and the methodological assumptions and uncertainties contained in each review, and make that information prominent in its communications to the public and all stakeholders.

Additionally, a specific methodological issue in ICER's Care Value Analysis process is the use of quality adjusted life years (QALYs). As you know, while QALYs have a long history in economic modeling and research, their practical use in health plan and public policy decision making is much more complex and challenging. QALYs are inherently not accounting for intangible aspects of treatment benefits that are often extremely important to patients and their families. Those unaccounted for aspects of the value of treatments are particularly evident for chronic or disabling diseases such as multiple sclerosis, rheumatoid arthritis, and some cancers that may reduce patient's ability to care for themselves as measured by their ability to conduct Activities of Daily Living. As noted above, because of the problems inherent with QALYs, we recommend that ICER derive alternative methodologies that encompass the broader clinical, social, and patient perspectives beyond its current unquantified Contextual Considerations, and not use narrowly calculated QALYs in its reviews because they can both lead to skewed results and non-experts can easily misunderstand the meaning and real-life significance of QALY numbers.

As a final, more general matter, our members have expressed concern about uncertainties involving ICER's critical calculations, data extrapolations, and assumptions underlying the care value and provisional value measures, and their inability to receive the underlying data when requested. These ambiguities not only make peer review impossible but significantly limit the ability to reproduce ICER's calculations so that others - including manufacturers and other researchers - can test the assumptions and modeling used in ICER's reviews in order to deliver useful and appropriate feedback. We suggest that, for future drug reviews, ICER be as transparent as possible regarding underlying assumptions, data extrapolation and calculations so that manufacturers and stakeholders better understand the various limitations of the underlying data, assumptions and ICER's associated conclusions with respect to each drug reviewed.

Again, on behalf our members, we thank you for this opportunity to comment on certain aspects of the Framework. We look forward to continuing these discussions going forward. Please do not hesitate to contact me if you have any questions about any of the comments above.

Sincerely,



Robert K. Coughlin  
President & CEO



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September 12, 2016

Via Electronic Submission

Steven D. Pearson, MD  
President  
Institute for Clinical and Economic Research (ICER)  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

**RE: ICER National Call for Suggestions to Improve its Value Assessment Framework**

Dear Dr. Pearson:

On behalf of the Medical Device Manufacturers Association (MDMA), a national trade association representing the innovative sector of the medical device market, I am submitting the following comments in response to the call for suggestions to improve the Value Assessment Framework from the Institute for Clinical and Economic Research (ICER). MDMA represents hundreds of medical device companies, and our mission is to ensure that patients have access to the latest advancements in medical technology, most of which are developed by small, research-driven medical device companies.

MDMA is commenting on the ICER Value Assessment Framework because it has been used in the past by ICER affiliates, such as the California Technology Assessment Forum (CTAF), to evaluate medical technologies. We appreciate ICER's request for comments on the Value Framework, but need more information on how exactly ICER will consider and incorporate stakeholder input. This will help ICER meet its stated goal to "work collaboratively with patient groups, clinical experts, and life science companies." All too often device companies have found the value assessment process to be inappropriate for capital equipment/medical devices and arbitrary for reasons we describe below.

**Assessment Inputs**

Based on our review of value assessment inputs, there is little medical device organization participation in the process. Principle too all inputs, the patient should be ICER's most important stakeholder and should be included broadly and comprehensively throughout the process.

**Comparative Clinical Effectiveness**

Regarding clinical effectiveness, supporting evidence can be obtained from several study protocols, including prospective cohort analysis, which allows for real-world, non-experimental, data to be obtained. Randomized controlled trials (RCTs) are not always the most appropriate protocol design and assessments should be structured to include other designs. MDMA agrees with getting input from patients to obtain outcomes related to clinically meaningful improvement of function and/or quality of life, and how a procedure or device allows the patient to return to function. The Framework should have validated methodological standards as its backbone, and these standards should be applied transparently and consistently, but with an understanding of the differences between device and biopharma therapies and with the patient and their condition at the center.

### **Cost-Effectiveness and Cost per Outcomes Achieved**

When evaluating cost effectiveness, cost needs to be expansive and look beyond a single procedure or encounter. The evaluations should also consider costs that are avoided, such as the need for additional procedures or therapy, inpatient length of stay, risk of infection or readmission, etc. Further, the cost and quality-adjusted life years (QALY) considerations of ICER's current Value Assessment Framework seem to be more drug than device focused. It is important to assess the value of different therapies to an individual patient. The final decision of which treatment is most appropriate for a given patient should be made by the patient working with his or her physician considering that patient's individual circumstances, values, and needs.

MDMA recognizes the importance of and broadly supports value assessments, but ICER and its affiliates, such as CTAF, should refrain from applying the Value Assessment Framework to devices until the framework is changed to accommodate the unique requirements of medical devices (such as frequent, incremental changes to the products).

Noted above, CTAF has in the past attempted to apply the Value Assessment Framework to capital equipment. For example, in 2008, CTAF completed a technology assessment for stereotactic body radiation therapy (SBRT) for lung cancer in medically inoperable patients. As part of this review, CTAF reviewed criteria to determine the clinical efficacy of SBRT and found SBRT to only meet one of the five criterion for safety, effectiveness and improvement in health outcomes.[1] Stakeholders submitted comments and gave testimony at the public meeting to review the assessment. As part of this public process stakeholders brought the panel's attention the National Comprehensive Cancer Network (NCCN) guidelines on non-small cell lung cancer. While the NCCN guidelines were listed in the "recommendations of others" section of the assessment, they appeared to have not been considered to determine whether a subset of patients could meet the clinical criteria. During the meeting, the panel chair put forth an alternate recommendation for peripheral tumors (consistent with NCCN guidelines), which was approved by a majority panel vote.[2] In 2011, the SBRT technology assessment was completed again, and the assessors determined that all five criteria had been met, reaffirming the panel's recommendation, as supported by NCCN. We believe the recommendations of expert bodies

[1] Blue Shield of California Foundation - California Technology Assessment Forum. June 2008 - Summary of Panel Actions. Accessed online: [http://icer-review.org/wp-content/uploads/2016/01/746\\_image\\_CTAF\\_Mtg\\_Summary\\_061808\\_final\\_JS.pdf](http://icer-review.org/wp-content/uploads/2016/01/746_image_CTAF_Mtg_Summary_061808_final_JS.pdf)

[2] *Ibid.*



such as NCCN and specialty societies should be consideration in ICER, given the assessment criteria may not always be appropriate for medical devices.

MDMA believes that the framework should take into account the value of innovation and seek to foster the innovation ecosystem. This ultimately will lead to new treatments and cures, driving down cost and improving quality of care. MDMA appreciates the opportunity to submit comments and looks forward to working with ICER as it works to improve its Value Assessment Framework.

Sincerely,

**Mark Leahey**

Mark B. Leahey

President and CEO

Medical Device Manufacturers Association

[1] Blue Shield of California Foundation - California Technology Assessment Forum. June 2008 - Summary of Panel Actions. Accessed online: [http://icer-review.org/wp-content/uploads/2016/01/746\\_image\\_CTAF\\_Mtg\\_Summary\\_061808\\_final\\_JS.pdf](http://icer-review.org/wp-content/uploads/2016/01/746_image_CTAF_Mtg_Summary_061808_final_JS.pdf)

[2] *Ibid.*



# National Health Council

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September 12, 2016  
Institute for Clinical and Economic Review  
Steven D. Pearson, MD, MSc, President  
Two Liberty Square  
Ninth Floor  
Boston, MA 02109

RE: ICER National Call for Proposed Improvements to Value Assessment Framework

Dear Dr. Pearson,

The National Health Council (NHC) appreciates the opportunity to provide input on the 2017 update to ICER's Value Assessment Framework. The NHC is the only organization that brings together all segments of the health community to provide a united voice for the more than 133 million people with chronic diseases and disabilities and their family caregivers. Made up of more than 100 national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient advocacy organizations, which control its governance and policy-making process. Other members include professional and membership associations, nonprofit organizations with an interest in health, and representatives from the insurance, pharmaceutical, generic drug, medical device, and biotechnology industries.

Understanding and defining the value of health care treatments and interventions has become a national priority. The patient community is eager to take part in the value discussion. Patient<sup>1</sup> perspectives on value can differ significantly from other groups such as clinicians and payers. These perspectives often integrate considerations beyond clinical outcomes and cost, such as a treatment's ability to help patients achieve personal goals.

The NHC recognizes ICER's recent efforts to engage the patient community by, for example, outlining a plan for gathering patient input in the scoping documents that inform ICER's reviews and appointing a patient representative to the governance board. However, we strongly recommend ICER adopt an open and collaborative process for identifying and appointing additional patient representation in your governance as well as create additional opportunities for patient engagement.

The NHC offers comments on the four areas ICER has identified as the highest priorities for potential revision to the framework.

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<sup>1</sup> Throughout this letter, the term "patient" refers to patients and their family caregivers.



***1. Methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value intended to fall in the current value framework within “additional benefits or disadvantages” and “contextual considerations”***

We commend ICER for including methods for integrating patient and clinician perspectives as a high-priority area for improving ICER's value assessment framework. The NHC agrees there is a significant gap in appropriate, validated methods to integrate patient and clinician perspectives into value assessments and appreciates ICER's effort to solicit more input in this area.

We are concerned, however, that the scope of this priority as articulated in the call for comments is too narrow and assumes that relevant patient-centered data is widely available for assessment. Specifically, the current scientific literature does not adequately incorporate patient and clinician perspectives, which underscores the need for a paradigm shift in how research is both conducted and evaluated. To imply that the current literature in any way includes appropriate incorporation of patient perspectives misrepresents the state of the field and, unfortunately, downplays the underlying need for gathering and considering these perspectives and the potential impact their inclusion can have on value assessments. This will result in the need for ICER to rely on other means for capturing this information, either directly or through partnerships that include patients and patient groups. We encourage ICER to more openly acknowledge the fundamental deficiencies, gaps, and challenges in this area, which can help set the tone and appropriately frame ICER's efforts to credibly incorporate the consideration of the patient voice in its value assessment process.

Because of these existing deficiencies, gaps, and challenges, it is of utmost importance that ICER develop a robust, systematic process for incorporating the patient perspective into its reviews. We urge ICER to develop this process in partnership with patients, patient organizations, and other experts in the field and make the process transparent and understandable to patients. Doing so will greatly improve the output of ICER's work and lead to greater credibility for the organization.

To facilitate the integration of patient perspectives in value discussions, the NHC convened a multi-stakeholder roundtable to develop a Patient-Centered Value Model Rubric<sup>2</sup>, a tool that the patient community, physicians, health systems, and payers can use to evaluate the patient centeredness and to guide developers on the meaningful incorporation of patient engagement throughout their processes. The roundtable participants identified six domains that encompass patient centeredness:

1. **Patient Partnership**, involving patients in every step of the value model development and dissemination process
2. **Transparency to Patients**, disclosing assumptions and inputs to patients in an understandable way and in a timely fashion
3. **Inclusiveness of Patient**, reflecting perspectives drawn from a broad range of stakeholders, including the patient community.

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<sup>2</sup> Learn more at: <http://www.nationalhealthcouncil.org/patient-centered-value-model-rubric-released>

4. **Diversity of Patients/Populations**, accounting for differences across patient subpopulations, trajectory of disease, and stage of a patient's life.
5. **Outcomes Patients Care About**, including outcomes that patients have identified as important and consistent with their goals, aspirations, and experiences.
6. **Patient-Centered Data Sources**, including data sources that reflect the outcomes most important to patients and capture their experiences to the extent possible.

The NHC strongly recommends ICER develop a formalized patient-engagement process as part of its value assessment framework that addresses the six domains outlined in the Rubric to ensure its value assessments are patient centered. Part of this formalized process could include an open process for stakeholders to nominate individuals from the patient and clinician communities to serve on relevant committees. The NHC would welcome the opportunity to work with ICER on this effort.

The NHC recommends that as part of each assessment, ICER explicitly describe how patient input and preferences were considered and incorporated to help ensure accountability to patients, demonstrate responsiveness to patient input, and help patients better understand the information ICER finds useful. Specifically, ICER should publicly make available its rationale for including or not including submitted comments. We recognize ICER has already made efforts in this area, for example in seeking patient perspectives for the draft scoping document on multiple sclerosis treatments and indicating specifically the aspects of the scoping document (such as choice of interventions or outcomes) that were informed by that input. Understanding why certain patient considerations were included and others were not underpins constructive collaboration. We urge ICER to produce outputs like this to demonstrate the impact of its engagement efforts.

Finally, we understand through recent public comments by ICER staff that the Institute is currently developing a roadmap for advocates to engage ICER. We commend you for this work and encourage you to seek input from the patient community on the roadmap. The NHC and our members look forward to working with you to further strengthen this document and all of ICER's patient-engagement activities.

## ***2. Incremental cost-effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures***

The NHC recognizes the importance of evaluating treatments and services to understand their comparative clinical and cost effectiveness. However, we stress that the appropriateness of outcomes selected is critical to the relevance and accuracy of determining value to patients. Whether in the context of QALYs or other measures, ICER should aim to gain a better understanding of whether a QALY and or the data it is based on, are from relevant patients and are meaningful to patients. We caution that endpoints that are translated into value assessments must be derived directly from information provided by patients to be relevant for value determination. Reliance on population-based assessments that do not reflect the heterogeneity of disease subpopulations and patient treatment responses, and patient preferences run the risk of mischaracterizing the imputed value of the treatments being compared. In addition, meaningful endpoints specific to patients and a disease state, such as alleviation of symptoms or the ability to be productive in work or home settings, may not be reflected by global or specific clinical measures that feed into a QALY, losing the opportunity to assess value on patient-centric outcomes. Again, input from the appropriate patient populations for identification of outcomes

that are important to them is critical to support a value assessment approach that is meaningful and has utility for patients.

**3. *Methods to estimate the market uptake and “potential” short-term budget impact of new interventions as part of judging whether the introduction of a new intervention may raise affordability concerns without heightened medical management, lower prices, or other measures.***

We are concerned that this priority appears to focus solely on identifying methods that would help assess short-term affordability from the payer perspective and result in restricted access to treatments as an unintended consequence for patients. The NHC urges ICER to, at minimum, consider long-term outcomes and impacts from the patient and payer perspective. While many interventions may have high short-term budget impacts, they may not only greatly improve patient outcomes but can reduce the costs for a patient and the health care system over a longer period of time by reducing the likelihood of more costly interventions and/or poorer outcomes such as frequent hospitalizations and/or surgeries. Many of these cost savings will not be realized for years and will likely be spread between patients – alleviating potential financial hardships – and entities such as private health plans, Medicare, Medicaid, and other social safety net programs.

Focusing on short-term (5 years or less) budget impacts in isolation, de-coupled from approaches that consider longer-term impacts over a lifetime horizon, is not an appropriate or meaningful patient-centered approach to assessing the impact and value of interventions and services. As articulated, this priority appears to focus too narrowly on the short-term impact on siloed costs.

**4. *Methods to set a threshold for potential short-term budget impact that can serve as a useful “alarm bell” for policymakers to signal consideration of whether affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.***

Again, the NHC has serious concerns with focus on short-term budget impact models. We urge ICER to acknowledge through its value assessment process that the measure of value to patients inherently extends beyond the short-term perspective that payers often adopt. We are concerned that emphasizing the budget impact of treatments using assumptions and arbitrary thresholds for short-term budget impact may be used as a rationale to restrict patient access, particularly when they are established without the context of any offsetting long-term benefits that are important not only to payers, but to patients and their families. This is particularly important in cases of chronic conditions, which impact patients during the course of their lifetime.

The NHC also suggests ICER move away from the terminology, “alarm bell,” which might incite knee-jerk reactions that lead to inappropriate access restrictions and other unintended consequences. Shifting to something like “indicator for proactive management to improve impact and outcomes” would be more conducive to collaborative, patient-centered approaches.

The NHC is eager to continue to partner with ICER as it works toward promoting greater patient engagement and integrating patient perspectives in the value assessment process. We would like to thank you for this opportunity to share our comments. Please do not hesitate to contact Eric

NHC Comments on ICER's Proposed Improvements to Value Assessment Framework

September 12, 2016

Page 5 of 5

Gascho, our Vice President of Government Affairs, if you or your staff would like to discuss these issues in greater detail. He is reachable by phone at 202-973-0545 or via e-mail at [egascho@nhcouncil.org](mailto:egascho@nhcouncil.org).

Sincerely,

A handwritten signature in black ink, appearing to read 'MBoutin', with a long horizontal stroke extending to the right.

Marc Boutin, JD  
Chief Executive Officer



National  
Multiple Sclerosis  
Society

September 12, 2016

Steven Pearson, MD, MSc, FRCP

President

Institute for Clinical and Economic Review

Boston, MA 02109

Via electronic mail: [publiccomment@icer-review.org](mailto:publiccomment@icer-review.org)

Dear Dr. Pearson,

The National Multiple Sclerosis Society (Society) appreciates the opportunity to respond to the Institute for Clinical and Economic Review's (ICER) national call for input for proposed improvements to its value assessment framework. The Society works to provide solutions to the challenges of MS so that everyone affected by this disease can live their best lives. To fulfill this mission, we fund cutting-edge research, drive change through advocacy, facilitate professional education, collaborate with MS organizations around the world, and provide services designed to help people affected by MS move their lives forward.

**ICER should ensure that its value assessment framework adequately emphasizes the patient's perspective**

We recognize that the concept of value is a fundamental component to the healthcare and health delivery system. We believe that considerations of value must include the perspectives of all stakeholders, especially those of people who live with MS and other diseases. Determining and incorporating the patient perspective on value is critical to strengthening ICER's value assessment framework. In our previous engagement with ICER, we have noted that patient preferences vary greatly through disease states and have cautioned against the use of a one-size fits all model.

We recommend that ICER incorporate the National Health Council's value rubric into the next iteration of its value assessment framework to help evaluate the patient-centeredness of its value model and aide in the development of a formal process for patient engagement throughout ICER's review process. The rubric, available in full [here](#), outlines the domains that must exist for a value framework to be considered patient-centered:

- Patient Partnership, involving patients in every step of the value model development and dissemination process;
- Transparency to Patients, disclosing assumptions and inputs to patients in an understandable way and in a timely fashion;
- Inclusiveness of Patient, reflecting perspectives drawn from a broad range of stakeholders, including the patient community;
- Diversity of Patients/Populations, accounting for differences across patient subpopulations, trajectory of disease, and stage of a patient's life;
- Outcomes Patients Care About, including outcomes that patients have identified as important and consistent with their goals, aspirations, and experiences; and

- Patient-Centered Data Sources, including data sources that reflect the outcomes most important to patients and capture their experiences to the extent possible

Incorporating the patient perspective in value discussions is a relatively new effort. Patient perspectives towards value tend to differ greatly from those of payers; therefore, there is a paucity of data regarding patient perspectives on value and how best to incorporate those attitudes into value frameworks.

Many organizations are working on methods and best practices to help facilitate the patient perspectives into value discussions. The Society is currently funding studies to better understand how people who live with MS view value and will share the findings of these studies with ICER when they are available. Additionally, we are participating in FasterCures and Avalere's Patient-Perspective Value Framework (PPVF) Initiative, which seeks to develop a value framework for assessing therapies, diagnostics, and other healthcare services, which is in line with patients' concepts of value. We recommend ICER develop a formal process to routinely solicit feedback from all relevant stakeholders, as new information and data is generated that will help incorporate the patient's perspective on value into frameworks that assess the value of new innovative treatments and therapies as they are utilized by the health care system.

### **ICER Should Actively and Transparently Engage Patient Community and Stakeholders**

We believe that ICER should expand its engagement with patients, patient and caregiver organizations, and clinical experts throughout its review of the specific diseases areas. The Society would like to thank ICER for implementing its survey to gain insight directly from people living with MS during its *Review of Drugs for Relapsing-Remitting and Primary Progressive MS* and believe that this type of engagement with patients should be part of a formal process for engaging with patients, patient organizations, and stakeholders. Ideally, this engagement should begin well in advance of ICER's review process to ensure that background, scoping documents and review reflect the consensus of these communities within the particular disease area.

Additionally, ICER could improve its current process by being more transparent regarding its consideration of the feedback it obtains from stakeholders during its outreach. We appreciated the engagement and incorporation of feedback from the MS community as a part of ICER's MS review, but believe this engagement could be strengthened by providing a formal transparent process that identified what feedback was or was not incorporated into the final ICER review and stating the reasoning behind these decisions.

### **ICER should utilize alternatives to the Quality Adjusted Life Year**

The Society has previously recommended that ICER should clarify its calculation of the quality adjusted life year (QALY), particularly as there are concerns that a cost-per-QALY cannot adequately account for the value of substantially improving the life of a person with a disability or serious medical condition. ICER should examine both alternative approaches and health utilities such as disability adjusted life years, which may enable payers to develop policies that better reflect individual patient values.

**ICER should examine health care utilization outcomes by gauging direct and indirect costs**

We believe that any model used should examine both direct and indirect costs of the disease area under review: including long-term care, lost wages, the cost of drugs, the cost of outpatient care, the cost of rehabilitation, and the cost of assistive technology. These are all critical economic impacts that are not reflected by traditional health care utilization outcomes such as emergency room visits or inpatient stays. Additionally, ICER should allow public comment on the economic model that is used to allow for feedback on new or innovative models that would better reflect the economic costs of different disease areas.

**ICER should incorporate additional sources and types of data for evidence reports**

The Society believes that ICER should look beyond randomized clinical trials (RCTs) within its evidence reports. In our previous correspondence to ICER, we noted that RCTs are not designed, controlled, conducted, or powered to establish the cost effectiveness of a therapy or the impact of a therapy on the evolution of disability in the course of MS over a clinically-relevant time period. RCTs provide limited data, real-world treatment impacts, or information on patient reported outcomes and therefore alternative data should be utilized. Additionally, information on the range of studies that ICER uses should be discussed amongst stakeholders before scoping and background documents are released for public comment, so that stakeholders can understand and help assess the usefulness of those studies for decision-making.

**ICER should broaden its cost perspectives beyond 5 years**

ICER's current practice of using a five-year timeframe for calculating budget impact may not fully capture the benefits of the current disease modifying therapies, especially for chronic diseases like MS. ICER should utilize feedback from stakeholders and clinical experts to determine an appropriate timeframe to accurately assess the full impacts based on available data.

Specifically in MS, the five year timeframe is problematic as it is unlikely to fully capture the economic benefits of delaying disease progression, particularly lower health care utilization costs, thought to result from the use of disease modifying treatments. There is growing evidence that suggests early and consistent treatment will have benefits for people living with MS that extend for a decade or longer; therefore we believe that at least 10 years will be needed to determine the impacts for a review of MS therapies.

Thank you for the opportunity to comment on this iteration of ICER's value assessment framework. If you have any questions, please contact Leslie Ritter, Senior Director, Federal Government Relations at [leslie.ritter@nmss.org](mailto:leslie.ritter@nmss.org) or 202-408-1500. We look forward to continued discussions.

Sincerely,



Bari Talente, Esq.  
Executive Vice President, Advocacy



September 12, 2016

Institute for Clinical and Economic Review  
Two Liberty Square  
Ninth Floor  
Boston, MA 02109

**Re: ICER National Call for Proposed Improvements to its Value Assessment Framework**

Dear Dr. Pearson:

On behalf of the 30 million Americans with one of the nearly 7,000 known rare diseases, NORD thanks the Institute for Clinical and Economic Review (ICER) for the opportunity to provide comments on the Institute's proposed "Value Framework Assessment 2.0".

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

We are committed to fostering an ecosystem that encourages the development and accessibility of safe and effective therapies for rare disease patients. We are excited by the advent of value frameworks, and believe that value frameworks, if developed collaboratively and used responsibly, can provide objective analysis for assessing the value of therapeutic interventions.

People with rare diseases have a uniquely important role to play in value framework development. Almost every input into a value framework involves the personal experiences of people with rare diseases and their families. With patient-centricity fueling innovations in rare disease research and drug development, it is critical that any and all value frameworks place the patient at the center of its creation.

It is for these reasons that we are pleased to provide comments on ICER's "Proposed Improvements to its Value Assessment Framework". The below comments are organized to reflect ICER's prioritized areas for improvement.

**1. Methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value intended to fall in the current value framework within "additional benefits or disadvantages" and "contextual considerations"**

We commend ICER for the stated goal of appropriately integrating patient perspectives on the value of interventions. While laudable, we are unconvinced the proposed practices will achieve this goal.



First, due to the inherently small and dispersed patient populations common in rare diseases, there is often a dearth of scientific literature or understanding in the disease. The vast majority of rare diseases are rarely researched or given any attention by the scientific and medical professions. It is for these reasons that if ICER is looking to integrate existing publications for rare diseases into their value assessment, they will likely come up empty.

Even when there is current scientific literature available, it is often outdated, or archaic in its formulation. We are only now starting to conduct scientific and medical research in partnership and collaboration with the patient. For ICER to rely on existing scientific literature without assessing its patient-centricity, ICER will be departing from its stated patient-focused goal.

We understand this may limit ICER's ability to use existing sources, perhaps precluding their use entirely. This underscores even further the importance of partnering with patients and patient organizations in assessing "additional benefits or disadvantages" and "contextual considerations".

In doing so, ICER must not make the same mistakes many others have already made. ICER cannot rely on one or two patients to represent the entire patient population with the disease. ICER cannot rely on one or two researchers or physicians who treat the disease.

ICER must not even rely on one patient organization to collaborate with. People with rare diseases who have a patient organization representing them are actually quite fortunate, as most rare diseases have no representative organization. ICER must consider this, and work to collaborate with the existing networks of patients in place if no established organization exists. But some rare diseases are fortunate to have multiple organizations representing the population. It is critical to include all viewpoints, perspectives, and opinion across the patient, physician, and patient organization landscape.

ICER must also give patient organizations the required amount of time to appropriately participate. It is our understanding that ICER's public comment period for various documents generally are allotted three to four weeks. This is entirely inadequate, particularly for rare disease patient organizations. NORD has over 250 rare disease patient organizations as members. Over 70 percent of our members have fewer than five full-time employees (FTEs) conducting the entirety of the organization's operations. To require these organizations to comment on a lengthy and incredibly esoteric economic analysis in a matter of weeks is absurd.

If ICER is truly committed to collaboration with patients and their organizations, they will recognize the realities rare disease patient organizations operate under.

Finally, we understand that "a comprehensive Patient Participation Manual is under development". It is our understanding that ICER is partnering with one patient representative in the development of this manual. While we thank ICER for the intent of this effort, ICER is committing one of the errors we are concerned about: using one person as the sole representative of the entire patient and patient organization community. It is not enough to request feedback from the patient community on the patient engagement manual once completed. The patient community must be involved in its development from its inception, just as if it was a value framework.

## **2. Incremental cost-effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures**

The use of incremental cost-effectiveness ratios using QALYs has become a standard practice in the health economics and value framework field. However, we are concerned these methods used within ICER's framework could inaccurately assess the therapy's value for the patient population.

Similar to the problems with using existing scientific literature (or lack thereof), the willingness-to-pay (WTP) values used to evaluate quality-of-life improvements or declines, in many, if not most, existing assessments were not developed in coordination with patients. As discussed in ICER's publication titled "Addressing the Myths About ICER and Value Assessment", the "QALY was developed by health economists and doctors..." Notably absent are the patients.

ICER later adds that it "select(s) quality of life scores whenever possible from individuals who have the condition rather than asking people without the condition to judge 'how bad' it would be to have that disease". While this is certainly preferred, it is incredibly unlikely that existing WTP valuations exist for individuals with most rare diseases let alone subpopulations within those diseases. It is not enough to include patient-generated data only when available.

For ICER to craft truly representative incremental cost-effectiveness ratios, they must do several things in collaboration with patients and patient organizations. ICER must survey a representative sample of patients with the disease across the entire disease progression and spectrum on their WTPs for quality-of-life improvements or declines. ICER must also craft a disease-specific and subpopulation-specific assessment of the baseline quality-of-life assessment for each subpopulation. Simply extrapolating existing analyses on the quality-of-life from other diseases or symptom estimates would result in fallacious findings. ICER must also include the WTPs of families and caregivers for each specific subpopulation.

Again, partnering with patients and their organizations is critical to overcoming these hurdles.

## **3. Methods to estimate the market uptake and "potential" short-term budget impact of new interventions as part of judging whether the introduction of a new intervention may raise affordability concerns without heightened medical management, lower prices, or other measures.**

We join many in the patient community in finding ICER's prioritization of short-term budget impacts troubling. It is our understanding that ICER assesses therapies within the short-term budget impact of one-year because this is the window of time in which payers assess their actuarial soundness, set their premiums, and structure their benefit design. While we understand the need to be useful to payers by fitting within their schedule, it should not come at the cost of accurate valuation of therapies.

In addition, using a five-year time window for "long-term budget impacts" will also substantially devalue various therapies. For example, we are on the cusp of a medical breakthrough in gene therapy and gene editing technology. We will likely see within the next decade the availability of cures for previous incurable genetic disorders.

If ICER only values these therapies over a five-year window, ICER will ignore years, perhaps even decades, of vastly improved quality-of-life for these patients. ICER should craft its time windows to specifically reflect the therapy and disease it is treating instead of adopting a one size fits all approach.

**4. Methods to set a threshold for potential short-term budget impact that can serve as a useful “alarm bell” for policymakers to signal consideration of whether affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.**

Here again we are concerned with ICER’s approach. ICER again appears to be prioritizing short-term budgetary impacts through the lens of the insurer. Arbitrary thresholds should not be used for incredibly case-specific analyses. We also agree with the National Health Council in suggesting “ICER move(s) away from the terminology ‘alarm bell,’ which might incite knee-jerk reactions that lead to inappropriate access restrictions and other unintended consequences”.

Overall, we implore ICER to be cognizant of the responsibility they bear in crafting these value frameworks. While ICER’s motives may indeed be patient-centric, their work can very easily be used in anti-patient ways. We believe it is ICER’s duty to take responsibility for how their analyses can be used, and do everything in its power to responsibly and collaboratively craft an unbiased publication.

We are unsympathetic to defenses of ignorance or time constraints for publishing analyses that misrepresent the value of therapies and lead to limited access to patients. For ICER to succeed, we expect them to carefully, thoughtfully, and collaboratively assess the value of therapies no matter the time and resource investment it takes.

We thank ICER for the opportunity to comment, and we look forward to working with ICER to accurately and collaboratively assess the values of therapeutic interventions. For questions regarding NORD or the above comments, please contact me at [mrinker@rarediseases.org](mailto:mrinker@rarediseases.org) or (202) 588-5700, ext. 102.

Thank you in advance for your consideration.

Sincerely,

A handwritten signature in blue ink, appearing to read "Martha Rinker", is written over a light blue rectangular background.

Martha Rinker, J.D.  
Vice President, Public Policy



September 12, 2016

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

**RE: Call for Proposed Improvements to ICER's Value Assessment Framework**

Submitted electronically via: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

Dear Dr. Pearson:

The National Pharmaceutical Council (NPC) shares your interest in recognizing the many components of health care value, and in using evidence as the cornerstone for making the health care system more effective and efficient. With this view in mind, NPC appreciates ICER's call for comprehensive and directed suggestions for improvements to the ICER Value Assessment Framework. NPC recognizes the changes you have made to the framework to date, including the two highlighted in the call for comments.

As you know, NPC is a health policy research organization dedicated to the advancement of good evidence and science, and to fostering an environment in the United States that supports medical innovation. NPC is supported by the major U.S. research-based biopharmaceutical companies. We focus on research development, information dissemination, education and communication of the critical issues of evidence, innovation and the value of medicines for patients. Our research helps inform critical health care policy debates and supports the achievement of the best patient outcomes in the most efficient way possible.

As stated in NPC's *Guiding Practices for Patient-Centered Value Assessment (Guiding Practices)*,<sup>1</sup> we believe value assessments can be an important tool for the complex decisions organizations and patients face when considering treatment options. Assessments that adhere to the *Guiding Practices* can support optimal value for patients. There are several key areas where changes to ICER's current value assessment framework will create more alignment with the *Guiding Practices*.

The most critical of these areas is the assessment of budget impact and the way it is intertwined with value, most notably the calculation of a "value-based benchmark price." The *Guiding Practices* state that budget impact assessments — which are measures of resource use, not of value — should remain completely separate from value assessments. Other key areas are highlighted below.

## I. Care Value

ICER's evaluation of "care value" is aligned with the *Guiding Practices* in several areas. For example, the time horizon is long-term, a broad array of factors that are important to patients and society are considered (albeit qualitatively, which does not give these important, patient-centered factors sufficient impact), and cost offsets are included. However, there are areas of misalignment in the care value evaluation, most notably the use of a single quality-adjusted life year (QALY) threshold across all populations and diseases (further detail below).

ICER does reach out proactively to manufacturers and provides high-level information. However, this level of information is not sufficient to enable reviewers to reproduce the results and provide meaningful, real-time input. Full transparency — down to the equation level — is needed to enable reproducible results and support fully informed stakeholder collaboration. NPC recommends releasing the model to all stakeholders along with the draft report, perhaps on a protected web-based platform. Furthermore, (expedited) peer review of the model before it is finalized is recommended.

NPC recommends the routine use of sensitivity analyses. Many judgements come into play when conducting meta-analysis and cost-effectiveness analysis, thus, sensitivity analyses are critical to examine whether the findings were influenced by any decisions made in the analysis. Sensitivity analysis can also be used to explore heterogeneity of treatment effects, avoiding an over-reliance upon methods based on averaged estimates. The accuracy of these analyses is in question when no sensitivity analyses have been performed to test the assumptions of the model.

Heterogeneity occurs not just at the patient level, but at the payer level, too. The health care system in the U.S. includes quite diverse payers and payment systems. Applying a framework and decision criteria that are similar to those used in a relatively homogenous and centrally driven payer health care system does not include the range of decision attributes for relevant U.S. stakeholders. Ideally, the value framework should present a transparent and modifiable output that allows the user to adjust any cost-effectiveness results according to user/health plan preferences and decision needs, and to include the range of factors of interest to that user.

### A. Integrating "Additional Benefits or Disadvantages" and "Contextual Considerations"

*ICER seeks: Methods to integrate patient and clinician perspectives on the value of interventions that might not be adequately reflected in the scientific literature, elements of value intended to fall in the current value framework within "additional benefits or disadvantages" and "contextual considerations."*

As noted above, ICER assessments attempt to include a broad array of factors that are important to patients and society. However, these factors are currently incorporated in a qualitative manner as "additional benefits and disadvantages" and "contextual considerations," and it is incumbent upon the voting panel to recognize the value of these factors and reflect them in their care value vote. This qualitative inclusion does not allow these important, patient-centered factors to have a strong enough — or consistent — impact on an assessment. ICER is seeking methods for more

formal integration, and NPC agrees it is important to include these factors in a more robust and representative manner.

ICER's current approach leaves the consideration of these factors up to the discretion of the voting panel, which may not have the expertise or appropriate context to meaningfully evaluate them. Moreover, this valuation approach is heavily dependent upon the perspectives and values of a small group, and is not transparent. This approach is insufficient to incorporate the impact of these important patient-centered factors.

Previous work by ICER identifies many examples of these factors (see tables below),<sup>2</sup> which can indeed be quantified and incorporated into a composite measure of benefit or effectiveness.

| Stakeholder                 | Additional Benefits  |
|-----------------------------|--|
| Patient, Family, or Society | Benefits of treatment that extend beyond patient-specific health improvement, e.g. reduction in care needed from friends and family, earlier ability to return to work |
|                             | Allows expansion of eligible population for treatment  |
|                             | Removes or reduces barriers to treatment through new route or delivery mechanism   |
| Providers/Delivery System   | Presence of quality target(s) for which the treatment will improve performance   |
|                             | Other practical advantages related to preparation/storage/delivery of the treatment  |

| Contextual considerations                       | Contextual considerations favoring coverage/preferred status                                  |
|---|---|
| Other treatment options                         | No other acceptable treatments exist  |
| Heterogeneity of Treatment Effect               | New/different mechanism of action in setting of significant heterogeneity of treatment effect |
| Professional standards                          | Consensus among professional statements on appropriate use                                    |
| Societal values regarding the illness/condition | High severity and/or priority condition<br>Vulnerable population (e.g. children)              |

There are many precedents and good examples of cost-effectiveness in health care that optimize the assessment of clinical effectiveness with both individual and composite measures (rather than the sole use of the QALY).<sup>3,4,5</sup> Research — particularly in worksite health promotion — has shown how some aspects can be quantified and used to incorporate indirect costs into cost-effectiveness models. A notable example is quantification of productivity loss using the Work Productivity and Activity Impairment (WPAI) Questionnaire in the assessment of absenteeism, presenteeism, and daily activity impairment due to general health or due to a specific health condition; it has been widely used and validated in the study of many diseases.<sup>6</sup>

In instances where it is feasible to do so, quantitative credit should be given for these factors. In instances where there is not yet a quantitative path forward, the qualitative inclusion of such factors in the models should be formalized as part of the framework so patient-centered concerns can be meaningfully considered in the care value assessment. Examples of transparent methods of structuring qualitative assessments come from both EMA and the FDA in how they conduct their benefit-risk assessments.<sup>7,8</sup>

Recognizing the heterogeneity of payers in the U.S., the value framework should acknowledge that different users will have different preferences for including/excluding these factors, and allow for user customization of factors and weights for said factors.

## **B. Incremental Cost-Effectiveness Ratios**

*ICER seeks: Incremental cost-effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures.*

ICER's current assessments apply the threshold range of \$100,000 to \$150,000 per QALY. This approach is inconsistent with the *Guiding Practices*, which emphasize that no single threshold can or should be universally applicable, as thresholds are likely to vary by population and disease. In setting particular thresholds, the *Guiding Practices* also recommend a multi-stakeholder evaluation process reflecting societal values.

The thresholds are used by ICER to set a “value-based price,” on which stakeholders and the media focus. Using a threshold that is not applicable for a population or disease produces an invalid value-based price, yet decisions will be made based on this price. NPC recommends moving away from a cost-effectiveness-derived, value-based price as a single number to a discussion about the implications for various parameters/assumptions in the cost-effectiveness evaluation for a specific disease or condition. ICER could instead lead the conversation about what the best parameters and assumptions are when it comes to modeling cost-effectiveness for a specific disease. (NPC notes this recommendation is specific to the “care value” value-based price and not the “budget impact” version.)

## **1. The QALY Has Serious Limitations and Caution Should be Exercised in its Use**

A cost-effectiveness ratio is used to determine if a treatment provides good value (expressed as a health outcome) relative to its cost.<sup>9</sup> Different treatments produce different health outcomes and it can be difficult to compare across such a wide variety of outcomes. The QALY is designed to express a variety of outcomes in a composite measure (that combines length and quality of life) so they can be compared more easily. However, the QALY has not proven fit for purpose for this goal.

Use of the QALY poses several serious limitations, primarily ethical considerations, methodologic issues, and disease-specific considerations.<sup>10</sup> The QALY is designed to maximize health, which excludes other treatment benefits that are of importance to patients (e.g., productivity). Maximizing health is not always the focus of treatment, particularly for drugs that treat the elderly, in which case health care and social care are inevitably intertwined.<sup>11</sup>

The QALY traditionally includes physical domains (e.g., mobility), but does not effectively capture mental and social domains, which have been rated as more essential for inclusion in a health-related quality of life measure than physical domains.<sup>12</sup> This is especially important for treatments for conditions that improve quality of life but do not extend life per se.

Other shortcomings of the QALY include:

- QALYs may undervalue survival benefits in populations presumed to have poor quality of life, e.g., Oncology and CHF patients;
- Cost per QALY approaches may under-incent development of orphan/rare disease products, which face a number of economic cost-effectiveness challenges;<sup>13</sup>
- Treatments for acute conditions may be undervalued;<sup>14</sup> and
- Age differences are inadequately managed, i.e., interventions in youth are inherently valued above those targeted for later in life.

The ECHOUTCOME project tested the validity of the assumptions underlying the use of the QALY and found it to be an invalid measure. The researchers note its use leads to inconsistent recommendations on access to innovative health technologies and medicines, and that HTA groups should use other methods.<sup>15</sup>

ICER itself identifies some of the key problems with the QALY:

Whereas many international payer agencies have adopted the QALY as a universal metric of health outcomes by which to analyze comparative net health benefit across different types of medical interventions, very few payers in the US use the QALY in a systematic way. In part this is because of methodological concerns about whether the QALY adequately reflects the preferences of patients for different types of health outcomes. There are long-standing concerns that QALYs fail to capture important societal values favoring health benefits for patients with the most severe illnesses. And QALYs usually



must be estimated from published literature through analyses that can be complex, time consuming, and ultimately lacking in the degree of transparency that is one of the most important goals of a value framework. The methodological concerns are most relevant when QALYs are used as part of analyses comparing the incremental cost-effectiveness of treatments for different conditions.<sup>16</sup>

ICER's current approach of using the QALY as the sole measure of effectiveness in its evaluations is not addressing the very limitations stated above.

Taken together, these serious limitations should be acknowledged and alternative weighting/approaches included in ICER's value framework. No single measure or set of measures will be optimal across evaluations. Measures of benefit and effectiveness can, and should, vary across evaluations.

Ideally, alternative approaches should be designed by the research community to incorporate the additional benefits and contextual considerations referenced in the previous section. This would mean that the QALY would be replaced with more appropriate and sensitive measures. Cost-effectiveness analyses do not require that the QALY be used; given that the QALY is often not fit for this purpose, it should be replaced with suitable alternatives. Caution should be exercised with its use, and the limitations of its use should be explicitly stated when it is used.

## **2. Thresholds Will Vary Across Diseases and Populations**

If the QALY is used (despite the limitations noted above), it should be recognized that no single threshold can or should be universally applicable, as thresholds are likely to vary by decision-maker, population, and disease. Neumann states:

...it is impossible to find a single threshold to represent society's willingness to pay for QALYs gained, because different approaches yield different values, each of which is based on different assumptions, inferences, and contexts. Searching for a single benchmark is at best a quixotic exercise because there is no threshold that is appropriate in all decision contexts.<sup>17</sup>

Evidence exists that willingness to pay for minor conditions is less than that for life-saving conditions.<sup>18</sup> Willingness to pay for oncology suggests thresholds as high as \$300,000/QALY.<sup>19,20</sup> QALY thresholds are ill-defined for acute, short-term treatments such as anesthesia, for which the benefit of reduction of pain and suffering is measured in literally minutes or hours. The resulting cost per QALY calculation can be stratospheric, but no one would realistically suggest operating without anesthesia because a QALY threshold has been crossed.

It is very hard (and politically unpalatable) to declare one condition more important than another. However, just because it is hard does not mean that it should not be done. Given this evidence, thresholds should vary for different decision-makers, diseases, and populations, if they are used at all.

### 3. Perspective

Cost-effectiveness should, at a minimum, take a societal perspective and not a payer perspective. The societal perspective can allow for many additional constructs to be considered, such as “value of innovation” and “value of scientific spillover.” A societal perspective will ensure that appropriate cost-offsets are included and not just those that will be accrued by the payer.

An even better approach would be to take the emerging importance of a “Patient Perspective,” which is usually consistent with the societal perspective but allows for constructs that matter significantly to patients (e.g., the “value of hope”) to be considered. Finally, ICER should clearly state the perspective it takes and be ready to address issues of inclusion and exclusion in both its assessment of benefit and cost.

### 4. Indirect Treatment Comparisons

The limitations of indirect treatment comparisons are well known. ICER’s reliance upon this approach is problematic and can lead to significantly flawed conclusions. Use of indirect treatment comparisons in the absence of direct head-to-head comparative data suffers from an inability to fully adjust for differences in trial populations and protocols.

For example, for the review of relapsing-remitting MS (RRMS), comparisons across trials on annualized relapse rate (ARR) may be complicated by changes in relapse rates over time, suggesting changes in the natural history of disease. The time periods over which ARR are calculated also differ from one trial to another. Differences in inclusion and exclusion criteria, baseline characteristics between trials, and even variability in definition of key outcomes can introduce bias in indirect treatment comparisons across MS trials.<sup>21,22</sup>

Indirect treatment comparison is especially problematic in the instance of emerging/unapproved products or for evaluation of off-label usages for products, for which available comparative information is very limited and the overall evidence base has not been finalized by regulatory organizations. ICER should focus on FDA-approved products and evaluate indications based on well-controlled clinical trials (rather than integrating earlier reviews of unapproved products and incorporating products used for off label purposes), and limit firm comparative conclusions to circumstances when direct comparative data exist and heterogeneity between populations and studies is limited.

## II. Budget Impact

ICER’s evaluation of “health system value” — which confounds budget impact and value — is not aligned at all with the *Guiding Practices*. Addressing this misalignment is of paramount importance to support informed health care decision-making.

Budget impact assessment is a measure of resource use, not a measure of value, and it has no role in value assessment. Eliminating budget impact assessment completely from ICER's reviews is the most definitive way of keeping the concepts separate. An alternate (but less definitive) method of keeping the concepts separate is to refrain from moving beyond an estimate of budget impact into an assessment of affordability. NPC strongly recommends that ICER revise the framework in a manner that ensures this separation of budget impact and value.

Accordingly, "Health System Value" should be renamed "Short-Term Budget Impact." The name "health system value" is misleading and suggests that the assessment is representative of health system benefit relative to health system cost. In fact, ICER's assessment is simply an estimate of budget impact, and should be referred to as such.

#### **A. Market Uptake and "Potential" Short-term Budget Impact**

*ICER seeks: Methods to estimate the market uptake and "potential" short-term budget impact of new interventions as part of judging whether the introduction of a new intervention may raise affordability concerns without heightened medical management, lower prices, or other measures.*

An estimate of budget impact is a necessary but insufficient part of evaluating affordability. NPC offers recommendations on estimating uptake rates and short-term budget impact with the explicit caveat — as per the *Guiding Practices* — that it is not appropriate to hold a budget impact estimate up against an artificial affordability threshold.

Budget impact assessments are important to payers. They will be most relevant to payers if the assessments are realistic and representative of the varied scenarios individual payers may face. Since there is no single U.S. national health care budget holder, the current approach is neither realistic nor representative of these scenarios.

There are three key components to the budget impact assessment: utilization, price, and time horizon, all of which need improvement under ICER's current approach. The current approach creates upwardly biased budget estimates, which can have unintended consequences for chronic diseases that impact large populations (e.g., Alzheimer's).

##### **1. Use Realistic Estimates of Utilization and Include Sensitivity Analysis**

The *Guiding Practices* recommend the use of realistic estimates regarding a treatment's uptake rate. ICER assessments currently unrealistically assume unmanaged utilization and incorporate ICER predictions for the level of uptake after five years. A recent study found that the ICER one-year uptake rate estimates for PCSK9 inhibitors were significantly overestimated.<sup>23</sup> More realistic utilization estimates would: (1) be based on the typical medication management that payers would use to impact utilization in the clinical area of interest, (2) incorporate uptake predictions from manufacturers, clinical experts, and/or analysis from claims database of recently launched products or similar analogues, (3) be

limited to the populations in scope, and (4) use sensitivity analysis to capture uncertainty and the range of possible uptake rates.

## **2. Use Realistic Estimate of Price**

The *Guiding Practices* recommend use of costs that are representative of the net price most relevant to the user. The “list price” that ICER assessments currently utilize does not represent the actual discounted price that is relevant to, and negotiated by, payers. Using third-party data to obtain an industry-wide discount rate estimate and conducting sensitivity analysis around this rate (using a range of discount assumptions) would provide a more realistic price estimate. Following International Society for Pharmacoeconomics and Outcomes Research (ISPOR) good research practices for measuring drug costs is recommended.<sup>24</sup>

The *Guiding Practices* recommend incorporating reductions in cost due to generic entry. For example, in the multiple sclerosis class review, there are three oral medications (dimethyl fumarate, fingolimod, and teriflunomide), which will have generic alternatives available during the assessment time horizon. Third-party data and existing research<sup>25,26</sup> can be used to provide estimates of the expected reduction in price due to generic entry, and this reduction should be included in the budget impact estimate.

## **3. Use Multiple Time Horizons, Including Lifetime**

For the time horizon, budget impact assessments face the tension between payer budget windows (1-2 years) and long-term horizons that matter to patients and capture more cost offsets. ICER assessments currently use a five-year window as a compromise. Projecting budget impact should include time horizons that are relevant for the specific assessment. Using multiple time horizons, including a lifetime horizon (when applicable), could better satisfy the needs of all stakeholders.

Using uptake rates and prices that are higher than the managed uptake rates and discounted prices that payers will actually face biases ICER’s budget impact estimates upwards. A recent analysis by the Partnership for Health Analytics Research (PHAR) estimated the difference in ICER’s one-year prediction of the cost for the PCSK9 inhibitors and actual spending.<sup>27</sup> ICER predicted \$7.2 billion, while actual sales are estimated to be \$83 million. The magnitude of the difference between these two estimates is so large that it raises significant concerns over using the ICER budget impact estimates for decision-making.

## **B. Affordability**

*ICER seeks: Methods to set a threshold for potential short-term budget impact that can serve as a useful “alarm bell” for policymakers to signal consideration of whether affordability may need to be addressed through various measures in order to improve the impact of new interventions on overall health system value.*

### **1. Separate Budget Impact from Affordability**

Short-term budget impact is a measure of resource use and should remain separate from affordability. Affordability is an important concept for society. Evaluating affordability involves making assessments and trade-offs at an overall health system level (i.e., a broad assessment of all investments in a health care system) and beyond the health system (i.e., spending on health care vs. other societal considerations such as education, police, and roads).

A comprehensive approach to affordability requires considerations of concepts such as disinvestment and willingness to pay, needs to be informed by cultural and societal values and by health and non-health needs, and requires broad stakeholder involvement. ICER’s current approach to assessing affordability — setting an “alarm bell” threshold — is not a comprehensive consideration of the health care system, does not consider societal values, and does not adequately measure affordability. In addition, it creates unnecessary fear and anxiety around the numbers.

Not only would an affordability assessment require decisions about health care spending vs. non-health care spending, it would also require societal decisions about intra-health care spending — tradeoffs regarding spending on the elderly versus the young, rare versus common disease, curative therapies versus prolonging life versus quality-of-life enhancement, as well as allocations between medications, surgery, hospital care, and physician services. ICER’s current framework and stakeholder input process does not incorporate these broader factors required to assess affordability and therefore its focus should not extend beyond an assessment of budget impact; the assessment of affordability should be eliminated.

### **2. Artificial Affordability Caps and Derived Prices are Inappropriate**

The *Guiding Practices* state that an assessment of budget impact should not be judged against artificial affordability caps. As noted above, an affordability assessment needs to look broadly at all health care spending that is relevant to achieving a given health outcome. ICER looks more narrowly at a particular treatment and determines whether spending on that treatment might exceed a fixed portion of drug expenditures.

ICER’s current approach of setting a uniform “alarm bell” threshold based on a fixed portion of drug expenditures creates an artificial affordability cap that does not conform to historical

drug spending patterns and could have negative, unintended consequences. A forthcoming analysis by IMS and NPC demonstrates this fact.<sup>28</sup> It shows that substantial variability exists in new-drug spending across years, as well as for individual drugs within years. Setting a single spending cap at the individual product level as ICER does presupposes that drug spending is relatively uniform and predictable across and within years.

Furthermore, the IMS/NPC analysis shows that only a very small percentage of drugs each year exceed the artificial cap created by ICER. Since the large majority of products are well below the threshold, that makes headroom for those very few products which might have a larger expected budget impact. A single threshold applicable to all new drugs does not consider this empirical reality. Since substantial variation does exist, and very few products exceed the ICER-specified cap, setting a single budget threshold at the individual product level and using it as a revenue cap is inappropriate and has the potential for significant unintended consequences.

One such unintended consequence is the disincentivization of development of drugs for broad populations with unmet need. Predictions for budget impact will increase as the predicted number of patients increases, causing a treatment for a broad population to be more likely to trigger an “alarm bell” threshold. However, a comprehensive affordability assessment that considers societal values and the broader public health perspective would likely result in a higher spending allocation for such a treatment.

The ICER threshold equation assumes that the allocation of health care spending among drugs, hospital care, imaging, and physician care is the “correct” allocation across resources. Perhaps more should be spent on drugs and less on imaging for optimal resource allocation, or vice versa. The derived threshold assumes that the current allocation is optimal, an unproven assumption that is likely incorrect.

Additionally, the ICER threshold equation is benchmarked to the annual GDP growth rate plus one percent. This is counter to innovation patterns that may occur periodically rather than at a constant rate.

ICER could provide a ranged budget impact assessment based upon sensitivity analysis. Linking that assessment to “affordability” to derive “value-based prices,” however, would not be appropriate based upon the issues highlighted above. Identifying the potential range of budget impacts and raising the need for public dialogue among all stakeholders for high budget impact therapies is more appropriate.

### **III. Assessment Process**

ICER’s assessment process includes advance notifications of assessment topics and an opportunity for all stakeholders to submit public comments on scoping documents and reports (albeit the time to do so is too short), which are in alignment with the *Guiding Practices*. There are, however, many areas of concern where the assessment process can be made more robust.

## **1. Bring Broader Stakeholder Representation into the Process**

ICER has sought to improve stakeholder engagement over the past year. The introduction of engagement guides for manufacturers and patients has been helpful to those groups. Some manufacturers have expressed appreciation for the proactive outreach and earlier engagement that ICER has implemented in more recent reviews, but much more can be done to bring broad stakeholder representation into the assessment process. Although outreach is occurring, much greater engagement and feedback of patient groups is needed. NPC recommends using “The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric” as a guide to ensure the patient community is engaged throughout the process.<sup>29</sup>

## **2. Include Broader Perspectives and Clinical Expertise to Voting Panel**

Although a variety of perspectives are represented at ICER meetings, comments made by panel participants during meetings often suggest they are approaching value assessment solely through a cost-focused lens. Panel members should have a broader view of value beyond cost, and should be more diverse in their views.

Providing a mechanism for stakeholder representatives (e.g., consumer, industry) to receive nominations for inclusion on a panel, which would be reviewed by a separate committee, could bring this broader perspective to the panels.

It also is important for multiple voting panel members to have expertise in the disease area under discussion to improve clinical accuracy of their assessments. Such expertise was lacking in the recent multiple myeloma panel.

Voting panel members should also receive some level of (independent) training on the fundamentals of cost-effectiveness and value assessments. It was apparent that some members of the multiple myeloma panel were unfamiliar with the concept of an incremental cost-effectiveness ratio and how to interpret it.

## **3. Extend Length of Time for Review and Seek Broader Feedback**

ICER has extended the time for stakeholders to submit comments on scoping documents and reports, but the amount of time is still too short. Patient groups, in particular, have reported difficulty with the limited time that is available to review an assessment report, identify key issues and concerns, and develop constructive comments. Additionally, smaller companies — which lack the manpower to address these labor-intensive requests for information in short order — may be at a disadvantage relative to larger firms with more resources and experts in residence.

The need for more time becomes even more important as ICER requests more detailed, technical feedback (e.g., in their recent efforts requesting information on preliminary model inputs and assumptions). Although the requests are welcome, manufacturers as well as patient groups and other stakeholders require sufficient time to review and respond to such detailed requests.

Only three clinicians chose to comment on NSCLC review, perhaps reflecting the difficulty and time intensiveness of this process. Thus, ICER should consider doing more outreach. ICER is trying to get reviews out quickly, which does not provide enough time for stakeholders to fully engage. Form should follow function, and sufficient time should be allowed for meaningful review and feedback by all interested stakeholders.

#### **4. Review Assessments Regularly**

The *Guiding Practices* recommend that assessments be reviewed regularly and updated to keep pace with and account for medical innovation. ICER currently has no plans to revisit and revise any assessments, let alone specify through what process they would update an assessment in the face of an evolving standard of care and/or new evidence.

The shelf life for ICER assessments is short, and some are already out of date as new evidence has become available and new treatments have been approved. For example, the multiple myeloma review was out of date within a couple of weeks of its publication, as new data were made public at the ASCO meeting that could not be shared prior to their presentation at a scientific forum.

NPC recommends that ICER have a clear process for managing the evolution of evidence, especially in the case of emerging therapies. This is of particular concern as these reviews are conducted in the absence of a full picture of a therapy's benefits and disadvantages, yet these reviews will continue to be relied upon by other stakeholders even after additional data (e.g., real-world evidence) emerge. Drawing firm conclusions is premature. For example:

- The MS Class review includes ocrelizumab, although this agent has not received final approval from the FDA, hence the evidence base is not well established.
- The RA class review includes sarilumab and baracitinib, although the PDUFA dates for these agents barely overlap the report development schedule and much information is still to be released.
- The PCSK9 inhibitor review should be considered for updating given the major differences that have been documented between assumed and actual utilization management/budget impact and the anticipated release of major outcomes trials.

Cost-effectiveness assessment at launch is not always accurate, as new information about a treatment's effectiveness in the real world can alter an early data-limited view. A relatively famous example is the HMG Co-Reductase Inhibitors, or statins, which were widely reviled at launch by academics and insurers for being outrageously cost-ineffective according to the same assessment techniques ICER is using — but within a few years and with new clinical outcome information, the statin class went from cost-ineffective to cost-effective to cost-saving, all before patent expiry. Had the early pronouncements shut down access prematurely, the U.S. public would have lost years of life. A similar story holds true for HIV treatments, which went through the same cycle.

NPC recommends that assessments be revisited on a regular basis and revised as significant new evidence becomes available.



## **5. Foster Productive Engagement Earlier in the Scoping Process**

ICER's recent efforts to establish an "open input" period prior to developing the scope for their review are welcome. However, more time is needed for organizations to respond.

Furthermore, ICER's draft scope documents are brief and thus limit productive engagement by stakeholders. This has improved in recent reviews with more opportunities for manufacturers or other stakeholders to speak with the review team or respond to more specific information (e.g., on draft model inputs). However, for most of the specifics, stakeholders typically have to wait for the draft effectiveness report, when analyses and conclusions are already far advanced. NPC recommends expanding the level of detail in the draft scope documents.

## **6. Increase Comment Transparency**

ICER is currently selective in its disclosure of comments and concerns raised to them. NPC recommends that all comments and their disposition should be publically available. Ideally, ICER should give its rationale for issues that it has chosen not to address.

## **7. Expand Topics and Topic Selection Process**

ICER's topic selection process should include multiple stakeholders with a significant representation by patients. ICER is currently over-reliant upon drug-to-drug evaluations. Given that drugs still represent a limited portion of the overall health care budget, ICER's impact would increase if its agenda was less concentrated and considered other interventions.

We appreciate this opportunity to identify ways to improve the ICER Value Assessment Framework and to bring it into closer alignment with the *Guiding Practices*. NPC's continued engagement with ICER signifies our commitment to the critical dialogue necessary to ensure the development of high-quality, meaningful tools that help patients, physicians, payers, and others make informed decisions. I look forward to the constructive dialog on September 30 around the key issues raised in NPC's, and other stakeholders', comments.

Respectfully submitted,



Robert W. Dubois, MD, PhD  
Chief Science Officer  
National Pharmaceutical Council

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**Our Mission:** To drive efforts to cure psoriatic disease and improve the lives of those affected.

September 12, 2016

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Two Liberty Square, Ninth Floor  
Boston, MA 02109  
Submitted via email: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

**RE: Response to ICER National Call for Proposed Improvements to its Value Assessment Framework**

Dear Dr. Pearson,

I write to you today on behalf of the more than 8 million Americans living with psoriatic disease to offer public comment on the Institute for Clinical and Economic Review (ICER) *National Call for Proposed Improvements to its Value Assessment Framework* released on July 14, 2016. We thank you for the opportunity to provide input on the 2017 update of the methods used by ICER to develop evidence reports on new therapies and health care interventions. We are pleased that you have invited all interested parties to react to the current ICER value framework. As patients are the ultimate beneficiaries of the therapies and interventions reviewed by ICER, the National Psoriasis Foundation feels strongly that the perspectives of individual patients, patient representatives and those that care for patients should be of central concern to you as you move forward with this update.

This spring ICER began a review of psoriatic disease therapies. This review – now focused only on psoriasis therapies only – will culminate in the New England CEPAC convening on November 18, 2016 to deliberate and vote on evidence presented in ICER's report on treatments for psoriasis. As we are only “half-way” through the review process, our comments are reflective of our experience to date. We urge you to give considerable reflection to the input of other patient advocacy organizations and the National Health Council (NHC), which may be more comprehensive in scope.

***Methods to integrate patient and clinicians perspectives on the value of interventions***

When the NPF reached out to ICER earlier this year in advance of the psoriatic disease treatment review, one of the key points we wanted to convey was that psoriasis is a relentless and unpredictable disease, individual and diverse, presenting differently from one person to the next. Answering the simple question of “what is important to patients” is, therefore, quite challenging. Patients have told the NPF they place value on a number of items including the expected efficacy of the treatment, the ability to access all psoriatic disease treatments, the safety of the treatment, the burden of utilizing this particular treatment, the impact that the therapy may (or may not) have on related or concurrent health conditions (including physical, mental and emotional health), and cost – among others.

In raising these items with ICER, we noted that these perspectives are so varied and patient preferences so diverse that the Food and Drug Administration (FDA) chose to spend an entire day hearing from the psoriasis community as part of FDA Patient Focused Drug Development (PFDD) initiative. It has been fortunate for our

community that we had the benefit of pointing ICER toward the March 17, 2016 psoriasis PFDD meeting webcast <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm470608.htm> as a way to give the institute an opportunity to hear directly from more than 100 patients about symptom challenges and treatment preferences. Time and again during this day-long meeting, patient participants shared their frustrations and the challenges of managing the wily symptoms of psoriasis and the unpredictable nature of the body's response to treatments. The second panel of this meeting, in fact, focused specifically on discussing patient perspectives on treatments. While some of the perspectives offered that day are captured in scientific literature, many of the unique – and very personal and sensitive – reflections of patients are often not known or understood by clinicians and researchers.

Assuming the model aims to consider each of the relevant benefits of interest to patients, the absence of a trusted, validated, and uniformly utilized outcomes measure for psoriasis that includes patient preferences and incorporates all these end points is a concern of the NPF with regard to the review underway. As ICER proceeds with this review and others in the chronic disease space, any reliance on outcomes measures that fail to properly capture the most bothersome symptoms of the disease (as in the case of psoriasis) is a concern. We raised this in a comment on the draft scoping document this summer. We disagree with the use of outcomes such as Psoriasis Area Severity Index (PASI) and Psoriasis Global Assessment (PGA) as "surrogate outcomes" en route to "key measures of clinical benefit." Focusing on PASI and PGA is but the tip of the iceberg and will limit one's ability to measure the total benefit of treating and will also fail to account for the transformational nature of biologic therapies.

Any discussion – or review – of treatments should also bear in mind that treatments that work for one person may not for others. Many patients cycle through accepted treatment options unsuccessfully, or temporarily successfully, and are ultimately left at the end of the treatment road with no alternatives. As we noted on several occasions during our discussions with ICER staff, this frustration is often one of compounded by insurance policies and practices that erect barriers for patients in urgent need of treatment.

The NPF has long recognized the importance of systematically gathering patient perspectives on all these issues and involving patients directly in research and clinical efforts including the development and validation of outcome measures and the identification of research priorities. Even for an organization such as the NPF which has devoted significant time and resources to doing this well, we note how challenging it is to engage patients and encourage them to share their perspectives in a way that can inform future efforts. This should be of particular concern for ICER which has neither a natural link to patients nor direct relationships with the experts who serve communities such as ours on a day-to-day basis. Analyses that fail to take real-life patient preferences, needs, and socio-economic challenges (among other considerations) into account will produce a value-discussion in a vacuum with little relevance or usefulness to patients, providers, and payers.

***Cost effectiveness ratios, appropriate thresholds, budget impacts and best practices***

As we shared earlier this year, an NPF survey of more than 400 patients done in 2012 found that two-thirds of these respondents were angry, frustrated, and/or helpless. While these numbers are stunning, the stories shared by patients are even more powerful than the statistics and expose the multiple challenges faced by patients on a daily basis. Talk to almost any patient with moderate to severe psoriasis – about 30 percent of whom often have both psoriasis and psoriatic arthritis, thus contributing to the intensity and cost of treatment – and they will tell you about the life changing experience it was for them when they (finally) got on a treatment that worked or the devastation they felt when a therapy lost efficacy, or they lost access to a therapy that was working for them. As it is, NPF annual surveys find that many patients are unable to obtain their first-choice prescription because the insurer would not cover it (21%), the co-pay was too much (18%), or they could not find a provider (8%)— (a problem often associated with costs and/or narrow networks). Talk to a patient who has been unable or ashamed to be intimate with a spouse, or who has suffered social stigma, endured bullying, shunning, embarrassment,

and maybe have even contemplated suicide due to their disease – it will not take long to hear that patients know the personal benefit of treating their psoriasis as clinically recommended.

Yet inherent challenges with identifying and assigning value to the benefits at both an individual level and societal level are large. According to the psoriasis scoping document released this summer, the aim of the report is to evaluate both the comparative clinical effectiveness and value of targeted immunomodulators for adults with moderate-to-severe plaque psoriasis. It is unclear, though, exactly what question(s) will be answered as part of this review. Regardless of the academic value of conducting such an evaluation, the real world challenge of attempting this sort of cost-benefit analysis on the psoriatic disease community where benefits of treating psoriasis are so difficult to monetize is concerning. Important cost questions to address include the need to up-dose, the use of combination therapy, costs associated with lab monitoring, impact on comorbid conditions – most of which are not captured in the literature or captured only for limited periods of time. Cost benefit analyses that are based on short term outcomes from trials (which fail to assess long term health consequences) do not properly account for the lifetime nature of these diseases. Finally, estimates of the cost of psoriasis frequently underestimate the impact of the disease because they fail to factor in costs associated with lost or reduced productivity or the financial impact associated with a lower quality of life.<sup>i,ii</sup>

### **Conclusion**

As ICER moves ahead with reviews such as the one for psoriasis therapies, we acknowledge the benefit of bringing forward sound science and evidence that informs patients and providers about treatment options. We encourage the Institute to consider the concerns raised by the NPF, and other patient representatives as it completes the 2017 methods updating.

No relationship in the health care landscape should be more sacred than that of the patient and provider. It is critical that patients and physicians have access to all of the therapies approved by the FDA - both new and those that have been on the market for more than a decade - along with those that come to market in the future. Only when physicians are able to access all the tools in their treatment toolbox, will they be able to provide individual patients with the care most appropriate for them and their disease.

Any framework that fails to meaningfully include patients, and ultimately disrupts the sanctity of this relationship through policy recommendations that limit access to treatments, will only serve to grow the 55% of patients with moderate to severe psoriasis who are not being treated to the appropriate standards of care. On behalf of National Psoriasis Foundation, thank you for your consideration of these comments which we hope will positively inform this review. We again invite you to call upon us, our Medical Board, and our patient community as you move forward. Please contact me with any questions.

Sincerely,



Leah Howard, JD

Vice President, Government Relations and Advocacy

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# **Novartis Response: ICER's National Call for Proposed Improvements to the Value Assessment Framework**

(September 12, 2016)

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Novartis appreciates the opportunity to provide feedback on the Proposed Improvements to ICER's Value Assessment Framework. We recommend the following considerations to be taken into account when developing the Value Assessment Framework v2.0.

### **Change in terminology: "Care Value" & "Provisional Health System Value"**

- Novartis recommends revising the term, "Care Value." Value is subjective and can be misleading to stakeholders. In addition, the current structure of "Care Value" does not sufficiently take into account the patient perspective. Therefore, the cost-effectiveness assessment and budget impact aspects should be considered independently.
- The term "Provisional Health System Value" does not accurately represent its true purpose. Since budget impact is a major driver of the ICER evaluation, it would be more appropriate to use the term, "Provisional Health System Budget Impact."

### **Capturing & Weighing "Other Benefits or Disadvantages" & "Contextual Considerations"**

- The current Value Assessment Framework should capture quantitative aspects of patient input and incorporate this input into the cost-effectiveness models. ICER should conduct comprehensive due diligence and collect data on direct and indirect benefits of treatments to patients, including real world evidence and clinical data, and incorporate all patient factors into the models. Examples of these types of data include productivity loss, patient-reported outcomes (e.g. impact of symptoms), and caregiver burden.
- Patient engagement should be increased during the ICER evaluation process. Following the recent National Health Council guidelines, patients should be considered full partners and integrated in all aspects of model development. This can be accomplished by engaging patients in every step of model development including pilot testing and refinement.<sup>1</sup> Ample time should be built into the process to achieve this goal.
- In order to avoid discriminating against specific populations, ICER should use population-specific data. Taking productivity loss as an example, the population should be segmented by age to characterize the working population vs non-working population.
- In order to evaluate value, it is necessary to have a clear framework that defines the intrinsic value of a drug. At Novartis, we define the value of our medicines based on four dimensions: meaningful outcomes, patient experience, healthcare system impact, and societal value. Of course, the successful implementation of this framework is based on input in advance – before implementation - from stakeholders such as payors, providers, academics and patient groups. Fully realizing the promise of science, and ensuring maximal patient benefit requires the entire system to collaborate toward a new understanding of value, one centered on better utilization of medicines and resources to improve outcomes.

## **Technical aspects of the Cost/QALY**

- The loss of exclusivity (LOE) of medications and associated impact on generic alternatives should be accounted for when evaluating cost-effectiveness and budget impact of medications. Also, the significant historical decrease in price of small molecule generic medications should be differentiated from biosimilars, which maintain a higher price due to the significant investment required for development and production. Recognition of the impact of generics will enhance the accuracy of the budget impact model over the proposed time horizon. Specifically, IMS health published a report in January of 2016 titled, “Price Declines after Branded Medicines Lose Exclusivity in the U.S.” This report describes the changes in prices after oral and non-oral small molecule medications lose their exclusivity. ICER should use this report to inform incorporation of LOE inputs in their models.<sup>2</sup> Additionally, ICER should garner input from a diverse set of stakeholders on LOE to ensure relevance and accurate representation.
- Novartis understands the reasoning behind using Wholesale Acquisition Cost (WAC), as it is the only publicly available drug price. However, ICER should make clear in their reports and press releases with a disclaimer that WAC pricing may not be reflective of the actual price in the real world. Given this fact, there is an inherent uncertainty in any conclusions utilizing the WAC price, which should also be noted in reports.
- The Cost/QALY threshold should not be standardized across different disease states since a standardized threshold can be difficult to apply to varying conditions. Additionally, once the threshold is set as a fixed value for a specific disease state, there should not be elasticity present in final voting as was observed in recent reviews.

## **Calculating the budget impact threshold**

- Currently, ICER’s framework uses a historical number of medications that came onto the market over two years (cf. 2013-2014) to calculate the budget impact threshold. This approach is not an accurate representation of current approvals. Alternative options to achieve a more accurate number for the budget impact threshold could include considering willingness-to-pay approach or evaluating the number of approvals over a 5-year period.
- When developing cost-effectiveness models, the range of potential results/sensitivity analyses should be included in the framework and weights should be added.

## **Potential short-term budget impact**

- The current time frame for the budget impact analysis is five years, and it does not accurately reflect the benefits of the medications, including both curative medications as well as chronic medications. The benefits of these medications are often observed over a longer period and they should be captured holistically. Novartis recommends that the budget impact model employ multiple time horizons to address the needs of multiple stakeholders.

## **Uptake Assumptions**

- ICER's market uptake scenarios are based on an unmanaged environment and are not a true representation of the current marketplace. Specifically, a 75% uptake over a 5-year horizon is highly improbable for any medication and should not be of the high end of ICER's uptake scale. More transparency is needed to understand how ICER calculates these estimates with references, reasoning and weighting behind each of the six criteria.
- When performing class reviews, it is not appropriate to assume or project a higher uptake of medications than already established for products already on the market. In addition, it is important to be consistent in the methods used to evaluate market uptake versus economic models. Currently, medications are evaluated sequentially for market uptake, but methods are comparative in economic models.
- Disease state should be factored in when calculating the uptake of medications as the uptake percentage varies significantly across conditions.

## **Meaning of "Alarm Bell"**

- Novartis does not agree with the use of "Alarm Bell", as the term can be misleading and it is not accurately represented in any of the published ICER reports. Certainly, the term 'Alarm Bell' carries more weight when applied to discount recommendations.
- The term itself carries different weight based on the sequence of the medication approval within the medication class. For example, if the medication is the first approved in the class, the "Alarm Bell" is louder and has a higher impact. Due to these inconsistencies, Novartis considers that it is not appropriate to make final discount recommendations based on these threshold values.
- Novartis recommends the use of "Budgetary Impact Estimation" as a substitution for the "Alarm Bell" as it more accurately describes the results of the ICER evaluation.

## **Comparators**

- ICER has not specified the comparator in any of the analyses that are planned. We suggest using the International Society for Pharmacoeconomic and Outcomes Research (ISPOR) Good Practice and Outcomes Research Report guidelines to inform comparator choices.<sup>3</sup> ISPOR recommends using the standard of care, or the comparator that best characterizes natural disease progression. Additionally, ISPOR Good Practices state that the comparator of interest should be selected based on the standard of care identified for each "context of use".<sup>4</sup>
- There is currently inconsistency in comparator selection across ICER class reviews. While the Multiple Myeloma class review included only medications that had multiple myeloma as a part of their Food and Drug Administration (FDA) label, the Multiple Sclerosis (MS) class review includes rituximab, which is not FDA approved for use in MS.

- We do not support the use of off-label medications in ICER evaluations due to the potential lack of adequate safety evidence, insufficient effectiveness data, and the potential to promote and lead to an increase in off-label use of medications.
- Off-label use of medications does not allow the FDA to monitor for potential adverse drug events. However, if ICER decides to continue the use of off-label medications they should develop two reports, where one excludes off-label medication use (which should be used as base case) and another that is all-inclusive. This approach is particularly prudent in situations when the government and/or commercial insurers will not reimburse for off-label use of medications.
- Novartis does not support the inclusion of unapproved medications that are early in their lifecycle in ICER evaluations. Unapproved medications should only be included if the FDA review is imminent and robust Phase III data is publically available.
- When performing class reviews, we recommend not using unapproved drugs as comparators as they lack pricing information. In addition, unapproved medications are not utilized by other health technology assessment entities such as the National Institute for Health and Care Excellence (NICE) as it could be considered as promotion of preapproved medications.

### **Increase the Patient-Centered focus of the framework**

- Novartis believes that the cost to the insurer is not a direct patient-centered value and the current framework poses a potential risk to decreasing patient access to medications. This concern has also been raised by patients, providers and caregivers in response to the Multiple Myeloma class review.
- The current ICER framework also puts an overemphasis on the cost of the drug and underemphasizes patient benefits.
- While Novartis understands that cost is an important factor of medication evaluation, we want to encourage ICER to incorporate patient input into the cost-effectiveness model. Currently, budget impact is a major driver of the ICER evaluation. The National Health Council recently published guidelines on including patient voice in the value framework. The guidelines recommend using data beyond randomized controlled trials such as patient registries and health-related quality-of-life studies. Additionally, processes should be in place to identify and incorporate emerging data sources, in particular patient-generated health data and outcomes important to patients.<sup>1</sup>
- The modeling process conducted by ICER is traditional and is not reflective of the innovative methods used to manage patients today. For example, in oncology, many tests are conducted to target appropriate patients with the goal of enhancing treatment efficacy/effectiveness. The current Value Assessment Framework accounts only for the cost of these types of tests and does not evaluate the benefits for patients.

**Lack of a system-wide perspective & broader stakeholder representation**

- In previous ICER reviews, the members of the voting panel were largely composed of payers. The lack of inclusion of patient and clinical subject matter experts in public panels or as voting members is not inclusive and should be addressed to ensure diverse and balanced perspectives are reflected in the final votes.
- In the past, public comment periods and testimony periods at public meetings have been inadequate.

**Transparency**

- Novartis recommends an increase in transparency in ICER documents. Currently, stakeholders are unable to replicate the ICER economic models based on the documents published because they do not include all details on data input, assumptions, and comparators. Thus, making the model more transparent and publicly available would increase inclusiveness of all stakeholders.
- An alternative approach would be for the ICER process to include submissions of manufacturer's product value dossiers and economic models, which should be kept confidential – in a manner similar to the HTA process of other countries (e.g., NICE in the UK). The goal of this approach would be to enhance the dialog between different stakeholders and establish a true partnership between stakeholders and ICER. It would also potentially be less resource intensive for ICER.
- Thus far, ICER methodology is not transparent on the process of choosing a comparator in their evaluations. The comparator strongly influences the outcomes and therefore determining a comparator is crucial. To perform an accurate assessment, it is critical that ICER chooses appropriate comparators as a benchmark. Specifically, selecting the least costly therapy as a comparator might not be appropriate for cost-effectiveness evaluations. The full rationale for comparator selection should be provided for stakeholder review and input.

**Current framework disincentives innovation**

- Using the current ICER framework, the treatment for conditions with large target populations and broad unmet need are very likely to have a high budget impact and ring the 'Alarm Bell.' Thus, negatively impacting the development of treatments for such diseases. Also, the clinical, humanistic, and economic benefits of innovative medications are understated. In addition, it is inappropriate to make comparisons between innovative medications and therapies/classes that are all generic or medications that are infrequently used (e.g. off-label, follow-on indications) for the treatment of a disease. Therefore, Novartis recommends making the "Alarm Bell" threshold more flexible to account for innovative and first-in-class treatments by incorporating the societal value and the value of innovation in the final benchmark, rather than disincentivize innovation.

**References:**

- 1) The National Health Council. The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric. Available at: <http://www.nationalhealthcouncil.org/sites/default/files/Value-Rubric.pdf> (Accessed September 5, 2016)
- 2) Price Declines after Branded Medicines Lose Exclusivity in the U.S. IMS Institute for Healthcare Informatics. Available at: <https://www.imshealth.com/files/web/IMSH%20Institute/Healthcare%20Briefs/PhRMA%20Generic%20Price%20Brief%20January%202016.pdf>. (Accessed September 5, 2016)
- 3) Ramsey SD, Willke RJ, Glick H, et al. Cost-effectiveness analysis alongside clinical trials II-An ISPOR Good Research Practices Task Force report. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. Mar 2015;18(2):161-172.
- 4) Walton MK, Powers JH, Hobart J, et al. Clinical Outcome Assessments: Conceptual Foundation—Report of the ISPOR Clinical Outcomes Assessment—Emerging Good Practices for Outcomes Research Task Force. *Value in Health*. 2015;18(6):741-752.

# LEADING THE FIGHT TO END DUCHENNE

Institute for Clinical and Economic Review  
Steven D. Pearson, MD, MSc, FRCP  
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## **Re: National Call for Proposed Improvements to the ICER Value Assessment Framework**

September 12, 2016

Dear Dr. Pearson,

On behalf of Parent Project Muscular Dystrophy (PPMD), we are pleased to submit the following comments in the National Call for Proposed Improvements to the Institute for Clinical and Economic Review (ICER) Value Assessment Framework.

### **Introduction to PPMD**

PPMD is the world's largest organization focused on ending Duchenne muscular dystrophy. Duchenne is a progressive disease diagnosed in early childhood that affects skeletal muscle and the cardiac and pulmonary systems. There currently are no FDA-approved disease-modifying treatments, and children diagnosed with Duchenne typically live only into their 20s. In short, Duchenne is 100% fatal. PPMD is the leading voice for the Duchenne Muscular Dystrophy community and, as such, is actively engaged in all stages of advancing medical innovation for our families. Our PPMD community is comprised of clinical and scientific experts and an engaged and diverse network of patient families.

The advent of the Patient Focused Drug Development (PFDD) provisions within the 2012 Prescription Drug User Fee Agreement (PDUFA V) and corresponding FDA Safety & Innovation Act (FDASIA) aligned perfectly with the dawning of a new day for our Duchenne community – one in which basic laboratory breakthroughs had evolved into clinical trials, enabling the Duchenne pipeline of experimental therapies to become more robust than ever. PPMD immediately embraced the opportunities presented to us through PDUFA V and have worked over the past few years to evolve the science of patient input and advance the field of Patient-Focused Drug Development.

Since that time, we conducted the first-ever scientifically rigorous survey of parents of Duchenne patients to obtain quantitative evidence as to their views on benefit-risk and are now conducting subsequent expansions of our patient-preferences studies into a broader caregiver demographic and young people living with Duchenne.

We have published a series of white papers analyzing PDUFA through the lens of the Duchenne community including *PPMD's Putting Patient's First* and *PPMD's Benefit-Risk Assessments in Rare Disorders* publications. We have also led a comprehensive and multi-stakeholder effort to prepare draft guidance to industry developing Duchenne therapies. This PPMD-led guidance,



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*“Guidance for Industry Duchenne Muscular Dystrophy Developing Drugs for Treatment over the Spectrum of Disease”* was submitted to FDA in June 2014 and – along with a Duchenne Community Policy Forum convened by PPMD in December of 2013 - was the foundation used by the agency to develop its own draft guidance on the same topic issued in June of 2015 entitled, *“Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment”*.

Additionally, we have been the first patient community to use scientifically validated preference methods to measure patient and caregiver preferences. By partnering with social scientists and health economists from Johns Hopkins University, we have completed two patient preference studies involving subsets of the Duchenne community and are in the midst of analyzing data from a third. These studies are the first-ever quantitative studies of Duchenne community preferences on potential benefits and corresponding risks of emerging candidate therapies. This summer, to further advance the field of PFDD and to ensure that the lessons that have been learned to date are shared broadly -- the Biotechnology Industry Organization (BIO) and PPMD convened the world’s leading experts in the science of patient preferences to develop and publish *Key Considerations for Developing and Integrating Patient Perspectives in Drug Development: Examination of the Duchenne Case Study*.

In all of this work, we have used scientific methodologies for obtaining patient preferences, moving beyond qualitative statements from community members. PPMD conducted the first-ever scientifically rigorous survey of caregivers of Duchenne patients to obtain quantitative evidence as to their views on benefit-risk. This is being done in recognition of the reality that regulators and payers need and deserve quantifiable data on which they can make important review and coverage decisions. Today, we are expanding our patient-preferences studies to include a broader caregiver demographic and young people living with Duchenne. This work will add to the expanding body of evidence and hopefully be factored into agency decision-making.

PPMD is appreciative of ICER’s renewed commitment to patient engagement and appreciates the opportunity to reflect on the ICER Value Assessment Framework.

## **1. Integrate the Patient, Caregiver, and Clinical Expert Perspective Into the Expert Review Across the Assessment Process**

Patient engagement is increasingly defined by a combination of rigorous evidence with direct, material participation of those most affected by the decision-making process. **PPMD encourages ICER to bring patient representatives from the area under study - as well as clinical experts from the specific disease area - into the study team and assessment, as deeply and as early as possible.**

In PPMD’s experience, patient representatives are involved from generating research topics to implementing the research study and serve an invaluable asset to the entire research team. Our experience with working collaboratively within PCORNet and the general medical and research community is that prioritizing the patient voice is making a positive impact on all aspects of care and research.



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## 2. Recognize the Dynamic Nature of Value at the Individual Patient Level

PPMD's work to improve patient care and support clinical research has provided robust insights into the way in which patient and caregiver perspectives evolve over time. In particular, our work in benefit-risk analysis within the Duchenne community has informed this understanding.

Each and every family within the patient community has their own personal story. And within our community, each family has a unique story about Duchenne. Disease progression varies. Each family's ability to provide care and physical support varies. And the needs of each individual with Duchenne changes significantly as the disease progresses. Each and every family is able to relate a story of gradual loss, the 'little deaths' experienced as their loved one loses function. But we recognize that regulatory agencies make decisions based on rigorous data, and to that end, we, the patient community believed it would be critical to the decision making processes if we were able to provide data related to caregiver and patient preferences. So, we as a community set out to 'quantify the tears', in an attempt to turn the voice of the patient into accessible data.

In order to accurately measure opinions or preferences we used scientifically validated stated preference methods ensuring greater confidence in the value of the data we collected. We partnered with social scientists and health economists from Johns Hopkins University. Our research partners helped us develop an appropriate instrument that we used to survey nearly 120 Duchenne parents, the first-ever quantitative survey of Duchenne community preferences on potential benefits and corresponding risks of candidate therapies. Specifically, we used the best-worst scaling (BWS) method that measured respondents' views on six relevant and understandable benefit or risk scenarios such as stopping or slowing progression of muscle weakness, longer lifespan, nausea, and risks of bleeding. In addition, we collected the narrative stories of our families and found that the stories provided qualitative data in support of the quantitative data collected.

Example Task:

| Best                  | Treatment  | Worst                 |
|-----------------------|--|-----------------------|
| <input type="radio"/> | Slows the progression of weakness                      | <input type="radio"/> |
| <input type="radio"/> | 2 year gain in expected lifespan                       | <input type="radio"/> |
| <input type="radio"/> | 1 year of post-approval drug information available     | <input type="radio"/> |
| <input type="radio"/> | Causes loss of appetite                                | <input type="radio"/> |
| <input type="radio"/> | Increased risk of bleeding gums and increased bruising | <input type="radio"/> |
| <input type="radio"/> | Increased risk of harmless heart arrhythmia            | <input type="radio"/> |

The primary study objective was to explore how parents/guardians of individuals with Duchenne prioritize risk and benefit in the context of new therapies.

In the survey, participants were provided with sets of simulated treatment scenarios and asked to choose the best and worst of each treatment scenario; later, participants were provided with sets of Duchenne-related concerns and asked to choose the one they worried about the most in

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the past seven days and the one they worried about the least. Thus, participants evaluated and compared their preferences toward the attribute levels and selected the pair of attribute levels that they perceive to be furthest apart.

Overall, we found that parent participants prioritized protection of muscle function over any other attribute, including longer lifespan, two serious risks, nausea, and having more information about the drug's risk and benefits. Participants' most significant worries were related to disease progression and care needs. The study suggests a parent population that is highly concerned about Duchenne's effect on their child's strength, and that is willing to accept risk and uncertainty for a treatment that would slow or stop muscle weakness.

PPMD has been working to expand this work further to examine how preferences may or may not change throughout the trajectory of the disease progression.

More recently, we partnered with an industry collaborator to understand patient preferences regarding a specific pulmonary candidate therapy. We once again used best-worst scaling methodology, but for the first time surveyed patients as well as caregivers. The survey involved more than 130 patients and caregivers, and we again found that patients are willing to accept risks and burdens to achieve pulmonary benefits, notably improvement in cough strength.

Example task

| Best                  |   | Worst                 |
|-----------------------|---|-----------------------|
| <input type="radio"/> | Cough strength:<br><b>Maintained for 10 years</b>         | <input type="radio"/> |
| <input type="radio"/> | Lung infections during your life:<br><b>Half as many</b>  | <input type="radio"/> |
| <input type="radio"/> | Your chance for diarrhea:<br><b>1 in 2 (50%)</b>          | <input type="radio"/> |
| <input type="radio"/> | How often you need a blood test:<br><b>2 times a year</b> | <input type="radio"/> |

|  |
|--|
| Would you choose this treatment?                         |
| <input type="checkbox"/> Yes <input type="checkbox"/> No |

Overall, respondents chose to accept a strong benefit with an accompanying high risk more than two-thirds of the time, and the majority of respondents assigned low perceived burdens to three side-effects of taking medication, sustaining blood draws, and diarrhea. Interestingly, there was little difference between caregiver and patient preferences. The study results showed how much patients and caregivers value improved pulmonary outcomes in Duchenne.

Our efforts – as well as those of many sister organizations conducting similar work in their respective communities – have demonstrated that rigorous data is being generated by patient communities. **Given these findings, we respectfully recommend that the ICER Value Assessment Framework allow for the inclusion of evidence developed through PFDD mechanisms, to reflect the dynamic nature of value at the individual patient level, where**

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relevant to a disease-area or specific treatment. Doing so will recognize the movement toward PFDD and will signify the importance of such data when relevant to an application and when developed and produced in a quantifiable and scientifically validated method.

### 3. Incorporate Patient Preference, Patient-Reported Outcomes and Other Patient Engagement Evidence in Assessments

Patient engagement science and related tools are developing rapidly and should have a material role in ICER assessments. PPMD and other voluntary health organizations are making investments into this field which can be leveraged by ICER. Below are examples of evidence generated to date by the Duchenne community and stakeholders that are representative of the critical insights patient communities can bring to the value analysis.

- B/R findings
- Other surveys
- DuchenneConnect patient reported data
- Quantitative data collected from patient preference studies
- Qualitative data collected from patient experience surveys

In a study led by Dr. Stanley Nelson at UCLA, he and his team evaluated patient-entered data within PPMD's DuchenneConnect registry and found that the DuchenneConnect data could be used to evaluate comparative effectiveness of steroid therapy in patients with Duchenne in a similar way a clinical trial does <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4207635/>.

**PPMD urges ICER to expand your framework to allow for an algorithm that is inclusive of the expertise, experience and evidence around patient-preference – and the trade-offs and considerations patients make when seeking treating options.**

### 4. Include Impact on Caregiver Burden within ICER Assessments

Many diseases, particularly those that are profoundly disabling to the patient for long periods of time, carry immense indirect costs related to the burden on caregivers. We see this phenomenon becoming even more impactful as patients with Duchenne live further into adulthood due to modest advances in clinical care that are not disease-modifying. In a burden of disease study of Duchenne muscular dystrophy published in the Journal of the American Academy of Neurology in 2014 (Erik Landfeldt et al. Neurology 2014;83:529-536), annual household burden was a mean of \$75,820, with a mean informal caregiver burden of \$13,370 and mean indirect costs of \$45,080. Costs were further stratified over disease trajectory. **The opportunity for therapies that can slow disease progression and improve quality of life for these families should be fully considered in the value assessment.**

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## 5. Leverage Evidence and Analysis for Shared Decision-making

PPMD encourages ICER to continue its efforts to broadly engage relevant communities in the assessment process to both strengthen the work product as well as to develop sustainable implementation channels. This collaboration should include efforts to educate both patients/caregivers and clinicians on the underlying evidence and conclusions in a manner that fosters shared decision-making in the real world.

The integration of patient perspectives and meaningful patient data in the process of shared decision making for the value assessment framework. Patients are continuing to contribute to the growing body of evidence regarding value of potential therapeutic interventions. This integration is already occurring earlier in the drug development process, with patients and caregivers contributing to the understanding about what is most meaningful to them when it comes to developing potential therapies. This interaction should be occurring throughout the arc of drug development, from discovery on through delivery.

PPMD is grateful to ICER for its continued commitment to improvement and engagement of the patient community in the value assessment framework process. We understand that valuation of emerging products is a complex science and that in the context of rare, progressive diseases with few treatment options the complexity increases. What we ask ICER to allow for within your framework is an algorithm that is inclusive of the expertise, experience and evidence around patient-preference – and the trade-offs and considerations patients make when seeking treating options. We hope that we have provided some meaningful and inspirational comments for you to consider. We stand ready to collaborate with you. For more information about any of the resources referenced within this comment or Duchenne community engagement, please feel free to contact Annie Kennedy PPMD's Senior Vice President Legislation & Public Policy at [annie@parentprojectmd.org](mailto:annie@parentprojectmd.org) or 703-655-6838.

Sincerely,



President & CEO  
Parent Project Muscular Dystrophy

September 12, 2016

Steven D. Pearson, MD, MSc  
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Dear Mr. Pearson:

The undersigned organizations are pleased to join the Partnership to Improve Patient Care (PIPC) on this letter providing input in response to the national call for input issued by the Institute for Clinical and Economic Review (ICER). In a debate that often is dominated by the perspectives of other stakeholders – payers, manufacturers and researchers – we seek to elevate the voices of those who might otherwise not be heard – those of patients, many of whom have serious and life-threatening chronic conditions, their caregivers and people with disabilities. Simply put, if we aren't paying for care that patients' value, we aren't really paying for value-based care.

As noted by ICER and many other organizations, rising health care costs, as well as changing benefit designs, place increased pressure on care access and affordability. In this environment, it is more important than ever to address the issue of value, and to make sure these efforts are centered on care and outcomes that patients value. One important element of this is making sure that patients, providers and other decision-makers have sound information and decision-support tools available to them.

ICER's particular approach to value assessment underscores long-standing concerns that many patients and consumers have about how the value of individual patient care will be judged, and whether these judgments will be applied in ways that ignore individual patient differences and needs or deny access to treatments or services that are valued by individuals or patient subgroups. In recent months, these concerns have been amplified as proposals have emerged that would misapply assessments like ICER's in ways that would impede patient access to optimal care by imposing one-size-fits-all value judgments.<sup>1</sup>

While we recognize the steps your organization recently took to improve the procedures it uses to conduct value assessments, it is our hope that the changes to ICER's process lead to the meaningful incorporation of the voice of patients, people with disabilities, and those who care for them throughout its work. We are concerned that the effect of identifying the concerns of patients and people with disabilities as myths per ICER's recent report entitled "Addressing the Myths About

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<sup>1</sup> CMS Proposed Part B Drug Payment Model, 81 FR 13229

ICER and Value Assessment” is to dismiss their very real concerns about both ICER’s methods and, more broadly, the standards to be used to judge the value of patient care. We urge ICER to give sincere and careful consideration to the input of all organizations representing patients and people with disabilities, many of which have direct experiences with ICER’s process and whose input would be very constructive. We may not always agree, but we should be able to agree that all voices matter, especially the voices of patients and people with disabilities that are directly impacted by your work.

Our input is informed not only by long-standing concern about the need to advance more patient-centered approaches to value assessment and value-based decision-making, but also by in-depth work that many of our organizations have participated in over the past year on the topic of value assessment. As you may know, PIPC held an in-depth roundtable discussion earlier this year with organizations representing patients and people with disabilities, also including Avalere Health and the Patient-Centered Outcomes Research Institute (PCORI). The PIPC roundtable report elicits and captures diverse perspectives on patient-centeredness in value assessment. We share the concerns in the PIPC report and support ICER’s use of the National Health Council’s Patient-Centered Value Model Rubric, as discussed below. We look forward to ICER’s incorporation of patient perspectives systematically and consistently throughout its assessments.

We would like to bring to your attention to several significant concerns from patients related to the process, methods, and end use of value assessment. Where appropriate, we also recommended steps ICER could take to address these concerns.

### **Process: ICER Should Make Substantial Improvements to Its Process for Conducting Value Assessments to Ensure It Receives and Considers Input from Patients and Their Caregivers**

It is imperative that ICER proactively reach out to patients, patient advocates and clinical experts for their input, and explain the process through which assessments are developed. Based on our experience with organizations such as the Patient-Centered Outcomes Research Institute (PCORI), we know that patients and people with disabilities, and the organizations who serve them, are able and willing to offer input and expertise. The data, information, and perspective that these groups bring to the conversation around value assessment is vital to driving value in health care, as is supporting their capacity to contribute. For example, patient groups offer expertise on the conditions they represent, both from the perspective of patients, but also via their close collaboration with the medical community. Specifically, we propose the following changes to ICER’s process.

- ICER should be engaged with organizations representing the impacted patient communities and clinical experts in the specific treatment area under consideration in advance of scoping



their projects to ensure that ICER's assessments are achieving consensus on the assumptions (such as predicted uptake of the treatment), definitions and underlying questions. We suggest that ICER conduct briefings for the organizations representing patients that are candidates for the potentially studied treatment, as well as the clinical experts that provide services to those patients, as part of the scoping process.

- ICER should provide stakeholders representing patients and clinical experts with a meaningful role in developing the construct and operation of ICER's advisory panels to ensure that participants have specific expertise on the treatments under consideration.
- ICER should develop realistic timeframes to provide comments throughout their process. We applaud ICER's recent efforts to extend certain comment deadlines.
- ICER should respond to feedback by making it clear what input was incorporated and why certain input was not incorporated into its final reports. Meaningful engagement requires not only getting input from patients, people with disabilities and clinical experts, but also *incorporating that feedback* into your final reports. It is a positive first step that ICER is making comments to its draft reports publicly available.

### **Methods and End-Use: ICER Should Significantly Revise Its Methods To Achieve the Goal of Ensuring Patient Needs and Preferences Are at the Center of Its Work, Even When Assessments Are Intended for Payer Decision-Making**

We recognize that ICER's assessments are not generally intended for use by patients and people with disabilities. However, we are concerned that ICER's work could hinder efforts to advance best practices in shared and supported decision-making that are being developed for patients. We would ask that you consider methodological changes that would help individual patients or providers disaggregate your assessments in ways that help them understand how the assessment relates to them and the decisions they are making, similar to the manner in which Congress called on PCORI to make its research findings relevant to individual patients.<sup>2</sup> If ICER's work is to be considered a reference for private payers in determining coverage and value of treatment options, then ICER must take responsibility for the impact its work will have on real patients and people with disabilities. Therefore, PIPC recommends several changes to ICER's methods that would support decisions by payers that reflect value as defined by patients and people with disabilities, thereby improving health outcomes and reducing costly adverse events.

- *ICER should avoid the "one-size-fits-all" mentality that does not recognize diversity among patients and people with disabilities by adopting alternative approaches to the use of quality-adjusted-life-years (QALYs).* Patients and people with disabilities do not support the use of QALYs in research related to the assessment of treatment value. Additionally, a societal impact

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<sup>2</sup> 42 U.S.C. 1320e(d)(8)(A)(ii)

analysis based in cost-per-QALY may not account for the value of substantially improving the life of a person with a disability or serious medical condition. ICER acknowledged it is “aware of this possibility” of the discriminatory potential of QALYs in its recent report, making it disingenuous to call the concerns of patients and people with disabilities about QALYs a “myth.” Alternative approaches could better enable patients and people with disabilities to understand how the evidence on clinical and economic value relates to them, and enable payers to better develop policies that reflect value from an individual perspective (not just at the population level).

- *ICER should expand the sources and types of data it relies upon for its evidence reports, thereby reinforcing the importance of changing the culture of research to recognize the value of patient data sources, without viewing such a change as an assault on evidence-based medicine.* Randomized Clinical Trials (RCTs) provide limited data, representing only a small part of the population and do not represent real-world treatment impacts as do other sources such as patient and clinical data registries. While RCTs provide strong assurance of validity within the study, they do so at the expense of offering limited insight on value for patients or endpoints beyond the study. ICER should also provide clear consistent guidance on the range of studies relied upon by ICER to help all stakeholders assess its usefulness for decision-making.
- *ICER should be transparent about the evidence on which its assessments are based, as well as the limitations presented by that data such as the limited populations and outcomes captured by the evidence.* Stakeholders should understand the evidence used to develop value assessments, the quality and source of evidence, and the limitations of the evidence. By better articulating the limitations of the data that informs the development of ICER’s value framework, it will be clear where evidence gaps exist to inform future research efforts. For example, PCORI was called upon by Congress to articulate the limits of its research and could provide a useful model for consideration.<sup>3</sup>
- *ICER should better reflect patient-centered outcomes.* Quantifying value in a way that is useful and meaningful to patients and people with disabilities requires a basic understanding of their values and preferences. Doing so will benefit both patient and payer as they identify and integrate the appropriate patient-centered criteria in assessing the value of treatments for a particular condition. ICER’s assessments should not conflate value considerations at the population level with value considerations experienced at the individual level, where real-world personal and financial cost considerations differ from population-based models.
- *ICER should not develop assessments that result in a single universal “value score” for patient populations. Patient sub-groups, and individual patients, define value differently based on their particular disease mutation, their preferences and their unique characteristics that result*

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<sup>3</sup> 42 U.S.C. 1320e(d)(8)(A)(iii)



*in very real differences in the impact of treatments.* We are concerned that payers use ICER determinations of value to restrict access to treatments without consideration of the varying value presented by a treatment or technology for the individual patient or person with a disability. Treatments impact patients differently based on their comorbid conditions as well. Value to patients and people with disabilities simply cannot be captured in a single number.

- *ICER should recognize a holistic cost perspective.* By focusing on short-term costs, ICER limits the relevance of its reports only to the short-term actuarial analysis of a payer. ICER's assessments have a limited perspective on the economic component of value, while there are long-term, personal and societal costs that are not being considered in its value assessments, such as risk of disability and the potential need for caregiving. Broader costs should be considered rather than focusing only on short-term costs so that ICER's work is relevant to decision-making by patients, people with disabilities and their providers.

We support the work of the National Health Council to provide a guide to evaluate the patient-centeredness of value models and to guide value model developers on the meaningful incorporation of patient engagement throughout their processes. The rubric outlines the domains that must exist for a value framework to be patient-centered:

- **Patient Partnership.** Patients should be involved in every step of the value model development and dissemination process.
- **Transparency to Patients.** The assumptions and inputs into the value model itself – and each step in the process – should be disclosed to patients in an understandable way and in a timely fashion.
- **Inclusiveness of Patients.** The value model should reflect perspectives drawn from a broad range of stakeholders, including the patient community.
- **Diversity of Patients/Populations.** The value model should account for differences across patient subpopulations, trajectory of disease, and stage of a patient's life.
- **Outcomes Patients Care About.** The outcomes integrated into the value model should include those that patients have identified as important and consistent with their goals, aspirations, and experiences.
- **Patient-Centered Data Sources.** The value model should rely on a variety of credible data sources that allow for timely incorporation of new information and account for the diversity of patient populations and patient-centered outcomes, especially those from real-world settings and reported by patients directly. The data sources included should reflect the outcomes most important to patients and capture their experiences to the extent possible.

Following NHC's rubric as a guide to improve ICER's framework would be a constructive first step in addressing the concerns of patient groups. We appreciate your consideration of the views

and concerns above, and look forward to being engaged in a version 2.0 of ICER's framework for assessing value.

Sincerely,



Tony Coelho  
Chairman, Partnership to Improve Patient Care

And the Undersigned Organizations:

ALS Association  
American Association of Neurological Surgeons/ Congress of  
Neurological Surgeons  
American Association of People with Disabilities  
American Association on Health and Disability  
American Autoimmune Related Diseases Association, Inc. (AARDA)  
American Foundation for the Blind  
Association of University Centers on Disabilities (AUCD)  
Asthma and Allergy Foundation of America  
Autistic Self Advocacy Network  
Brain Injury Association of America  
CancerCare  
Christopher & Dana Reeve Foundation  
Cognitive Compass  
Cutaneous Lymphoma Foundation  
Depression and Bipolar Support Alliance  
Epilepsy Foundation  
Global Liver Institute  
Hepatitis Foundation International  
Hydrocephalus Association  
International Cancer Advocacy Network  
Kidney Cancer Association  
Lakeshore Foundation  
Lung Cancer Alliance  
LUNgevity  
National Alliance for Hispanic Health  
National Alliance on Mental Illness (NAMI)  
National Council on Independent Living (NCIL)

National Viral Hepatitis Roundtable  
No Health without Mental Health  
Not Dead Yet  
Parent Project Muscular Dystrophy (PPMD)  
Parents Reaching Out in New Mexico  
Patient Services, Inc.  
Patients Rising  
RetireSafe  
Spina Bifida Association  
The Arc of the United States  
The diaTribe Foundation  
The Hepatitis C Mentor & Support Group, Inc.  
Tuberous Sclerosis Alliance  
United Cerebral Palsy  
United Spinal Association  
VHL Alliance

September 12, 2016

Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

By electronic delivery

Re: Proposed Process Improvements to ICER's Value Assessment Framework

Dear Dr. Pearson:

I am writing on behalf of the Personalized Medicine Coalition (PMC) in response to ICER's recent call for suggestions on how to improve its value assessment framework.

PMC is comprised of more than 240 member institutions representing a wide range of stakeholders, including patient groups, provider groups, payers, health care delivery organizations, diagnostic and pharmaceutical manufacturers, and clinical laboratories. Our members work to address issues in science, business and policy that impact personalized medicine.

We appreciate the opportunity to respond to your call for proposed improvements to ICER's evaluation process. Below, we outline some improvements for that process that would help ensure meaningful engagement with the scientific and research communities. Our comments focus on the following five areas:

1. Open Comment Periods
2. Length of Comment Letters
3. Inclusion of Relevant Clinical Expertise
4. Peer Review
5. Transparency in Stakeholder Engagement

## Open Comment Periods

PMC and its members have the ability to provide in-depth, technical insights on the subject matter of ICER's evaluations. As a coalition, any insights we offer must represent the interests of a range of disciplines and balance the perspectives and needs of our many members. Meanwhile, the field of personalized medicine is moving at an incredibly rapid pace. In this context, it is impractical for many stakeholders, particularly coalitions like PMC, to fully understand and respond to ICER's complex and lengthy

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documents in a short period of time. In the past, the time length of ICER's open comment periods have not allowed for meaningful input by impacted stakeholders.

The length of open comment periods should reflect the importance, length, and complexity of the items to which the community is responding. We appreciate the recent steps ICER has taken to extend its comment periods, and hope it will build on them by accepting our suggestions.

### *Recommendations*

Allow 30 days for the community to respond to short, clear, single-issue documents such as draft scoping documents; allow 60 days for the community to respond to evaluations of single-therapeutic or therapeutic-class reviews; allow 90 days for the community to respond to complex requests such as changes to methodology, the public-engagement process, the evaluation process, or draft evaluations that cover multiple drug classes and diagnostic trajectories. Holidays should be avoided.

### **Length of Comment Letters**

Page limits for comment letters discourage thoughtful engagement with ICER. For example, the 185-page non-small cell lung cancer draft evidence report considers four populations, four interventions, four comparators, and a variety of outcomes. The subject matter of that document is also complicated by rapid scientific advancements and increased use of diagnostics. While innovators will rightly focus on their products, patient groups, professional societies, coalitions and others may want to respond to all aspects of the report. Removing page limits, like ICER has done with this call for suggestions, will allow for more descriptive contributions to ICER's process.

### *Recommendation*

To encourage feedback that mirrors the thoughtfulness and complexity of the documents in question, we urge ICER to discontinue the use of page limits for comment letters.

### **Inclusion of Relevant Clinical Expertise**

Personalized medicine is a fast-moving and complicated field. Targeted therapies are coming to market regularly while, concurrently, FDA is updating labels to expand or target the use of certain drugs based on new clinical research results. This leads to rapid changes in how clinicians diagnose and prescribe targeted therapies. It is imperative that ICER's evidence reports reflect the reality of how clinicians are currently using personalized therapies and accompanying diagnostics to diagnose and treat patients.

### *Recommendations*

To ensure that value assessments are relevant to current clinical realities and consistent with the movement towards personalized medicine, ICER should engage experts with disease-specific expertise. Stakeholders with relevant expertise should be represented on advisory panels reviewing ICER's draft evidence reports, and their feedback should be considered before work products are finalized.

## **Peer Review**

Peer review allows stakeholders with expertise and experience in a specific field of medicine to engage with ICER. Peer review also assures the public that ICER's materials are scientifically and clinically valid. Submitting evidence reports for peer review after the report has already been released publicly for use in making health care decisions is not sufficient. ICER's evidence reports should undergo thorough peer-review by an unbiased group of experts prior to their publication.

## *Recommendation*

To ensure that ICER's value assessments reflect the current state of science and clinical practice, ICER should develop and implement a peer review process that provides an opportunity for experts in appropriate fields who are not otherwise part of the evaluation process to review its work products.

## **Transparency in Stakeholder Engagement**

Many stakeholders are positioned to provide valuable insight on value assessments. We commend ICER for publishing those insights and encourage the organization to continue to do so. However, stakeholders would greatly benefit from understanding how ICER sets its priorities and incorporates the feedback it receives. Engaging stakeholders in ICER's process for setting priorities and making stakeholder comments (for draft scoping documents and evidence reports) publicly available alongside an explanation as to why ICER does or does not address the individual comments would greatly enhance the public engagement process and improve the impact that ICER's value assessments have on the field.

## *Recommendations*

ICER should ensure that feedback on all ICER materials, including scoping documents and evidence reports, is publicly available. Additionally, ICER should explain why stakeholder feedback is incorporated or not incorporated and engage the public while setting its priorities.

Thank you again for issuing a call for suggestions about ICER's value assessment process. While PMC

has commented only on general process improvements, many of our members have provided detailed suggestions. We request that you consider those suggestions.

We hope this is the first step in public engagement on this topic and we look forward to working with you to improve ICER's process so that the principles of personalized medicine are incorporated into its work. If you have questions about this comment letter or would like to reach us, please contact me by phone at 202-589-1769 or by email at [AMiller@personalizedmedicinecoalition.org](mailto:AMiller@personalizedmedicinecoalition.org).

Sincerely yours,

A handwritten signature in cursive script that reads "Amy M. Miller".

Amy M. Miller, Ph.D.  
Executive Vice President

- 1) If you ever want to have validity to any of your work on rare and complex diseases which have a short life expectancy you must have skilled experts in that field on the panel. Without this input your work will look as flawed, ignorant, and uninformed as it did during the myeloma presentation.
- 2) Because the focus is on reducing the cost per QALY to \$50,000 or less then this is the average, and an equal number can be over \$50,000 as can be below \$50,000.
- 3) This concept is an allocation concept and goes against the concept of insurance where all pay in and many will get no payback, but if you do have a very expensive illness it will be covered.
- 4) If you want to improve the cost per QALY do what the Europeans do which is to negotiate prices with the insurance companies. This results is a cost of drugs half of what it is in the USA. Let Medicare negotiate with drug companies and the same thing will happen in the USA and the cost per QALY is cut in half. Also use the antitrust laws to go after the criminals like Turing who increase one drug by 5500% overnight and Novartis the makers of Gleevec, who increased the price by 500% when inflation was just 35%.
- 5) Your thought that a life year can be less than that of a person who is well makes no sense to a terminal patient. If I am 50 and have a projected life expectancy of 35 years, and I am told I now have just 5 years to live. I would say they might just be 7 times more valuable than that of a person with 35 years left. Each year of life becomes so much more valuable.
- 6) Drugs represent a little less than 10% of the healthcare costs. Aren't you shooting at the wrong target. Hospital and doctor costs are 5 times this amount.



September 12, 2016

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

Re: Call for Stakeholder Feedback on Institute for Clinical and Economic Review Value Framework

Dear Dr. Pearson,

On behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA), I am pleased to respond to the Institute for Clinical and Economic Review's (ICER) call for stakeholder input on 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 a long-standing supporter of policies that ensure health care decisions are patient centered and grounded in the best available evidence,<sup>1</sup> recognizing that sound approaches to evidence-based medicine are an important building block in value-driven health care. PhRMA strongly believes that well-designed tools for value assessment can move our siloed health care system to a holistic system based on value, which is central to long-term solutions that meet the needs of both patients and our health care system. The right information and tools, of which value frameworks are one, can empower informed health care decision-making and ensure the right treatments reach the right patients, at the right time.

Consistent with this position, on January 22, 2016, PhRMA released a set of 15 Board-approved principles in support of value assessment frameworks (enclosed).<sup>2</sup> Our principles can help ensure value frameworks, including ICER's framework, meet patients' needs and support continued innovation in health care. Framework developers who incorporate these principles can improve health care decision-making and the efficiency of our health care system, while frameworks that are inconsistent with these principles will make it more difficult for patients to obtain treatments that best meet their needs and will discourage continued medical progress. As we noted in our prior letter to ICER, we are concerned that ICER's current framework does not

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<sup>1</sup> PhRMA. "Principles for Evidence-Based Medicine." (Enclosed)

<sup>2</sup> PhRMA. "Principles for Value Assessment." Available at: <http://phrma.org/principles-guidelines/principles-for-value-assessment-frameworks> (Enclosed)

yet incorporate the process or methods, as described in our principles, required to ensure it meets the goal of a sound, patient-centered tool for considering and weighing available evidence on value.

We agree with ICER's goal of providing "all participants in the health care system with a fair and objective view of the evidence," and the position that "the assessment of value for all decision-makers should be grounded in what matters most to patients."<sup>3</sup> We appreciate your recognition that, in order to meet these goals, there is a need for reconsideration of and improvements to the ICER model in your national call for input.

Given the nascence of ICER's Emerging Therapy and Assessment Program, and the ongoing discussion around how value should be defined and quantified, we believe it's imperative that ICER continue to revise and refine its framework. The need for ongoing refinement has been echoed by experts in the field, who have stated that emerging value frameworks, including ICER's tool, face substantial analytical challenges and require significant refinement before they are broadly applied.<sup>4</sup>

There are several key steps that PhRMA believes ICER must take as it revises its value framework, in order to establish a methodologically rigorous, patient-centered value framework that can effectively support decision-making by stakeholders:

- I. Development of a transparent, dynamic ratings system that presents information on specific components of the value of health care treatments and interventions, and removal of value-based price benchmarks from all evidence reports.
- II. Suspension of the use of budget impact estimates until more sound methods are developed and validated.
- III. Adjustment of the cost-effectiveness component of the framework to reflect the inherent and widely recognized limitations in traditional quality adjusted life years (QALY)-based cost-effectiveness analysis (CEA), including capturing a wider range of benefits in CEA, and presenting a range of care value estimates based on sound assumptions and varied approaches.
- IV. Implementation of a fully transparent process in which ICER meaningfully engages with stakeholders, including stakeholders with disease-specific expertise, in setting priorities for assessment and developing its evidence reports.

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. PhRMA has provided more detail below as to specific steps that ICER can and should take to address our concerns.

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<sup>3</sup> Institute for Clinical and Economic Review. "Addressing the Myths About ICER and Value Assessment."

<sup>4</sup> Neumann PJ, Cohen JT. "Measuring the Value of Prescription Drugs." NEJM. January 2016. Available at: <http://www.nejm.org/doi/full/10.1056/NEJMp1512009#t=article>

**I. ICER should adopt a ratings system that provides greater transparency on the evidence and outcomes of specific components of the value equation, and eliminate value-based price benchmarks from its evidence reports.**

ICER's framework emphasizes setting a "value-based price benchmark" at the time of a drug's launch. We appreciate ICER's focus on value, and the orientation of its framework to payer-level decision-making. At the same time, we are concerned that ICER's approach fails to recognize how the concept of value is personal, dynamic and complex, and as a result, all centralized assessments of value are subject to a high level of uncertainty. As an organization that seeks to make evidence-based determinations, it is incumbent upon ICER to recognize and effectively communicate the inherent uncertainties of its analysis. Failure to do so conveys a level of certainty and precision that is not supported by evidence. Additionally, ICER's attempt to link assessment of value to a price benchmark forces methodological choices that impede the goal of providing an "objective view of the evidence" to all stakeholders.

*The value of new medicines is dynamic and is not well-suited to static value assessments.* The uncertainties surrounding the value of a new medicine at the time of its launch are often substantial, and even greater than for items and services not subject to the same rigor of premarket review as new medicines. Notwithstanding the uniquely high combination of evidence and standards for new medicines, the inherent uncertainties of setting a single value-based price through centralized value assessment are exacerbated when analysis is conducted at time of launch. For instance, the apparent value of a new medicine can evolve due to changes to a therapy's place in a line of treatment and changes in the evidence base through both additional trials and the accumulation of real-world evidence. In oncology specifically, further clinical trials, changes in sequencing, changes in combinations, and additional indications can lead to new valuations of the drug in a different context.

A recent report by Boston Healthcare Associates underscores the central importance of recognizing that value evolves and is not static, with the clinical progress achieved by what proved to be important medical advances greatly underestimated based on data available at the time of launch. The report shows how ongoing research revealed greater clinical value than demonstrated in initial clinical trials of new treatments for lung cancer, renal cell carcinoma, chronic lymphocytic leukemia, and multiple myeloma.<sup>5</sup> Likewise, in its value assessment framework, the American Society of Clinical Oncologists acknowledged that understanding of a medicine's role and full clinical value typically evolves over time.<sup>6</sup> However, both ICER and many HTA bodies abroad use single point assessments of value due to the difficulties of

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<sup>5</sup> Sweeny N, Goss TF. "The Value of Innovation in Oncology: Recognizing Emerging Benefits Over Time." May 2015. Available at: [http://www.phrma.org/sites/default/files/pdf/bha\\_value\\_of\\_cancer\\_innovation-whitepaper.pdf](http://www.phrma.org/sites/default/files/pdf/bha_value_of_cancer_innovation-whitepaper.pdf)

<sup>6</sup> Schnipper, L, Davidson, NE, Wollins DS, et al. "American Society of Clinical Oncology Statement: A Conceptual Framework to Assess the Value of Cancer Treatment Options." JCO. June 2015. Available at: <http://jco.ascopubs.org/content/early/2015/06/16/JCO.2015.61.6706>

measuring value evolution. Alternative approaches involve pragmatic decision-making, flexible thresholds for incremental cost effectiveness ratios, and variations in the hazard ratios of clinical trial data used in value assessments to account for future potential value.<sup>7</sup>

Analysis at launch also may be especially prone to ignorance of a critical long-term perspective. For instance, experts have found that “across 19 molecules whose patents expired from 2005 to 2009, \$193 to \$436 billion in economic value will transfer to consumers over 10 to 20 years due to patent expiration. This suggests that, while prices were high during the patent period, creating an incentive for innovation, the transfers to consumers after patent expiration are significant, which is how the patent system was designed to function.”<sup>8</sup> As we understood ICER’s value assessment framework, it does not consider either incentives for innovation or the enormous transfer to consumers after patent expiry made possible only because of the innovation that created the treatment. With drugs whose patents are expired now the mainstays for medical care across many disease areas, neglecting to consider this source of value skews ICER’s results.

*Definitions of value vary significantly from stakeholder-to-stakeholder, and among individuals, depending on their personal preferences and characteristics.* PhRMA is concerned that ICER’s value framework fails to acknowledge the different perspectives stakeholders have towards value, as well as the significant heterogeneity among individual patients. Individual patient differences occur due to many factors, such as genetic variation, differences in co-morbidities, and quality-of-life preferences. Any value framework that derives a value-based benchmark price combining average estimates of effectiveness, cost and other elements of value will invariably and systematically neglect heterogeneity in treatment effect, and important differences in patient needs and preferences, and as a result, create barriers to access to the range of treatment options needed to tailor care to ensure the best outcomes for patients.

In addition to failing to recognize the variability in the way different individuals define value, ICER’s value-based price benchmark favors the payer perspective over the perspective of patients.<sup>9</sup> Again, while we recognize ICER’s framework is oriented to payer decision-making, we believe it should be refined so that relevant information is provided to payers in a more patient-centric manner. A study published in Health Affairs surveyed patients to determine how much weight patients may place on a therapy with a wider “spread” of outcomes when presented with two cancer regimens that seemed on the surface to result in the same average survival gains. The patients were asked to compare two treatment regimens – one regimen promised patients exactly 18 months of additional survival, and the other an alternative called the “hopeful gamble,” which promised a 50 percent chance of thirty-six months of additional survival but also

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<sup>7</sup> Towse A, Barnsley P. Approaches to identifying, measuring, and aggregating elements of value. *International Journal of Technology Assessment in Health Care* 2013. 29:4(360-4).

<sup>8</sup> McKellar MR, Frank M, Huskamp H, et al. “The Value of Patent Expiration.” Forum for Health Economics & Policy. 2012.

<sup>9</sup> This is reflected, for example, in ICER’s document “Addressing the Myths About ICER and Value Assessment,” which articulates the goal of “a price that insurers will recognize as aligned with value” and setting an “alarm bell” on affordability tied to payers’ decision-making needs.

a 50 percent chance of no additional survival. A determination of clinically similarity would view the two regimens as the same, since they offer equivalent survival gains, though the hopeful gamble provides a greater chance at a large survival gain, but also the possibility of a worse downside. Participants were asked which they preferred. Although the “sure bet” regimen provides assurance of a shorter survival gain, and “hopeful gamble” offers a 50 percent chance of twice the survival gain, a large majority of cancer patients chose the latter.<sup>10</sup> These preferences illustrate the value of hope, a facet of value that payers often fail to recognize, and which is often underrepresented in value assessment, including in ICER’s framework. Because they are tied to the goal of setting a price benchmark, ICER’s methods fail to capture and convey the different ways that patients value treatments and health care interventions.

Other studies have 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. A survey recently conducted by Cancer Support Community showed that patients consider quality of life-related factors as the most important factor in treatment decision-making, over length of life, impact on family, and financial cost of care. Sixty-five percent of survey respondents indicated that quality of life had much more of an impact on treatment decision than financial cost. The structure of ICER’s framework simply does not reflect these priorities.<sup>11</sup>

As it refines its framework, ICER should look to organizations that are developing research to identify what individual patients value, and tools to make value frameworks more patient-centered. This includes research by organizations like Cancer Support Community, and the value assessment rubric developed by National Health Council.<sup>12</sup>

Based on these considerations, we recommend that ICER take the following steps:

- We strongly recommend that ICER eliminate the value-based price benchmark as a component of its evidence reports, which is a significant oversimplification of the benefits and cost of health care treatments and interventions. PhRMA is concerned that ICER’s approach to setting “value-based” price benchmarks is unrealistic, biased against new treatments, and divorced from the realities of the market’s effectiveness in driving spending that aligns with value. In particular, we recommend adoption of an output that provides greater transparency on the evidence and outcomes of specific components of the value equation so individual decision-makers can better tailor the assessments to their needs. Displaying the different facets of a treatment’s value (e.g. clinical effectiveness,

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<sup>10</sup> Lackdawalla D, Romley J, et al. “How Cancer Patients Value Hope and the Implications for Cost-Effectiveness Assessments of High-Cost Cancer Therapies.” *Health Affairs*. April 2012. Available at: <http://content.healthaffairs.org/content/31/4/676.full>

<sup>11</sup> Buzaglo JS, Miller M, et al. “Cancer Patients Priorities When Considering a Treatment Decision.” Available at: [http://www.cancersupportcommunity.org/sites/default/files/uploads/our-research/presentations/Patient-value/2016\\_biennial\\_cer\\_value\\_poster\\_6.7.16final2.pdf](http://www.cancersupportcommunity.org/sites/default/files/uploads/our-research/presentations/Patient-value/2016_biennial_cer_value_poster_6.7.16final2.pdf)

<sup>12</sup> The National Health Council. “The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric.” March 2016. Available at: <http://www.nationalhealthcouncil.org/sites/default/files/Value-Rubric.pdf>

toxicity, and cost) separately allows the end-user of the evidence reports to assign a weight to those elements that is appropriate for their preferences.

- Given the evolving nature of value and evidence, ICER should provide greater clarity and detail regarding the limitations and uncertainties that are inherent in its report. ICER should consider clearly and prominently labeling its analyses conducted near the time of launch as “preliminary and based on limited data” to avoid false assumptions about the certainty of its findings. Additionally, when new data not considered in an analysis becomes available, promptly mark the analysis with a phrase such as “newly available data not included in results.”

**II. ICER should suspend the budget impact component of its framework until it can identify a more sound method of estimating affordability and addressing payer needs. At a minimum, ICER should refrain from combining the results of its budget impact estimates with its cost effectiveness estimates.**

PhRMA is concerned that the health system value phase of ICER’s framework focuses squarely on short-term budget impact from a payer perspective, rather than examining long-term value from a patient or societal perspective. While ICER attempts to contextualize the budget impact analysis into a larger framework, ICER’s focus on the potential for “short term costs [that are] so substantial as to displace more valuable services” is shortsighted and exacerbates well documented biases against long-term benefits for short term health care savings.<sup>13</sup> ICER should work to correct this myopic focus on short term costs by focusing on long term costs and benefits of treatments including those that have an impact outside the health care system but are relevant to patients and their families.

PhRMA acknowledges that the intended end-user of ICER’s evidence reports are payers, who are concerned about the affordability of treatments; however, budget impact analysis is simply not a component of value. To the extent ICER persists in providing information to payers on estimated budget impact, it should be entirely separate from the value assessment.

The significant focus on the affordability of health care treatments and reliance on methods rooted in budget impact assessments, rather than the true value of these interventions, is at odds with ICER’s goal of creating a “value framework.” Such significant flaws in any tool used to support health care decision-making could have potentially dire consequences for patients, whether they are intended for patients or not. Further, this element of ICER’s model seriously impedes the goal of assessments that are grounded in “what matters most to patients,” even at the payer level of decision-making. ICER’s claims that the budget impact component of its value

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<sup>13</sup> Chabris CF, et al. Individual Laboratory- Measured Discount Rates Predict Field Behavior. NBER Working Paper 14270. August 2008.

framework is simply an “alarm bell” do nothing to diminish its potential dangers. If anything, it’s concerning that ICER seeks to minimize the potential implications of its framework for patients.

In light of these concerns, we urge ICER to refrain from estimating budget impact until it can identify more sound methods for doing so. Should ICER decide to persist in estimating affordability, it should immediately replace its current approach based on a subjective, siloed budget threshold, and instead simply provide to users the budget impact estimates underlying these calculations. In view of the difficulty in accurately predicting short-term budget impact, ICER also should provide a series of estimates based on a range of valid assumptions, which payers can use to draw conclusions about what if any steps they should take based on the estimates. These estimates should be calculated and displayed separately from any calculation of value, as budget impact is not a true measure of value, no matter how useful the information is to payers. Below we provide additional detail as to our concerns and recommendations.

*ICER’s framework is inherently biased against innovation.* ICER’s budget impact assessment has an inherent bias against innovative technology, which could stifle innovation and lead to underutilization of services that could provide long-term benefits to both patients and the healthcare system. Based on the proposed methodology, ICER penalizes productivity in the biopharmaceutical industry by basing the budget impact of drugs on the estimated number of approvals. Even if innovative medicines are making the largest contribution to improved public health, under ICER’s framework, the resources allocated for new medicines are fixed while resources available for less productive sectors making smaller contributions to improved public health are unaffected. Due to the potentially limited return on investment, companies have less incentive to ride a new wave of technical innovation, which discourages development across the full range of medical possibilities.

*A five-year budget analysis is biased and unrealistic.* According to the Centers for Disease Control, chronic diseases are “among the most common, costly, and preventable” health conditions, with approximately half of all adults in the United States suffering from one or more chronic condition.<sup>14</sup> A five-year budget impact sends the wrong message to clinicians and patients as well as payers who need to begin thinking more about long-term interventions that can keep patients with chronic conditions healthy over the course of their entire lives. This concern is underscored by the evidence relied on by ICER itself in evaluating the clinical and economic value of interventions. For example, ICER’s report on diabetes prevention programs cited the Diabetes Prevention Program Outcomes Study, which measures outcomes of behavioral intervention and pharmacotherapy over a ten-year period. This divergence between the design of ICER’s framework and the evidence it relies upon underscores the conflict between an objective assessment of evidence on long-term value, and subjective short-term judgments of affordability.

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<sup>14</sup> Ward BW, Schiller JS, Goodman RA. Multiple Chronic Conditions Among US Adults: A 2012 Update. Centers for Disease Control and Prevention Preventing Chronic Disease. April 2014, Vol 11.

*ICER sacrifices potentially high value care to make more room for low value care.* In the past, ICER has stated that spending on treatments and interventions beyond its pre-determined budget threshold “could displace equally or more valuable care.” However, ICER has presented no evidence this is the case and seems to conflate “low cost” with “high value” – a striking contradiction for an organization that claims to make evidence-based determinations. Prescription medications are subject to rigorous scrutiny supported by extensive clinical evidence before they can enter the market – a much higher bar than many other health services offered to patients. In contrast, there is extensive evidence that a sizable share of care delivered in the United States is low value. A multistakeholder analysis spearheaded by the American Board of Internal Medicine and AcademyHealth categorized more than 400 common procedures and healthcare interventions as “low value.”<sup>15</sup> Among the interventions identified, more than 75 percent were non-drug related. PhRMA encourages ICER to refocus on health services and interventions that are truly “low value” rather than scrutinizing therapies based on aggregate expenditures and budget impact.

ICER’s misplaced focus on “high cost” rather than “high value” can be seen in its evaluation of treatments for Hepatitis C. By definition, curing HCV before it harms patients is higher value than the very large cost of treating the consequences of Hepatitis C infection. Yet the health system value phase of ICER’s evaluation of innovative Hepatitis C treatments does not acknowledge the costs of chronic infection and subsequent complications. There is well documented evidence that appropriate use of medicines can offset healthcare spending.<sup>16</sup> While ICER’s health system methodology lists “*net change in total health care costs*,” the summary of 2015-2016 budget impact calculations does not allow for including the potential offsetting savings from drugs by averting other healthcare needs. PhRMA encourages ICER to consider the true net change in all health spending, rather than expenditures on drugs in isolation.

*ICER’s “health system value” calculations are arbitrary and based on speculative information.* ICER argues its budget threshold, based on gross domestic product (GDP) + 1% is not arbitrary, but is supported by policies adopted in Medicare and other public health care programs. However, Congress recently repealed a GDP-based system, the sustainable growth rate, which was widely viewed as unworkable. Additionally, while we believe the Independent Payment Advisory Board system is severely flawed, its GDP + 1% target is distinct from ICER’s target in that it applies on a program-wide basis rather than to a small subset of care and spending. Moreover, ICER does not propose to adopt and apply a GDP + 1% budget threshold for any health care service other than new drugs and devices.

Additionally, ICER arbitrarily bases the budget amount on freezing – or in practice, diminishing (since the large majority of health spending would not be constrained by the same budget amount

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<sup>15</sup> American Board of Internal Medicine Foundation. Choosing Wisely. April 2014. Available at: <http://www.choosingwisely.org/>

<sup>16</sup> Congressional Budget Office. Offsetting Effects of Prescription Drug Use on Medicare’s Spending for Medical Services. November 2012.



and is likely to grow faster) – new medicines’ share of total health spending. As paradigms of care shift from resource-intensive inpatient hospitalization to more personalized treatment using prescription medications, considering the budget impact of prescription medicines in isolation and freezing the share of spending attributable these medicines does not allow for health systems’ evolution and changes in patterns of care. There is also no good basis for ICER’s assumption, which is unrelated to the either the value of different treatments however measured or the rate of progress of medicines compared to other types of care. In fact, a study examining patterns of cancer care in the United States found that while per capita spending has remained steady over time, there have been significant shifts away from hospital-based care towards medication-based therapy, while simultaneously achieving significant improvements in survival and health outcomes.<sup>17,18</sup> Further, the goal of supporting high-value care by ensuring interventions are well-grounded in evidence would argue for increased, not static or reduced, spending on prescription medicines relative to other health care items and services.

ICER also has a poor track record of projecting the uptake of new medicines and treatment, which is central to its budget impact calculation. For example, ICER significantly overestimated the uptake of products to treat high-cholesterol in a 2015 evidence report.<sup>19</sup> Overestimating the budget impact of new medicines and treatments, thereby reaching an inaccurate estimate of a treatment’s “value”, according to ICER, could have significant consequences for patient access. Finally, treating drugs used by larger populations as inherently less valuable than those used by smaller populations – with extreme reductions in value for drugs that make a difference for large populations – creates perverse incentives for innovators, disincenting improvements for larger populations.

*ICER’s siloed approach to assessing value discourages the movement towards value.* ICER further discourages the movement towards a value-based health care system by adopting a siloed approach to budget impact that fails to address the health care system holistically. ICER’s budget applies only to new drugs and a small minority of other health services, with the calculation of the budget threshold for new drugs based exclusively on drug spending multiplied by GDP + 1%. However, drugs interact with other health services and spending. The Congressional Budget Office now 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 use of drugs. There is evidence that in oncology, additional spending on medicines results in lower treatment spending overall.<sup>20</sup> ICER’s approach to setting a budget threshold for medicines makes no allowance for

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<sup>17</sup> Tangka F, et al. Cancer treatment costs in the United States: has the burden shifted over time? *Cancer*. July 2010; 116(14):3477-84.

<sup>18</sup> American Cancer Society. *Cancer Facts & Figures 2016*. Atlanta: American Cancer Society 2016.

<sup>19</sup> Available at: <http://www.medpagetoday.com/Cardiology/CardioBrief/55910>; Available at: <http://www.reuters.com/article/us-express-scr-cholesterol-drugs-idUSKCN0VL2AX>

<sup>20</sup> Newcomer L, et al. “Changing Physician Incentives for Affordable, Quality Cancer Care: Results of an Episode Payment Model.” *Journal of Oncology Practice*. DOI: 10.1200/JOP.2014.001488.

such effects, a serious problem that reinforces silo-based thinking about health care rather than helping break down barriers to better care.

PhRMA suggests that ICER take the following steps to revise its framework:

- If ICER cannot address the issues related to the health system phase of its value framework in a timely manner, it could have serious consequences for patient access and innovation. PhRMA strongly recommends that ICER eliminate the budget impact component of its framework until it can identify a more sound method of estimating affordability and addressing payer needs.
- If ICER persists with the health system value phase of its framework, it should at a minimum, clearly label the budget as conceptual only and state that numerous choices other than those made in the budget could lead to different results. ICER should also refrain from combining the results of its budget impact estimation with its cost effectiveness estimation. Budget impact is not a measurement of value, and should be calculated and displayed separately from the “care value” phase of ICER’s framework.

### **III. ICER should adjust its approach to presenting cost-effectiveness data to reflect the inherent and widely recognized limitations in traditional QALY-based cost-effectiveness analysis.**

While PhRMA appreciates ICER’s commitment to putting patients “at the center of the discussion,” we have several concerns regarding ICER’s approach to cost effectiveness analysis (CEA) for the larger value framework effort. ICER’s goal is to provide a “care value” estimate and “facilitate discussions around value at the broader population level” for assessed technologies. However, it is unlikely that these value assessments will be used solely at a theoretical population level discussion and not influence individual patient treatment plans. Thus, it is important to understand if these tools appropriately capture “value” at all levels – from the individual patient to the population level.

There is an inherent tension in using CEA to assess the “value” of a course of treatment or therapy for both societal resource allocation and as well as individual decision making. By aggregating the concept of value and outcomes across individuals, ICER’s framework shifts from putting the patient at the center of the discussion and lacks the specificity necessary for health care decision making in practice. ICER’s approach to cost effectiveness analysis relies heavily on the use of quality adjusted life years (QALYs), which were not originally intended to be used by individual patients for decision making.<sup>21</sup> Thus, the reliance on QALYs to assess

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<sup>21</sup> Weinstein MC, Torrance G, McGuire A. QALY: The Basics. Value in Health. 2009, 12(S1):S5-9

value is inherently at odds with ICER's stated desire that "the assessment of value...should be grounded in what matters most to patients."<sup>22</sup>

Additionally, the approach that ICER proposes for CEA, using traditional QALY measures, overlooks important differences in patient characteristics, preferences, and responses to treatment. QALYs combine changes in morbidity and mortality into a single number and overlook significant heterogeneity of patient preferences and treatment effect between and across these two outcomes. To inform decisions affecting individual patients, it is critical to "consider patient-specific data on quality and quantity of life rather than QALYs based on aggregated data that incorporate a societal perspective on the value of any health benefits." For example, two patients with the same condition may value quality of life (morbidity) and quantity of life (mortality) differently, but may end up with the same QALY score. By broadly applying QALYs derived from studies rather than individual patient histories or interviews, ICER again moves away from a more patient-centric value assessment.

Even at the population level, where the use of QALYs may be less problematic, numerous economists and researchers have acknowledged that QALYs fail to appropriately "incorporate certain fairness and distributional concerns that are important in group decision-making."<sup>23</sup> While the Institute of Medicine recommends that "in the absence of direct preference elicitation for health conditions of interest from the affected population, QALY estimates should be based on well-developed, generally accepted, and widely used generic [health related quality of life] HRQL indexes" researchers have found that the results of CEA can depend heavily on the measurement tools being used. For example, a study examining several commonly used HRQL indices found adjusted disutilities ranging from 0.059 to 0.104 for the same population, depending on the measurement tool being used.<sup>24</sup> As one of the hallmarks of a valid measure is replicability, the wide range of differing results being driven by measure selection rather than actual patient preference indicates that QALYs derived from standard HRQL indexes should be interpreted with extreme caution.

Additionally, it is unclear how ICER assesses costs associated with all available treatment options for the cost component of CEA. A narrow focus only on drugs misses the larger picture of the drivers of healthcare spending. Spending on prescription drugs is projected account for less than 15 percent of all health care spending through 2024.<sup>25</sup> Additionally, many patients suffer from multiple conditions, where medications are only a part of a complex constellation of therapies and services. To evaluate the cost effectiveness of a single drug in isolation from the

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<sup>22</sup> Institute for Clinical and Economic Review. "Addressing the Myths About ICER and Value Assessment."

<sup>23</sup> Lipscomb J, et al. Retaining and Enhancing the QALY. *Value in Health*. 2009 12(S1):S18-S26.

<sup>24</sup> Franks P, Hammer J, Fryback DG. Relative disutilities of 47 risk factors and conditions assessed with seven preference-based health status measures in a national U.S. sample: towards consistency in cost effectiveness analysis. *Medical Care*. 2006. May; 44(5):478-85.

<sup>25</sup> Altarum Institute. A Ten Year Projection of the Prescription Drug Share of National Health Expenditures Including Non-Retail. August 2015. Available at: [http://altarum.org/sites/default/files/uploaded-publication-files/Non-Retail%20Rx%20Forecast%20Data%20Brief\\_with%20Addendum.pdf](http://altarum.org/sites/default/files/uploaded-publication-files/Non-Retail%20Rx%20Forecast%20Data%20Brief_with%20Addendum.pdf)

larger treatment context does not provide patients, providers, or payers with the information that they need to make sound decisions.

PhRMA suggests that ICER consider the following changes to the CEA piece of its value framework:

- ICER should expand the range of benefits captured in its cost effectiveness analyses. Traditional cost effectiveness analysis attempts to quantify patients' health and HRQL across several domains such as physical health and functioning, pain, and mental health. However, while these domains may consider part of what is important to patients, they cannot capture the full range of benefits and heterogeneity of preferences that patients have for certain outcomes over others. While ICER has acknowledged these limitations and included an assessment of "other benefits and disadvantages" in the proposed value framework, PhRMA encourages ICER to explicitly include these in the cost-effectiveness analysis and provide transparency regarding their inclusion.

Many of the traditional methods of measuring HRQL that underpin cost effectiveness analysis are generic scales that are not specific to the population or condition being studied. Patient outcomes and utilities should be directly relevant to the patient population affected by evaluated health interventions. If the appropriate specificity of data are not available then ICER should seek to collect information directly from the patient populations and all relevant subpopulations to address heterogeneity in treatment effects and preferences.

To consider the full range of direct and indirect effects of healthcare interventions a number of additional elements of value can be considered by ICER, including clinical and patient reported outcomes, healthcare spending offsets, quality of life, labor productivity, treatment response certainty, delivery mechanism, patient functionality, hope for significant treatment benefit, potential for access to future treatment options due to life extension, and spillover effects, such as those related to family burden or scientific progress.

We emphasize the importance of considering a few select value elements in conducting CEA. In particular, including productivity gains due to reductions in absenteeism as an explicit benefit of certain therapies that reduce the burden of illness is increasingly accepted by experts in pharmacoeconomics and health economics. PhRMA also encourages ICER to include outcomes for data collection and synthesis of existing studies that consider non-traditional measures of patient quality of life.

High unmet need, as evidenced by expedited regulatory approval and clinical trial enrollment, should be considered. Further, the option value of a newly approved treatment allows for incorporating future, or evolving value into the assessment. Option

value is the value to be gained by new indications and new combinations commonly seen with oncologic agents. Baseline severity or prognosis should be considered, particularly for diseases like cancer, as a patient who has a projected median survival of 3 months will value an additional month more than a patient who has a projected median survival of 2 years.

Additionally, while ICER includes “methods of administration” as a factor to be considered outside of the formal CEA, PhRMA believes that benefits to patients from improved and simplified treatment regimens should be included in a formal CEA. Offering a patient an oral vs. intravenous formulation can have a significant impact on patient quality of life and adherence and should explicitly be included in any CEA. While recent analyses of breakthrough medications that simplify treatment regimens such as the direct acting agents for HCV and single treatment regimens acknowledge the vastly shortened treatment duration and simplified treatment regimen that these therapies offer, they do not attempt to quantify the benefit offered by these improvements; when assessing benefits, most analyses focus solely on biomedical markers such as viral load.<sup>26,27</sup> PhRMA encourages ICER to explicitly capture benefits such as these in their CEA.

- ICER should present a range of cost-effectiveness ratios based on sound, varied assumptions to address differences in treatment effects, patient clinical traits, and treatment and risk preferences. A single ratio does not acknowledge that the results of CEA may change over time as our understanding of the benefits of treatment options as well as their costs can evolve. In a recently released report, ICER states that it “repeats analyses using different quality of life assumptions in order to understand whether a change in baseline quality of life makes an important difference in the final results.” ICER should incorporate those ranges into its output. Presenting the results as a range of possibilities acknowledges that our understanding of costs, benefits, and value can also change as new data become available.

Because of the variable nature of these results, PhRMA encourages ICER to present results of any CEA as a range of potential cost-effectiveness, rather than attempting to reduce this complex measure to a single number. It is important for policy-makers, payers, providers and patients to understand the inherent uncertainty associated with any CEA; presenting a single numeric result implies a level of certainty that is not supported by the underlying data.

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<sup>26</sup> Institute for Clinical and Economic Review. The Comparative Effectiveness and Value of Simeprevir and Sofosbuvir in the Treatment of Chronic Hepatitis C Infection: A Technology Assessment Final Report. April 2014.

<sup>27</sup> Hill A, Pozniak A, Simmons B. No difference in the risk of virological failure between antiretroviral treatments using co-formulated versus individual drugs: meta-analysis of 9 randomised trials in 2,568 patients. BHIVA Conference. April 2015.

Additionally, rather than assigning thresholds for “low,” “intermediate,” or “high” value using absolute cost per QALY (i.e., \$100,000/QALY), ICER should only use CEA as a measure of understanding how treatments compare to other alternatives. As noted earlier, the results of any cost-effectiveness analysis are highly dependent on the measures used to collect and characterize patient preferences and context of the decision making process. The level of value is dependent upon the decision maker who can make their own judgement based on the evidence presented.

- ICER should also consider approaches to CEA other than a cost-per-QALY-based approach. Other approaches, such as Cost Consequence Analysis (CCA) that could be a very viable alternative to the QALY, and that would allow the inclusion of wider patient and societal impacts in a clear, disaggregated fashion. The CCA approach is consistent with the argument that ICER should provide a range of data given that their audience uses differing criteria to come to their decisions. To use CCA, ICER would provide the cost impacts and offsets, direct and indirect, in a table following CCA methodology. It would be up to a specific payer to take the relevant components from this table and the clinical/safety table and come to their own decision. Within oncology, this would allow the considerable potential cost offsets of avoidance of downstream expensive radiotherapy, income from being able to return to work early, and so forth.<sup>28</sup>

#### **IV. ICER should implement an improved process for conducting assessments that provides increased transparency and meaningful engagement with patients, physicians and other stakeholders, including stakeholders with disease-specific expertise.**

PhRMA strongly recommends that ICER improve the process through which it assesses value. This includes providing opportunities for meaningful engagement with stakeholders, including manufacturers, providers, and patient groups, as well as improving the transparency of the overall model design and assumptions. PhRMA commends ICER for taking several steps to improve its engagement with stakeholders since the launch of its ETAP program, including extending comment periods for draft materials, and conducting additional outreach to patient and provider representatives. However, PhRMA remains concerned that although ICER has increased the quantity of manufacturers, provider and patient organizations it speaks to in developing its reports, its engagement is not resulting in the incorporation of those stakeholders’ perspectives and expertise in its output.

Engagement with stakeholders who have expertise and experience is not simply a box ICER must check – it is essential to ensuring that ICER’s reports are accurate and reflect the outcomes and experiences of patients and providers. A common criticism of ICER’s evidence reports has been that they fail to reflect the clinical realities of treating patients. For example, the American

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<sup>28</sup> Mayskopf, J.A., Paul, J.E., Grant, D.M. et al. *Pharmacoeconomics* (1998) 13: 277.

Society of Hematologists noted in their comments to ICER in response to the draft multiple myeloma evidence report, comparing FDA-approved combinations of novel drugs to historical treatment, “that most patients who are prescribed new agents have typically already failed the historical standard treatment, making this comparison irrelevant.”<sup>29</sup> This error, which as ASH points out, has the potential to lead payers to constrain treatment decision-making, could have been avoided had ICER included a hematologist or a multiple myeloma patient on its Midwest CEPAC advisory panel. ICER should ensure that its materials, including the scope its assessments and the resulting evidence reports, are aligned with the perspectives of clinical societies, through meaningful engagement.

Many stakeholders, including the biopharmaceutical industry, have submitted feedback in response to ICER’s evidence reports. PhRMA applauds ICER for posting the comment letters it receives online following the issuance of its draft reports. ICER should do the same for all of its materials, including posting comments it receives in response to announcements of new assessments, and draft scoping documents. ICER should also post transcripts of advisory panel meetings online shortly following the meeting.

In addition, ICER should make its models and assumptions publicly available, as experts have noted that “choices in modeling can lead to widely varying assessments for the same treatment based on the same data.” One observer who found that ICER chose to include some clinical outcomes but exclude others (such as avoided coronary artery bypass surgeries) when it assessed a type of cholesterol lowering medicine comments, “Suffice it to say, if you make a different set of assumptions you can get a very different answer.”<sup>30</sup> Since the results of cost effectiveness assessments for a given treatment can vary more than 20-fold, it’s essential that stakeholders be able to examine and assess the full set of choices ICER makes in reaching its result.

PhRMA recommends that ICER make the following changes to improve in its process:

- ICER should ensure that its advisory panels are comprised of stakeholders with disease-specific expertise, including clinicians, patients, and manufacturers.
- ICER should allow 30 days for public comment in response to its draft scoping documents and 60 days in response to its draft evidence reports. ICER’s evidence reports often are 150 pages or more in length, and it is unreasonable to expect stakeholders, particularly those with fewer resources at their disposal, to provide constructive, concrete feedback in 10 or 30 days. Such a short comment period will be prohibitive for many stakeholders with valuable expertise and perspectives.

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<sup>29</sup> American Society of Hematology. Available at: <http://www.hematology.org/Advocacy/ASH-Testimony/2016/5512.aspx>

<sup>30</sup> Rubin R. “Value Pricing For Drugs: Whose Value, What Price?” Health Affairs Blog. March 2016. Available at: <http://healthaffairs.org/blog/2016/03/28/value-pricing-for-drugs-whose-value-what-price/>

- ICER should be transparent about the feedback it receives from stakeholders, as well as whether it incorporates the feedback into its revised materials. It is not simply enough for ICER to say that it has taken feedback received into account – ICER should explain how it has incorporated feedback, including comment letters, into its revised materials. If ICER chooses not to incorporate a suggestion or criticism into its framework, it should clearly state the rationale for not doing so.
- ICER should make the models it relies upon available publicly so that stakeholders can validate ICER's methods, data sources, and assumptions. Information regarding ICER's model, as well as the assumptions that inform its model, is necessary in order for stakeholders to effectively evaluate the reliability and validity of the model. Given the nature of the models ICER relies upon, 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 taking steps similar to that of the European Society of Medical Oncologists, which has made its value framework available for critique and validation to all stakeholders.
- ICER should consider subjecting its value framework and evidence reports to peer-review prior to the release of the evidence report. By submitting its materials for peer-review, ICER would be subjecting itself to critique by a diverse set of experts and thought-leaders who can evaluate the analyses with an objective eye. ICER would not only benefit from the knowledge and expertise offered by a peer-review committee, undergoing the peer-review process would enhance ICER's credibility with other stakeholders. ICER should consider following in the footsteps of other framework developers, such as ASCO, whose value framework has been peer-reviewed twice before ASCO intends to finalize the framework. While we appreciate that ICER submitted its review of high-cholesterol medications for peer review and recent publication, ICER should ensure that its reports are peer-reviewed prior to use by health care stakeholders.
- ICER should be transparent in its priority-setting process. In determining what diseases it will assess, ICER should meaningfully engage with all stakeholders to better understand their concerns and priorities. ICER should consider releasing a proposed list of topics, and permitting public comment on the proposed list. ICER should also consider holding a public meeting at which proposed topics for assessment are discussed. Topics for assessment should be voted upon by a diverse group of stakeholders, including patients, clinicians and biopharmaceutical industry representatives.



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PhRMA and ICER have a shared interest in supporting informed, evidence-based shared decision-making by stakeholders at all levels, including payers and patients. 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,



Randy Burkholder  
Vice President, Policy & Research

Enclosed:

PhRMA Principles for Value Assessment

PhRMA Principles for Evidence-Based Medicine

## **Principles on Value Assessment**

### **January 20, 2016**

PhRMA supports the use of sound evidence for informed decision-making in health care. When designed well and used appropriately, emerging frameworks to assess the value of medical tests, treatments and health care services represent one of the many tools that can be useful to support well-informed, patient-centered health care. At the same time, it is important to ensure value frameworks are not misused in ways that impose centralized, one-size-fits-all policies, impede patients' and physicians' ability to tailor care to individual needs and preferences, and hinder progress against unmet medical need.

The principles below can help ensure that value frameworks and assessments meet patients' needs and support continued improvement in health care. Frameworks that incorporate these principles can improve health care decision-making and the efficiency of our health care system, while frameworks that are inconsistent with these principles will make it more difficult for patients to obtain health care and treatment options that best meet their needs and discourage continued medical progress.

#### **Background: Description and Context for Value Assessments**

Emerging value frameworks incorporate an assessment of evidence on clinical and economic data, and can be viewed as a subset of, or novel methods for, health technology assessment (HTA). They are designed to inform a range of different audiences and health care decisions, including treatment and prescribing decisions by patients and physicians as well as pricing or policy decisions made by private payers. A framework may be limited to or give particular priority to one of these perspectives.

Value frameworks are emerging at a time when other significant changes are occurring in health care, including: increased focus on patient- and consumer-centered care; growth in payment models that seek to incentivize health care value; growing capacity for generation of real-world evidence of value by a range of stakeholders using electronic health data; and the emergence of personalized medicine enabled by a growing understanding of genomics and capacity for storing and analyzing large volumes of electronic health data. As value frameworks emerge, it is important for them to align with these trends.

Value frameworks can be useful decision-support tools but should not be viewed as providing a single, universally applicable answer to questions about a treatment's value. Value frameworks typically emphasize one of several perspectives (e.g., payer, patient, society, or innovator) and conclusions may not apply to individual patients. In addition, as with any economic model, value frameworks involve making choices about methods, assumptions and data that can yield important differences in results depending on the choices made. This is reflected in the disparate assessments produced by different frameworks. These factors, combined with lack of consensus on best practices and inconsistency in level of transparency, underscore the need to construct and use value frameworks appropriately, as outlined in the principles below. Experience in some countries outside the U.S. illustrates how value frameworks can be used in ways that deny access to care options that clinicians and patients recognize as highly valuable.

These principles are focused on emerging value frameworks and assessments in the context of the U.S. health care system grounded in market competition. At the same time, many of these principles

are relevant for HTA more generally. While HTA is traditionally focused on payer-level decision-making, value assessment frameworks may seek to inform physician and patient treatment decisions at the individual level as well as decision-making at the population level. Regardless of who is utilizing the framework, it is essential to keep the patient at the center and ensure that population-level decisions do not hinder progress against unmet medical need, or impede physician flexibility in treatment decision-making or patient access to high value care at the individual level.

### **Principles for Value Assessment Frameworks:**

- I. **Utilize open and transparent processes for developing value frameworks and reports:** Value frameworks should be developed through an open and transparent process that includes: advance notice of priorities for assessment and scoping documents for planned assessments; opportunity for technical input from organizations with expertise in the items or services being assessed, including manufacturers when relevant; opportunity for public input on draft reports and public responses to comments received. Panels used in the development of value assessments and frameworks should be balanced and well-versed on topics under review, have relevant expertise, and should be provided materials for review in advance of meetings. Meetings should be open to the public and meeting output publicly reported.
- II. **Communicate results of final value assessments consistent with the goal of patient-centered decision-making:** Results of value assessments should be communicated after they are finalized, and in ways that support or, at a minimum, do not impede physicians and patients in tailoring decisions to the needs and preferences of the individual patient. Developers of value frameworks should make clear their process for releasing both draft and final value assessments. Communication should be consistent with standards for comparative effectiveness research communication described in statute creating PCORI.<sup>1</sup> Results of draft reports should not be widely disseminated or communicated as providing actionable guidance for decision-makers.
- III. **Undergo thorough validation and testing:** Value frameworks should undergo thorough and transparent validation both before and after development to ensure that they do not negatively impact health outcomes. In addition, framework output (assessment reports) should be subject to ongoing validation to ensure that accurate, reproducible findings are being generated. Frameworks also should be subject to peer-review to ensure they are consistent with well-established standards and methods.
- IV. **Ensure a strong role for physicians and patients:** Practicing physicians and patients bring essential expertise and perspective, and should have a central role in the prioritization and development of value assessments to ensure they draw on physicians' clinical expertise, reflect patient values and respect patient differences.
- V. **Clearly state the intended use and audience:** The developers of value frameworks should clearly specify the intended audience of assessments and the level of decision-making they aim to support. Value assessments should incorporate design and content appropriate for the audience and intended purpose. Regardless of the type of decision-making the assessment seeks to inform, it should facilitate patient-centered care.

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<sup>1</sup> Affordable Care Act. Subtitle D—Patient-Centered Outcomes Research. PUBLIC LAW 111–148. March 23, 2010.

- VI. **Prioritize patient-focused value frameworks to support individualized treatment decision-making:** The greatest opportunity for patient-centered value frameworks is through the development of more robust tools and decision aids to help physicians and patients decide which care options are most valuable to the individual. Patient-focused value frameworks should align with and support the goal of shared decision-making, and allow a patient to customize the assessment based on their individual preferences. Regardless of the level of decision-making where they are used, value assessments should not be misused at the population level in ways that impede physicians and patients from tailoring evidence-based decisions to the needs and preferences of the individual.
- VII. **Use rigorous methods and make them transparent to researchers and users:** Methods for assessing value should be grounded in sound, recognized methods and be subject to meaningful and rigorous peer review. Value frameworks should provide transparency in methods to allow other organizations to replicate findings, give decision-makers confidence in the findings, and give innovators predictability in standards being used. This should include transparency in types of data used, economic models and assumptions made. Users need to understand assumptions that affect results, whether they have a strong foundation, and be able to assess the effect of alternative assumptions.
- VIII. **Ensure that models utilize accurate, relevant data for assessing and reporting costs and economic outcomes:** If cost or affordability information is incorporated into a value framework, it is important that the information is conveyed in a way that is accurate, appropriate, and relevant to the intended audience. Value frameworks should seek timely and accurate data on cost information, gather input from relevant stakeholders, including physicians, and provide full transparency surrounding economic models used while protecting any commercial confidential data. Value frameworks intended to support patient-level decision-making should provide cost information relevant to the individual patient, such as out-of-pocket costs.
- IX. **Incorporate a broad range of high-quality evidence:** Value frameworks should include a broad range of rigorous and widely available scientific evidence, as incorporating only a portion of available evidence will ultimately limit the utility of the framework in practice. Any information that is potentially proprietary or commercially sensitive should be protected. Similarly, developers of value frameworks should use sound methods for synthesizing evidence.
- X. **Consider the broad effects of health interventions:** Health care interventions can have a wide range of direct and indirect costs and benefits. Value assessment frameworks should capture these in ways that provide comprehensive, accurate information on value, and convey information relevant to the intended audience and use. Quality of life, patient-reported outcomes, survival, patient functionality and economic productivity are among the factors important to patients and society.
- XI. **Prioritize the inclusion of longer-term outcomes:** Assessments should appropriately consider both short term and long term outcomes. Assessments based only on short-term costs and benefits will likely de-value important advances, which often reveal longer-term clinical benefits and cost offsets through reduced complications (e.g., survival from cancer medicines, reduced heart attacks through management of cholesterol levels) and hospitalizations. Likewise, after the expiration of exclusivity on medicines, the treatment may be widely used by a large number of patients at a lower cost, generating benefits that should be recognized in value assessments.

- XII. **Value progress against unmet medical needs:** Value frameworks should recognize the value of progress against diseases in which there is unmet need by aligning with the processes through which that progress occurs. This includes: accounting for the inherent value of scientific and biomedical advances that add knowledge about diseases and interventions and provide stepping-stones to future advances; recognizing inherent uncertainty in the innovation cycle that often involves introduction of highly promising advances followed by ongoing research on longer-term clinical outcomes; the emergence of personalized medicine; and the step-wise nature of progress in which significant gains for patients are achieved via advances that build on one another. Current models that make conclusions based on global budgets or spending caps fall short of the goals of patient-centeredness and true value assessment, and as a result devalue many important advances against unmet medical needs.
- XIII. **Support value across the health system and continuum of patient care:** Value frameworks should have a holistic, system-wide scope of work that evaluates all relevant aspects and settings of care. Consistent with the Patient-Centered Outcomes Research Institute's (PCORI) mandate for its work on comparative effectiveness<sup>2</sup>, value assessment should examine the full range of health care items and services (e.g., medicines, devices, diagnostics, surgery) and the care management and delivery strategies that influence patient care. Several emerging value frameworks are intended to help guide decisions of health care resource allocation, which cannot be done in a meaningful, informed way without examining all relevant aspects of clinical care and patient management.
- XIV. **Examine patient subgroups to meet individual patient needs and optimize value:** Value frameworks should consider and reflect the needs of patient sub-populations, who often respond differently to medicines based on factors such as age, genetic variation, and comorbidities. Because patient sub-populations can differ in their response to therapy, a variety of treatment options may be required to optimize treatment and provide the most clinical benefit and the greatest value. Recognizing patient heterogeneity is particularly important to ensure alignment with the emergence of personalized medicine.
- XV. **Support availability of multiple value assessments from a range of organizations:** Value frameworks seek to meet the needs of a wide range of decision-makers, and involve the evaluation of complex interventions using sophisticated and variable methods and assumptions. Decision-makers will benefit from multiple value frameworks, along with other data sources, to support their decisions and ensure the availability of relevant, timely, and high-quality reports.

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<sup>2</sup> Affordable Care Act. Subtitle D—Patient-Centered Outcomes Research. PUBLIC LAW 111–148—March 23, 2010.



## **PhRMA Principles for Use of Evidence-Based Medicine: Advancing Patient Care and Health Care Value**

PhRMA supports evidence-based medicine and evidence-based decision-making in health care. Specifically, all health care decisions should be informed by the best available evidence. Evidence-based medicine (EBM) is at its core the use of best available evidence to support good decision-making by patients and physicians, and integrates current available evidence, clinical expertise and patient understanding and values. While evidence-based processes also have value in informing policy- and population-level decisions, EBM efforts at all levels should help inform and support decisions made by patients and physicians. Empowering patients and physicians with high quality information on the range of available treatment options and health services will help ensure that our health system efficiently delivers the best possible results for all patients. Application of evidence-based medicine at the policy level (for example, coverage or payment decisions made by health insurers or government agencies) should support, not supplant, physicians' and patients' ability to make treatment decisions that meet the specific needs and values of the individual. Policy-level uses of EBM also should support health care management strategies shown to improve health care quality.

### **Goals of Evidence-Based Medicine:**

#### **I. PhRMA supports evidence-based medicine that facilitates good decision-making by physicians and patients.**

The ability of physicians to apply expertise and evidence to meet the needs and values of individual patients is essential to the practice of high-quality, ethical medical care. Evidence-based decisions at the policy level play an important role, but rely on population averages that may not apply to the care of individual patients, who vary in important ways not reflected in population-level data. Therefore, application of evidence at the population level must be consistent with permitting physicians and patients to choose safe, effective health interventions that best meet the unique medical needs and values of the individual patient. Any uses of EBM that replace the physician's practice of medicine with population-based policy conflict with the goals of good patient care and improved health care quality.

#### **II. PhRMA supports use of evidence-based medicine to improve health care quality.**

The goal of evidence-based medicine must be to improve health care quality and patient outcomes across the health care system. Evidence-based medicine and decision-making can play a valuable role in addressing the "systemic nature of quality-of-care problems" identified by the Institute of Medicine by pointing to patterns of care that support optimal patient outcomes. Quality improvement is likely

the best strategy for optimal allocation of health care resources, and evidence-based medicine that starts with the goal of quality improvement will result in greater health care value and may yield higher or lower costs for different interventions.

**Developing evidence:**

**III. PhRMA supports quality health outcomes research by a variety of health system constituents.**

Health outcomes research provides valuable information when done well, but even the highest-quality research can not provide single, definitive answers to the wide range of questions that matter to physicians, patients and other decision-makers. Therefore, health outcomes research, like all other areas of scientific inquiry, proceeds best through a pluralistic approach. PhRMA supports development of evidence on health outcomes that addresses the full scope of health interventions available to patients and health care management strategies, and is performed by a variety of private sector organizations and government-supported programs, consistent with PhRMA's Principles for Government-Supported Health Outcomes Research.

**IV. PhRMA supports broad application of evidence-based medicine to the full range of prevention, diagnosis, and treatment options and health care management strategies** including but not limited to pharmaceuticals – to provide physicians, patients and other health care decision-makers with the information they need on the overall benefits and risks of different interventions.

**V. PhRMA supports evidence-based decision-making that employs the full range of different types and sources of valid data.**

Each type of evidence has different strengths and weaknesses as applied to specific health care questions and decisions. Randomized controlled trials play an essential role in medicine – new medicines approved by FDA are subject to rigorous randomized trials to demonstrate safety and efficacy. However, restricting evidence to randomized controlled trials eliminates a broad range of information and expert medical input from the decision-making process. Evidence-based policies should include relevant, scientifically produced health outcomes evidence available from many types of studies. Other sources of information such as clinical practice guidelines and health economics research also can play an important role in evidence-based reviews. Rigorously designed studies using observational data can play an appropriate role in evidence-based medicine by supplying data from the patient perspective and actual clinical practice, and enhancing generalizability of findings.

**VI. PhRMA supports evidence-based medicine that recognizes and appropriately uses evidence on the full range of health outcomes** including patient reported

outcomes such as quality of life, patient functionality and patient preferences that matter to patients and physicians.

### **Using Evidence:**

**VII. PhRMA supports effective communication of the results of evidence reviews to physicians and patients to help them make good health care decisions.**

Consumers, patients, physicians and other health care professionals should have access to the range of evidence on all treatment options and health management strategies in formats that are balanced and practical at the point of decision-making. Such information can help patients and physicians consider issues like the level of certainty the evidence provides, its applicability to their own circumstances, and the potential risks and benefits of different treatment options.

**VIII. PhRMA supports the use of evidence-based medicine to improve the appropriate use of medicines, other medical technologies and health care services and address their overuse, underuse and misuse. PhRMA supports using principles of evidence-based medicine to study the impact of various health care management strategies on appropriate use of health care interventions.**

**IX. PhRMA supports evidence-based medicine that facilitates timely, appropriate patient access to new health technologies, procedures and services.**

Evidence-based medicine should be used to help patients and physicians make informed decisions about available treatment options. Evidence-based policies should not be used to delay access to medically appropriate treatment options.

**X. PhRMA supports open, transparent procedures for application of evidence-based approaches to policy- or population-level decisions.**

To ensure that evidence-based decision-making processes meet the needs of patients, they should be open to the public, provide appropriate opportunities for input, ensure that input from medical experts is included whenever appropriate, and clearly explain the basis of decisions. Such processes also should provide meaningful, timely appeals mechanisms.





September 12, 2016

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

RE: ICER Value Framework Comments

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Dear Dr. Pearson:

As stated before, Patients Rising is a non-profit with a very specific mission: *We fight for access to vital therapies and services for all patients with life-threatening and chronic diseases.* We believe that if a patient needs medicines to survive and live a better quality and more productive life – access to those treatments is warranted and essential. This is part of our desire for a balanced dialogue and national conversation that tells the truth about healthcare.

In this work, we are committed to engaging patients, caregivers, physicians, the media, health policy experts, payers, providers and other allied health professionals to develop realistic, solution-oriented discussions around these issues so that those impacted with critical medical issues can amplify our collective voice and create lasting impact on the future of health care in the United States.

It is for this reason, and others, that we write today and offer our review and observations of ICER's value framework, what it represents and the manifest flaws we believe must be immediately addressed.

## **I. Use of the QALY**

ICER's statement that "The QALY was developed by health economists and doctors in the United States" is factually inaccurate.

The QALY was first developed not in the United States, but in Great Britain, specifically at the University of York's Centre for Health Economics. Specifically, the QALY was developed and advocated for by an economist named Alan Williams of the University of York in the 1970s – to enable the rationing of health care in the UK's National Health Service.

Last month, ICER defended its use of the QALY in describing value, defining it as "the gold standard" and intimating that it is used around the world. Yet, at an advocacy briefing held in Washington, D.C. on September 9<sup>th</sup>, ICER's COO Sarah Emond, remarked that ICER is open to a reworking of the QALY (or the adoption of a different methodology) in 2017. Whatever

methodology is used to describe or define “value” should be made completely transparent and published in a peer-reviewed journal meeting high scientific standards.

Patients Rising supports a systematic evaluation of the QALY and its appropriateness as a measure in determining value for patients. Furthermore, we recommend that ICER not use misleading terminology such as “gold standard” when referring to the QALY, given its documented flaws and biases as well as the ongoing debate within health economics and policy circles regarding its appropriate use. Patients Rising recommends an evidence-based, patient-centered approach to defining value that is based in science and eschews the possibility of ideological bias.

## **II. Shortfall of relevant, “in-field” medical experts as part of your voting panel**

While there are always a finite number of members for any official voting panel, we do not believe past ICER practice has demonstrated best practices among organizations that make clinical recommendations, nor that ICER’s practices are in the best interest of the patient.

In looking ahead to the October 20 CEPAC meeting on Non-Small Cell Lung Cancer, the voting panel selected by ICER does not include a single expert clinician or clinical researcher treating Non-Small Cell Lung Cancer patients, despite the fact that many of the world’s leading oncologists in this subspecialty are working in the United States, including in St. Louis, Chicago, and other major Midwestern metropolitan areas. The lack of inclusion of such experts is a major flaw in the implementation of your methodology. Patient groups are alarmed at the possibility that individuals who are not board certified in oncology could vote on an issue that would impact the availability of cancer drugs to NSCLC patients.

ICER must redouble its commitment to make certain its organization is asking the most appropriate questions, extracting and examining the best and most up-to-date data and, ultimately, delivering an accurate assessment both clinically and economically that takes into account the severity and gravity of the diseases it evaluates. Unfortunately, ICER’s current practices do not seem fit to credibly serve this purpose.

## **III. Lack of meaningful patient involvement**

At the New England CEPAC meeting in July, many patient advocates were curious as to ICER’s selection of a patient representative who would not actually be affected by the vote taken. Patients Rising believes that in policy discussions, the experts and stakeholders selected to participate should have specific relevance to the matter at hand. We recommend that ICER include on future panels patients who are taking or have taken the therapies being evaluated, or are current candidates for these therapies. We would be happy to provide individuals whose individual situations, whether taking a specialty medication or who have a mutation that necessitates a personalized medicine approach, would be appropriate members of the panels.

Patients may not understand the complexities and specifics of cost-per-QALY models or ICER’s budget impact calculations, but they understand when a group of people go into a room and vote

on their ability to access their medicines. You should make the input of patients a top priority, not an afterthought.

#### **IV. Exclusion of estimation of rebates**

According to Express Scripts, Dr. Pearson is one of the key thought leaders contributing to their Oncology Care Value Program. We believe that ICER should convene a fair and balanced forum with your pharmacy stakeholders –specifically the two largest in the United States (Express Scripts and CVS Caremark) – to develop a formula for the estimation of rebates as part of ICER’s economic methodology. ICER’s methodology contains dozens of estimates and assumptions to facilitate analysis and synthesis of complex information.

If ICER is unwilling to take a serious look at the flawed and inflated payment structure or the absurd length of time to develop new treatments, how can you expect to represent an honest cost dialogue?

#### **V. Conclusion**

The only value framework that will ever be the right value framework is one where patients and their doctors can input information based on the whole picture of the treatment journey. This is because treating the whole patient is the most cost-effective means of treating the larger patient population. While there is much to be addressed in streamlining our finite health care resources, sacrificing patient care to meet some arbitrary metric fails every professional and moral standard.

For ICER, a new methodology is absolutely necessary.

Sincerely,

A handwritten signature in cursive script that reads "Terry M. Wilcox".

Terry Wilcox  
Co-Founder & Executive Director, Patients Rising



Quorum Consulting

September 9, 2016

Institute for Clinical and Economic Review  
2 Liberty Square  
Boston, MA 02109

**RE: Comments on ICER Value Assessment Framework**

To Whom It May Concern:

Quorum Consulting, Inc. (hereafter "Quorum") is a premier health economics and reimbursement firm, based in San Francisco, CA, that places a high degree of emphasis on informed evidence development to our manufacturer and industry clients. Because of this, Quorum recognizes the important role the Institute for Clinical and Economic Review (hereafter "ICER" or "the Institute") plays in presenting guidelines and benchmarks for all stakeholders in evidence development, and we appreciate the opportunity to participate in this important discussion regarding the ICER 1.5 framework. This letter serves as a commentary in which we provide several recommendations that we think might result in more transparency and stakeholder-suitable results in forthcoming evaluations.

To acknowledge the present situation as we understand it, ICER is soliciting ideas to modify its current ICER 1.5 framework, which is used to suggest what ICER calls both long-term (incremental cost-effectiveness) and short-term (provisional health system budgetary impact or affordability) comparative value by September 12. Although I did not expect to hear anything new in the webinar, since I had attended two of these ICER meetings as an observer in person over the past year, there were two things that struck me, in particular:

- ICER is now outsourcing the majority of its modeling (to University of Washington).
- ICER panelists no longer vote on the provisional health system value; indeed, Dr. Pearson mentioned that ICER may abandon the budgetary impact calculations altogether.

Subsequent to the Institute's "myth-busting document" and call for comments on its 1.5 framework, Quorum's recommendations include:

1. Use of societal subanalyses in the case in which productivity may potentially have a large impact on cost-effectiveness analysis (CEA) calculations. Currently, Dr. Pearson stated that the Institute does not take the societal perspective because of the inherent bias against non-working populations, but this could be a subanalysis. Also, consideration of shorter-term outcome measures (other than quality-adjusted life-years or QALYs) may be appropriate to payers;
2. Open the modeling to RFP, rather than relying only on U. of Washington; and
3. Having the models peer-reviewed prior to presentation.

Each of these recommendations is discussed briefly below.

1. According to the US Public Health Service Panel on Cost-Effectiveness in Health and Medicine published some 20 years ago (1), which commented on the preferred perspective to be used in cost-effectiveness analyses (CEAs),

"... the comprehensive societal viewpoint has important methodological ramifications. It means that all costs and all effects should be incorporated **no matter who pays the costs** [our emphasis] or who receives the effects. ... It means that all types of resources of value to society should be included; thus, patient's time costs (lost work time, lost leisure time) are counted. ... It means that opportunity costs are the appropriate method of valuation ... , and it means that the general public is the appropriate source of preferences for health outcomes. ... "

As mentioned in the more recent ISPOR task force publication (2), however, very few CEAs include patient productivity or are reflective of drug prices as they are negotiated, often instead using average wholesale price (AWP) in US-oriented analyses. They advocate for a "limited societal" or "health system" perspective, in contrast to the typical definition of employing a true societal perspective. One rationale for pursuing a limited societal perspective, especially from a drug pricing standpoint, is that the United States marketplace is skewed due to taxes, the patent system, our insurance milieu, pricing negotiations, etc.; this proposed perspective would allow one to consider opportunity costs in a standardized, public policy forum. Another rationale is that they also define a preferred health system perspective as one that would take into consideration the payer perspective plus indirect costs and community preferences for utilities.

Indeed, it would also make sense to employ this methodology as the Institute has documented that the care value analyses thresholds they employ (\$50,000-\$150,000) are based on societal willingness-to-pay (WTP) from the World Health Organization of 1-3 times per capita GDP (3).

In terms of use of additional outcome measures beyond QALYs, although endorsed by authorities such as the US Public Health Service Panel on Cost-Effectiveness in Health and Medicine and by the UK National Institute for Health and Care Excellence (NICE) as an appropriate reference (base) case, Caro et al. mentioned that payers may not understand or accept this somewhat obscure outcome metric (4). Indeed, given the fragmented US healthcare market and patient turnover, shorter-term outcome measures, such as cost per thrombosis avoided, mmHg reduction, complication-free episodes and functioning graft, may be more transparent and readily accepted by payers than is the longer-term QALY (5-8).

2. We would suggest that the modeling be open to RFP, rather than relying only on U. of Washington. The Institute may benefit from opening the modeling to multiple bidders in terms of alternative methodologies, data sources, perspectives, etc. This may also possibly reduce the perception of bias in terms of model creation and give other organizations an opportunity to be involved in this unique effort. Moreover, this will help to ensure that the Institute chooses the most capable model developer, as well as medical expert, for the particular disease.
3. Lastly, we would suggest that the models be peer-reviewed prior to being presented at the ICER meetings. This would allow all stakeholders to undertake their own sensitivity analyses and suggest alternate scenarios that could be considered and vetted prior to release of a draft document, again reducing suggestions of bias and non-inclusiveness, while promoting transparency.

Once again, thank you for the opportunity to comment, and on behalf of my colleagues at Quorum, I welcome ongoing discussions.

Very truly yours,

Renee JG Arnold, PharmD, RPh  
Practice Lead, Health Economics and Outcomes Research

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# Proposal for Improvement of the Value Framework by the Institute for Clinical and Economic Review (ICER)

## Summary

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1. Ensure the determination of Care Value is comprehensive and defensible
  - 1.1. Use explicit multi-criteria decision analysis (MCDA) process
  - 1.2. Use the criteria of severity, unmet need and innovation as well as comparative clinical effectiveness
  - 1.3. Incorporate the patients' voice throughout
  - 1.4. Remove cost-effectiveness from the Care Value determination.
2. Modify the determination of an acceptable price
  - 2.1. Use the Care Value assessment directly in the determination
  - 2.2. Employ an evidence-based efficiency threshold
  - 2.3. Derive the acceptable price using therapeutic-area specific efficiency frontiers.
3. Discontinue the use of a budget impact ceiling, as both the methodology for estimating it and its interpretation are invalid.
  - 3.1. Focus on providing a tool that allows budget holders to estimate the impact relevant to them
  - 3.2. Follow budget impact analysis good practices guidelines
  - 3.3. Customize the method of estimating budget impact to the technology under evaluation.
  - 3.4. Estimate uptake of new technologies based on evidence from similar technologies
  - 3.5. Assess uncertainty in budget impact evaluations
  - 3.6. Develop customizable budget impact calculator tool rather than 'the' budget impact calculation for the entire US population.
4. Publish and follow formal written methodological guidelines (or quote existing ones) for all components of the process



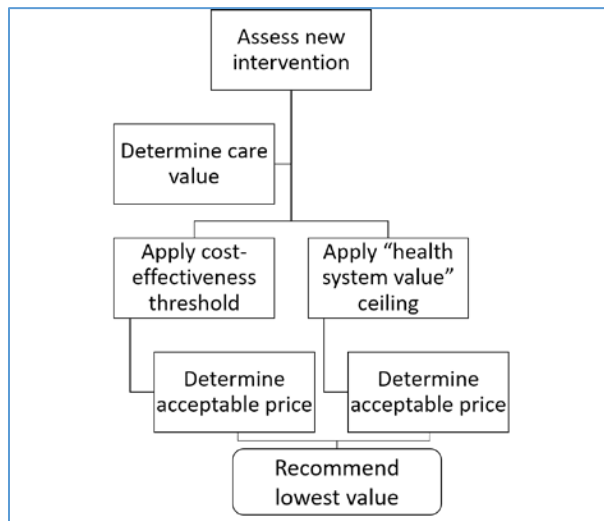
- 4.1. Create a publicly available list of stakeholders at the start of the process and formally invite them at the initiation of the assessment starting from the drafting of the scope
- 4.2. Ensure a good representation of clinical and patient organizations among the invited participants
- 4.3. Assess face validity of all aspects of the scope and value determination, using the stakeholder panel, and fully document the assessment in a validation section of the Evidence report describing who was involved and how the checks were done
- 4.4. Ensure a good representation of clinical and patient organizations among the invited participants
- 4.5. Include a detailed validation section into the Evidence Report regarding outcomes of the cost-effectiveness model
- 4.6. Make models available under appropriate agreements about non-disclosure.

# Proposed Approach

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The Institute for Clinical and Economic Review (ICER) aims to achieve the dual goal of improving patient care and controlling costs.<sup>1</sup> They consider the key elements for this to be the explicit and transparent assessment of value and the recommendation of value-based prices. The current process involves three separate determinations which are not linked (Figure 1). In one activity, ICER determines what it terms the “Care Value” based on comparative clinical effectiveness, incremental cost per quality-adjusted life year (QALY) gained, other benefits or disadvantages (acceptability/adherence, public benefit, productivity) and contextual considerations (high severity with no other treatment option, unmet need, other societal value). This Care Value is rated on a three-point scale of Low, Intermediate, and High. The result does not enter, however, into the setting of an acceptable (“value-based”) price. This is done by separately calculating two possibilities and taking the lower of the two. One possible acceptable price is derived by applying an assumed threshold cost-effectiveness ratio; the other looks at what ICER calls the “Health System Value”, which is really the application of a short-term budget impact ceiling.

*Figure 1. Current Value Assessment process involving three separate unlinked determinations*



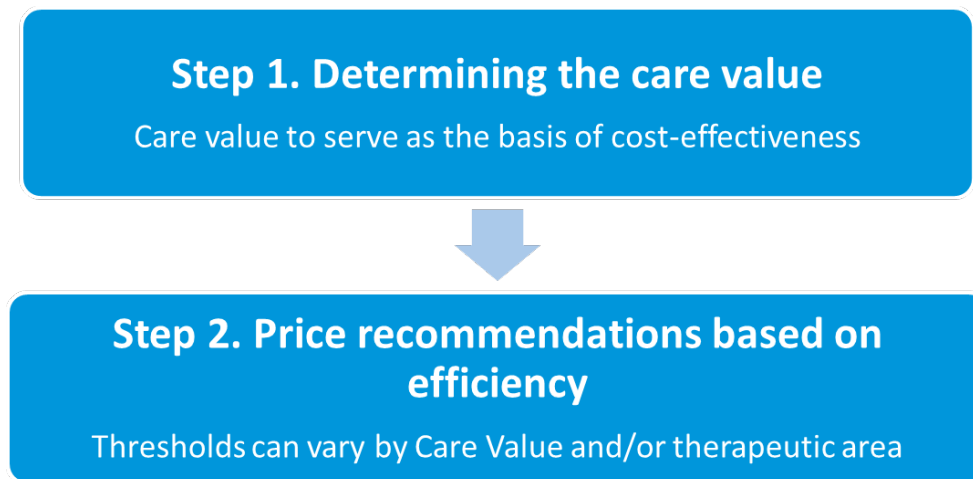
To achieve the aims stated by ICER, Regeneron recommends modifications in the methodology and process in the following areas:

- Determining Care Value and linking it to recommended price
- Calculation of budget impact
- Validity and transparency

## Determining Care Value and Linking it to Recommended Price

The Care Value determined by ICER should be an integral step in deriving a recommended value-based price. The first step, the determination of the Care Value should provide an explicit and transparent judgement of the health technology assessed based on the criteria established by ICER but not including efficiency (“cost-effectiveness”). The second step then takes into account the Care Value established in the first step and appropriate efficiency considerations to determine an acceptable price (Figure 2).

*Figure 2. Two-step approach recommended*



### Step 1: Determining the Care Value

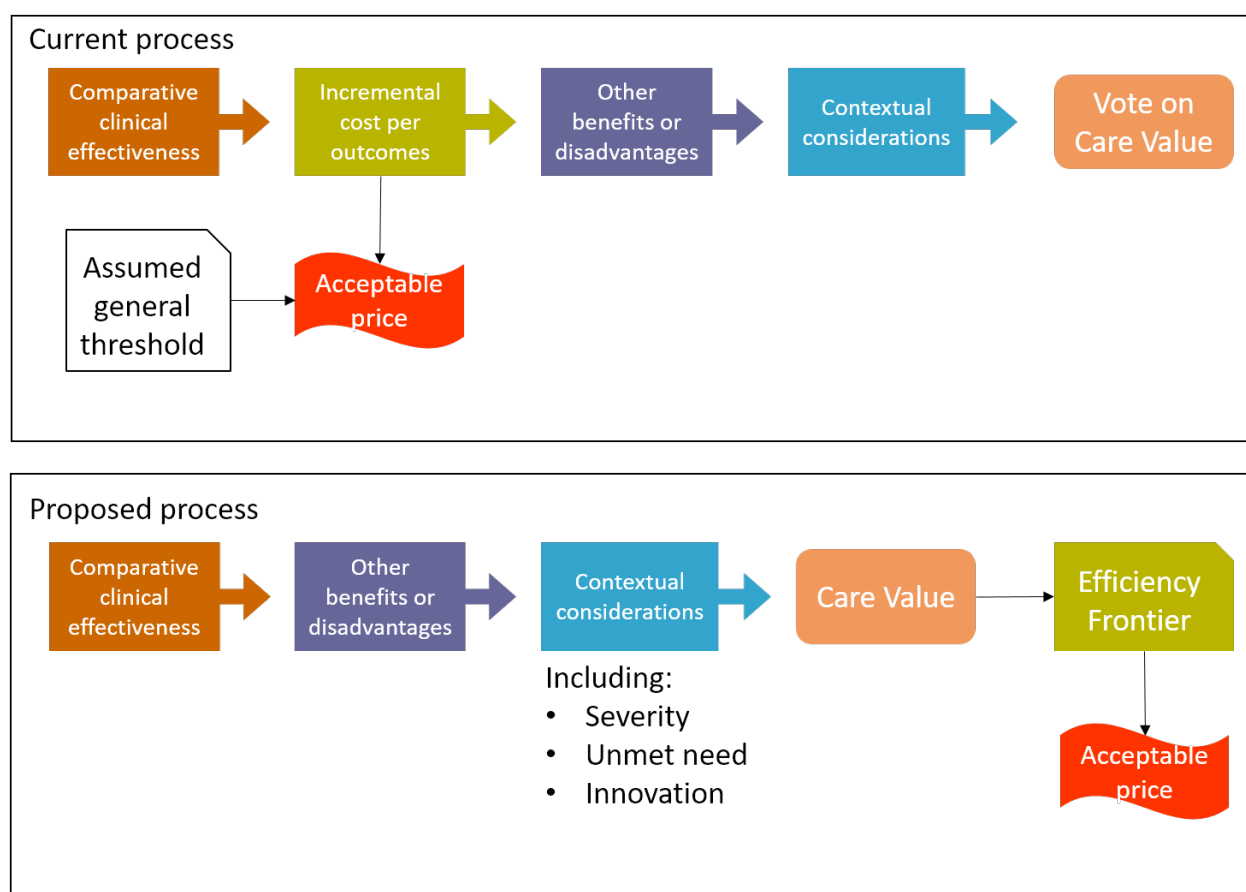
Among the criteria to be taken into account in the determination of the Care Value, comparative clinical effectiveness is essential. The incremental cost per outcomes achieved however, is currently included in both the determination of Care Value and as the basis of price recommendations (Current process on Figure 3), leading to double counting. More importantly, the Care Value is not used in the determination of the value-based price. At the moment, ICER assumes a general threshold loosely founded on what a few other jurisdictions have used (none of them evidence-based) and applies it to all interventions, regardless of their assessed Care Value. The assessed Care Value should not be ignored in deriving the acceptable price as it renders that worthy step moot: products judged to be of high value are subject to the same threshold as those of low value. We recommend the exclusion of the cost-effectiveness criterion from the determination of Care Value and taking it into account in Step 2, the estimation of the recommended value based price. This issue is further discussed below in Step 2.

The additional two criteria—other benefits and disadvantages and contextual considerations—center mostly on severity and unmet need, both of which have been shown to be supported by the

general population in a cross-sectional survey in the UK.<sup>2</sup> Severity can be defined by how much worse the disease is compared to others. A generally accepted method for doing this has not emerged but QALYs lost (e.g. through calculation of proportional shortfall<sup>3</sup>) could be the basis.<sup>4</sup> Unmet need can be based on how much of that lost health cannot be recovered using current treatment options (e.g. by having only symptomatic treatments as opposed to curative). Both severity and unmet need should take into account the patients' voice to the extent possible. While this is not straightforward, preference-elicitation studies exist that quantify the importance of aspects of treatments helping with the determination of unmet need.<sup>5,6</sup> Additional aspects of the other benefits and disadvantages and contextual considerations include those that can be taken into account in the efficiency calculations (e.g., productivity,) or with the inclusion of patients' voice (e.g. acceptability/adherence).

An additional criterion is recommended to be included in the determination of Care Value. The innovative nature of the treatment has been also shown to be supported by general population.<sup>2</sup> While innovation can manifest in better comparative effectiveness, it can also aid development leading to future benefit. For example a new mechanism of action, while not leading to substantially better response rates for the first drug in the class, or only providing better response at the expense of higher toxicities, could be the first step in discovering new treatments with considerably improved effects.

Figure 3 Current and proposed process for determining Care Value and acceptable efficient price



The assessment of how the new product performs according to the criteria can follow the current ICER process. The Care Value scale may remain ordinal, as it is currently (i.e., low, intermediate and high) or it can be modified to be an interval scale (e.g. on the scale of 0, or no value, to 100 for maximum possible value). However, the importance given to the different criteria and, therefore, the determination of Care Value by ICER's independent public appraisal committee should follow a more explicit multi-criteria decision analysis (MCDA) approach.<sup>7</sup> Not only is this more transparent and quantitative, it facilitates adaptation as required by the individual payers.

MCDA provides quantitative estimates of the value of an alternative when multiple factors must be considered. It involves four main steps: identifying options, defining and weighting relevant criteria and scoring each option on each criterion. MCDA has a sound mathematical basis, with a foundation in decision analysis.<sup>8</sup> It brings greater transparency and consistency to decision making, while facilitating discussions on what decision makers consider valuable.<sup>9</sup> It also offers the opportunity to engage the public on the criteria to be used and even regarding the weights assigned to them.

**Recommendations:**

1. Ensure the determination of Care Value is comprehensive and defensible
  - 1.1. Use explicit multi-criteria decision analysis (MCDA) process
  - 1.2. Use the criteria of severity, unmet need and innovation as well as comparative clinical effectiveness
  - 1.3. Incorporate the patients' voice throughout
  - 1.4. Remove cost-effectiveness from the Care Value determination.

**Step 2. Deriving Price based on Desired Efficiency**

ICER uses two approaches<sup>10</sup> to derive an acceptable price (and then recommends the lower of the two). One of these approaches is based on efficiency, measured by ICER using the cost-effectiveness (CE) ratio, or inverse of efficiency. A desirable efficiency is established (the “threshold”,  $T$ ) and the acceptable new price (NP) is then easily derived given the estimated benefit ( $B$ ):

$$NP = \frac{(B \times T - DiffOtherCost + CompPrice \times CompUsage)}{NewUsage}$$

where  $DiffOtherCost$  accounts for any differences in the costs of care induced by the new intervention and  $CompPrice$  and  $CompUsage$  refer to the comparator price and usage (i.e., amount used given by dose, duration and so on). All three of these aspects plus the benefit can (and should) be data driven, but the threshold CE ratio is problematic. At the moment, ICER assumes a general threshold loosely founded on what a few other jurisdictions have used (none of them evidence-based) and applies it to all interventions, regardless of their assessed Care Value.

**Determination of Disease Area-specific Thresholds for Categorical Care Values**

One possibility is to derive the threshold CE ratio specific to the level of value: high value products are appraised against a higher threshold and so on. Since the current threshold is purely an assumption, this modification could be very simple: make different assumptions for each level of Care Value. The drawback to conjecture as the foundation for the threshold—whether single or value-based—is that it leaves ICER's assessments open to repeated, unanswerable criticism.

A better approach is to use the observed efficiency of products already on the market grouped by their Care Value. This provides pragmatic, evidence-based estimates of the thresholds and allows for derivation of a price that is acceptable in the sense that it accords with extant efficiency for products of similar Care Value. That price has the favorable implication that health care delivery

is not losing efficiency<sup>1</sup>. Although this would involve some additional work to establish these thresholds, the resulting standards would be much more defensible and in accord with theory.

This basic evidence-based approach would be a substantial improvement but it harbors a problematic assumption: that a given level of Care Value in one therapeutic area is equivalent to that in another (i.e., high value in a rare fatal disease is the same as high value in a minor symptomatic illness). This untenable assumption can be avoided in two ways. One is to ensure that the measure of Care Value is common across all therapeutic areas. This has been the hope with the QALY but there is abundant evidence that it does not work that way [see for example Nord, 2015<sup>11</sup>] and, in any case, the QALY does not incorporate the contextual and other benefits, the inclusion of which is a major strength of the ICER approach. There have been various attempts at modifying the QALY to accommodate this but none have satisfactorily achieved it, and the fundamental problems with the QALY itself<sup>12</sup> remain anyway.

Rather than pursue a universal and comprehensive measure of benefit,<sup>13</sup> the problem of ensuring the thresholds cohere with the assessed Care Value can be addressed by finding the operating efficiency in each therapeutic area. This is not as daunting as it seems – most of the work is already done when a particular topic is addressed by ICER: the costs and benefits of available products in that therapeutic area are estimated. These can be plotted on a graph that has benefit on the vertical axis and cost on the horizontal (Figure 4).

This graph immediately reveals how efficiently benefits are being obtained in that therapeutic area, with products up and to the left providing benefits more efficiently. The line segments joining those products reflect the efficiency frontier and their slopes readily provide the evidence-based, coherent threshold for the new product.<sup>14</sup> A constructive side-effect is that the efficiency frontier also reveals any existing products that are inefficient, which means they are priced too high—dropping their prices to efficient levels would provide some of the funding for the new product. Yet another advantage is that by staying within a therapeutic area, ICER can avoid use of the problematic QALY because the unit of benefit has to be relevant only for that area. It can be based on a commonly accepted clinical score or anything that has strong face validity and recognition among clinicians and other stakeholders.

In the US, there is an additional nuance that should be considered. Whereas in most countries, the maximum reimbursable price accepted at the time of market access is the price paid, in the US that may not be the case. For the efficiency frontier to properly reflect the revealed

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<sup>1</sup> Of note, whether the existing efficiency in a therapeutic area could be improved further, or is already too strict, is a question that cannot be answered easily because it requires an external efficiency standard. Such a standard involves establishing what should be paid for a particular benefit and there is no agreement on this, or even on who ought to be the respondent. Moreover, not only do people find it very difficult to address this hypothetical question consistently, but there is no accepted basis for arbitrating differences of opinion.

preference of the market, the costs need to represent actual prices paid, which in turn, implies that there has to be sufficient uptake at that price. If a price is set but very few payers agree to reimburse at that price, then that point should not be used on the efficiency frontier. For older products, this is not likely to be a big problem but for newer ones where the reimbursed price may not yet have settled down, it may be difficult to fix their position on the frontier graph. In this situation, they should either be used only in the uncertainty analyses or be left out entirely from the derivation of the frontier.

**Figure 4. Illustration of the efficiency frontier**



### **Determination of a Threshold for a Numerical Generalizable Care Value Point Improvement**

One seeming disadvantage of therapeutic-area-specific thresholds is that they ignore efficiency in other areas. Creation of a numerical Care Value that has the same interpretation across therapeutic areas could ensure comparability of efficiency across disease areas. Creation of a universal measure of Care Value is a more complex task than defining different cost/QALY thresholds for Care Value categories, as it requires the translation of the disease-specific



effectiveness gain into a generalizable measure. If such a universal Care Value measure could be developed, for example by defining the maximum value as the Care Value of an innovative new product that restores the health status of the entire population of the world to full health, then efficiency could be measured on this new scale. The incremental cost per Care Value point improvement could replace the current cost/QALY measure, and a single threshold per Care Value point improvement would be enough to assess the efficiency of all new products. Initially the care value points would be less familiar than QALYs, but over time may gain acceptance.

While there are some theoretical arguments against disregarding cross-area comparisons,<sup>15</sup> these have been increasingly breaking down<sup>16-18</sup> and are inconsistent with practices involving efficiency in other areas of the economy (e.g., it would be ludicrous to insist that passenger vehicles and 18-wheelers adhere to the same fuel efficiency standard). Moreover, the theoretical requirements compelling use of a single, general efficiency threshold do not apply to the fractured, heterogeneous American health care system where there is no single budget and complete absence of a universally accepted global goal or measure of benefit (e.g., QALY maximization is not generally agreed upon).

### **Recommendations:**

2. Modify the determination of an acceptable price
  - 2.1. Use the Care Value assessment directly in the determination
  - 2.2. Employ an evidence-based efficiency threshold
  - 2.3. Derive the acceptable price using therapeutic-area specific efficiency frontiers.

## **Calculation of Budget Impact**

Besides determining a possible acceptable price based on efficiency, ICER also calculates another possibility based on a perceived budget impact that no single new product should exceed.<sup>1</sup> ICER calculates a potential short-term budget impact based on an assumption about the uptake of the new intervention. One of four uptake rates (75%, 50%, 25% or 10% uptake at 5 years) is assigned after examination of six characteristics of the drug or device and the marketplace: 1) Magnitude of improvement in clinical safety and/or effectiveness; 2) Patient-level burden of illness; 3) Patient preference (ease of administration); 4) Proportion of eligible patients currently being treated; 5) Primary care versus specialty clinician prescribing/use; and 6) Presence or emergence of competing treatments of equal or superior effectiveness. As the actual price paid for a new treatment is often not publically available, wholesale acquisition cost (WAC) is used as a proxy. Although this price may not correctly represent the actual price to a

payer, it is used together with the assumed uptake to predict the change in health care costs over an initial 5-year timeframe. This potential budget impact is compared to a presumed ceiling.

ICER supports the use of a ceiling by the statement that health care costs should not grow much faster than growth in the overall national economy. However, there is no theoretical justification for this statement. Allocation of resources between sectors of the economy is a complex decision influenced by economic, social and political judgments.

In ICER's own words, their goal is to "fill a gap in our country's health care system by producing independent, scientifically rigorous reports that help support discussions of how to achieve the broader goal of improving patient outcomes while making health care more affordable for patients now and in the future".<sup>20</sup> As pointed out by Paulden and colleagues, however, this goal cannot be achieved by focusing only on processes for funding new technologies.<sup>18</sup> According to the authors, achieving allocative efficiency would require "programme budgeting and marginal analysis on a grand scale".<sup>18</sup> Compared to this, the use of a single budget impact ceiling is such a crude instrument as to render its interpretation meaningless.

ICER defends its methods by stating that the ceiling is only used to sound an "alarm bell" if the short-term costs might increase health care spending significantly faster than the growth of the US national economy.<sup>20</sup> This is at odds with the fact that the budget impact ceiling is explicitly incorporated into the calculation of the value-based price benchmarks as described above (see Step 2. Deriving price based on desired efficiency).<sup>1</sup>

The use of such a budget impact ceiling however is not able to fulfill this role. Beside the theoretical issues mentioned earlier, the derivation of the \$904 million value includes a number of arbitrary assumptions that impair its practical use and interpretation:

1. The same budget impact ceiling is imposed on all products regardless of the Care Value assessed in an earlier step. This implies that it is appropriate to spend the same amount on a low value product as on a high value one.
2. The estimates for many of the inputs (e.g. growth in US GDP, contribution of drug/device spending to total health care spending, number of new molecular entity or device approvals, etc.) are derived from a single year, ignoring the natural variability of these estimates over time;
3. The derived contribution of drugs/devices to total health care spending is assumed to remain the same in the future. This assumption discourages development of drugs/devices that would increase spend, but produce savings in other types of health care resources and/or provide wider benefit;

4. Application of the same average amount to all new drugs or devices, regardless of the prevalence of the underlying disease, makes it inappropriately easier for developers of products for rarer diseases to avoid sounding the ‘alarm bell’. This discourages innovation in diseases that are highly prevalent and, thus, leading causes of mortality and morbidity;
5. Using GDP+1% for allowed growth and doubling the resulting amount to obtain a ceiling per new drug or device is an arbitrary way to operationalize ‘significantly faster increase’ in health care spending.

In addition, the determination of the drug budget is different between payers in the US, so the recommendation of a price based on a national average assumed growth is not going to be applicable to the majority of payers. Thus, the budget impact ceiling is not able to fulfill its aim for theoretical and practical considerations, while providing perverse incentives to manufacturers.

While it is recommended that the budget impact ceiling be abandoned, locally applicable budget impact calculations are very useful for individual payers. The calculation of the budget impact itself, however, should also follow methodological guidelines, like those published by the ISPOR Task Force on Good Research Practices – Budget Impact Analysis.<sup>21</sup> The current ICER practice seems to apply the same modelling technique to all areas under evaluation, namely calculating the numbers of patients treated based on an assumption of constant number of eligible patients over five years, and the above mentioned assumed uptake (or in some cases even 100% uptake) of the new treatment. The annual cost of treatments is calculated and applied to the corresponding patient group during the time horizon. Therefore patients starting treatment in year one will receive treatment for five years, those starting treatment in year two will receive treatment for four years, etc. There is no mention of how the actual duration of treatment is considered if treatment length is shorter than five years. The model cost calculations seems to assume the same duration of treatment as the cost-effectiveness calculation, and it seems that patients discontinuing the treatment would not be replaced. However, this assumption underestimates the numbers of patients actually receiving treatment compared to the uptake inputs if treatment duration is shorter than five years. Furthermore, the constant patient number assumption does not hold in most disease areas. The calculated budget impact will be misleading for new drugs and devices that were developed for disease areas with changing incidence and/or changes in eligibility criteria compared to old treatments.

There is no single budget impact calculation method that should be applied to all areas. Guidelines recommend that the model should be tailored to the specific health condition.<sup>21</sup> This requires careful consideration of the way to estimate number of patients being treatment each

year as well as consideration of where individual patients are in terms of their treatment pathway and how long they would be on treatment. Categorizing uptake of the new technologies into four linear rates is too simplistic. More disease area- and new technology-specific estimates of the expected uptake curve could be estimated by looking at uptake trends of products in similar disease areas.

There is also considerable uncertainty in a budget impact analysis. Guidelines recommend that the analysis compute a range of results that reflect a plausible range of circumstances the budget holder will face.

Lastly, ICER develops the budget impact model for the entire US population, which is an irrelevant perspective for the fractured US health care system. Payers may find a budget impact calculator tool more useful. It should contain the model structure determined to be adequate for the condition, and the means for calculation of the costs of treatments, but it should allow the payer to customize the inputs according to their own context.

### **Recommendations:**

3. Discontinue the use of a budget impact ceiling, as both the methodology for estimating it and its interpretation are invalid.
  - 3.1. Focus on providing a tool that allows budget holders to estimate the impact relevant to them
  - 3.2. Follow budget impact analysis good practices guidelines
  - 3.3. Customize the method of estimating budget impact to the technology under evaluation.
  - 3.4. Estimate uptake of new technologies based on evidence from similar technologies
  - 3.5. Assess uncertainty in budget impact evaluations
  - 3.6. Develop customizable budget impact calculator tool rather than ‘the’ budget impact calculation for the entire US population.

## **Validity and Transparency**

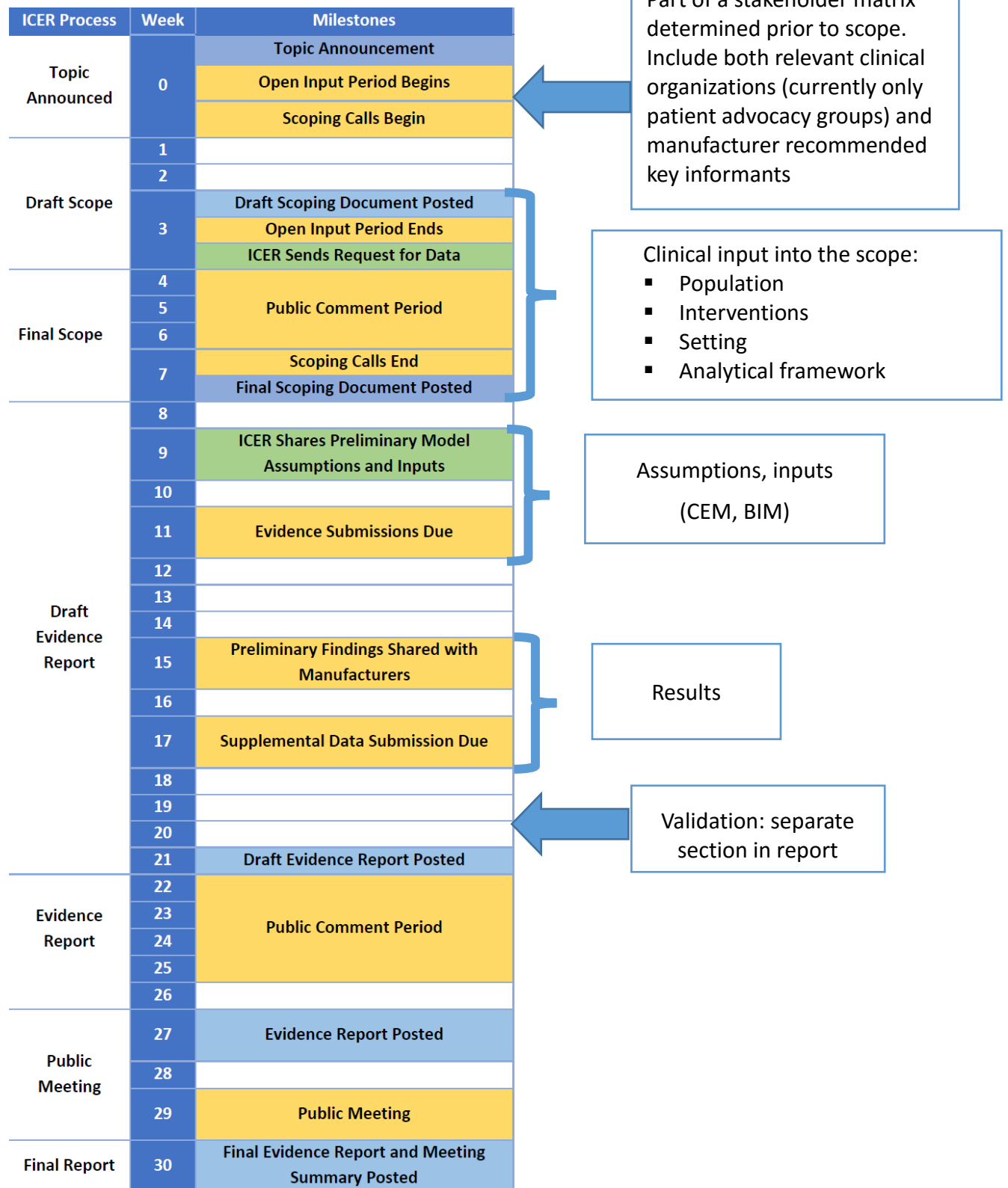
According to the ISPOR-SMDM Modeling Good Research Practices guidelines,<sup>19</sup> clinical face validity is essential in modelling. This includes the face validity of the structure, evidence, problem formulation, and results of the model. The validation should be conducted by experts in the therapeutic area, documented in detail and available to reviewers.

The assessment of clinical validity should be transparent, timely and explicit. To provide this, clinical organizations and clinicians (both selected by ICER and the key informant recommended

by manufacturers) should be part of a stakeholder matrix assembled as part of the scoping process (Figure 4). Clinical validity should be addressed at the scoping phase, where the appropriate population, interventions, setting should be assessed. The analytical framework, which incorporates the aspects of the disease that are relevant for patients and clinicians, and the intermediate and long term outcomes, also need to be clinically meaningful.

Assumptions, input and results for the assessment of Care Value, cost-effectiveness and budget impact should be validated by clinicians together with the model structure. These should be clearly described in a separate section in the Evidence report and provided to stakeholders.

**Figure 5. Recommendations for face validity checks**



ICER has made considerable effort to publish the elements of the process it takes to establish care value, the health system value and the price recommendations of new medicines and devices that are selected for evaluation. However, we believe that there is room for improvement in terms of transparency in some areas that would facilitate more constructive discussions with the stakeholders and adoption of the results by the various payers.

Stakeholder selection is critical to ensure that a wide variety of aspects are represented throughout the process. Engaging with a broad range of stakeholders, including multiple patient organizations, multiple clinical organizations and manufacturers ensures a 360° view of the disease with the most critical aspects presented for evaluation. All stakeholders should be engaged throughout the process. Currently, the stakeholders' role is emphasized in multiple ICER documents with some well-defined points of engagement throughout the process where members of the public can provide commentary and input, by sending them to ICER following the guidelines.

Systematic identification and invitation of all relevant stakeholders (clinical and patient organisations and manufacturers) with the publicly available list of invited stakeholders at the initiation of the process would increase the transparency the engagement, and therefore the confidence in the outcomes and the thoroughness of the process. Currently, which organizations are covered in the term “stakeholder” is unclear (and potentially different) at various time points; e.g. it is unbeknownst to the observers whether the list includes clinical or patient organizations, and if so, which ones.

Related to this, earlier involvement of manufacturers and clinical organizations in the scoping – i.e. before the draft scope is issued may benefit the process and reduce potential controversies later on in the process.

The second area where increased transparency would be beneficial is the estimation of efficiency. ICER does not require cost-effectiveness models to be submitted since it develops its own models and carries out efficiency calculations using various external partnering organizations. In order to ensure that models prepared by the various affiliated institutions are consistent and transparent methodologically to the extent possible, formal written methodology guidelines should be made available on the website or existing methods guidelines should be referenced.

The ICER website mentions following the general approach described in one of the seven-item series of ISPOR-SMDM guidelines regarding validation and transparency.<sup>22</sup> Nevertheless, currently no other methods guidelines from the ISPOR-SMDM series or elsewhere are referenced and no ICER-prepared methods guidelines are published. ICER analyses (both cost-effectiveness and budget impact) should follow the recommendation in these guidelines unless

adequate justifications are given for deviations. These would include, for example, a more detailed description of statistical methods used in survival extrapolations, a highly influential part of the models and the cost-effectiveness outcomes and hence of the price recommendations.

According to guidelines, reporting should also include external validation, as currently checking clinical face validity is restricted to the results of the comparative effectiveness review.

As the way of penultimate validation and scrutiny that is warranted by the potential impact of any evaluation conducted by ICER, models generated by ICER affiliated institutions should also be made available for review, under confidentiality and non-disclosure agreements to protect the intellectual property.

**Recommendations:**

4. Publish and follow formal written methodological guidelines (or quote existing ones) for all components of the process
  - 4.1. Create a publicly available list of stakeholders at the start of the process and formally invite them at the initiation of the assessment starting from the drafting of the scope
  - 4.2. Ensure a good representation of clinical and patient organizations among the invited participants
  - 4.3. Assess face validity of all aspects of the scope and value determination, using the stakeholder panel, and fully document the assessment in a validation section of the Evidence report describing who was involved and how the checks were done
  - 4.4. Ensure a good representation of clinical and patient organizations among the invited participants
  - 4.5. Include a detailed validation section into the Evidence Report regarding outcomes of the cost-effectiveness model
  - 4.6. Make models available under appropriate agreements about non-disclosure.



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# RetireSafe

**Standing Up For America's Seniors!**

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September 12, 2016

Steven D. Pearson, MD, MSc  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

Dear Dr. Pearson:

RetireSafe is a nationwide non-profit organization representing over 200,000 mature Americans. We believe that choice and access are important aspects of healthcare and applaud efforts that increase options for doctors and patients while maintaining cost effective access. We take our responsibility to be a voice for older Americans seriously, and we speak for them as we provide feedback in response to the national call for input concerning the value assessment framework issued by the Institute for Clinical and Economic Review (ICER).

ICER is a virtually unknown organization to most Americans and they are unaware of the impact that ICER's work may have on their healthcare. Some stakeholders focused on who finances ICER and who is on your board but it is ICER's products that concerns RetireSafe. The burden to monitor and respond to unknown organizations like ICER falls on stakeholder groups like RetireSafe and other organizations who provide healthcare to older Americans. It is also our responsibility to report back to those we represent about the response we received from organizations like ICER.

ICER indicated that, in reference to input concerning the value framework, the "highest priority areas for potential revision are" and then listed four areas. These areas were;

- Methods to integrate patient and clinician perspectives . . . in the current value framework within "additional benefits or disadvantages" and "contextual considerations"
- Incremental cost-effectiveness ratios: appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures
- Methods to estimate the market uptake and "potential" short-term budget impact. . .
- Methods to set a threshold for potential short-term budget impact that can serve as a useful "alarm bell" . . .

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**[@retiresafeorg](https://twitter.com/retiresafeorg)**

It concerns us that these high priority areas for revision are all within the confines of the value assessment framework and thus assume that the underlying methodology of the framework is sound. RetireSafe thinks this is a false assumption.

RetireSafe agrees with other stakeholders, including many patient advocates, who believe the foundation of ICER's framework ignores the efficiency and long term benefits of personalized medicine. We think an emphasis on short term budget concerns have clouded ICER's vision of the future of healthcare. The mere fact that quality adjusted life years, which tend to overlook important differences among patients and persons with disabilities, is used as a measure of value shows a disregard for the true value of healthcare and a reliance on a measurement used in the UK to ration access to healthcare. This is not what older Americans want or expect and is not where efforts to define healthcare's value should be focused.

There are many organizations and entities focused on driving patient-centered value in healthcare. It would have been prudent for ICER to recognize, understand and incorporate some of these approaches into the value assessment framework. Instead we are left with an approach that asks for input and ideas that will help an already-broken framework move forward. We are concerned that CMS has already started considering some of the approaches detailed in the framework, that the train has already left the station and its destination will be a reduction in choices, and a one-size-fits-all approach that will reduce innovation and ultimately be of less value. . . as the patient calculates value.

In the end it's the patient that will be impacted by decisions that ICER makes. RetireSafe's goal is to work as hard as we can to ensure that those final decisions are based on forward thinking, long range, patient focused metrics.

A handwritten signature in black ink, reading "Thair Phillips". The signature is fluid and cursive, with the first name "Thair" and last name "Phillips" clearly distinguishable.

Thair Phillips  
President/CEO  
RetireSafe



September 12, 2016

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

**RE: “ICER Opens National Call for Proposed Improvements to its Value Assessment Framework”**

Dear Dr. Pearson,

Sanofi appreciates ICER’s call for proposed improvements to its value assessment framework <sup>1</sup> and welcomes the opportunity to comment. Sanofi supports a comprehensive, holistic definition of value that balances patient, clinical, societal and economic perspectives. We actively contribute to the development of comprehensive evidence to demonstrate the value of our products and are committed to collaboration with stakeholders to ensure patients’ timely access to innovative medicines, improved health outcomes, and support the efficiency of the healthcare system.

We acknowledge that clinical value assessments, if properly conducted, can be an important means to inform evaluation of treatment alternatives by patients, clinicians, and healthcare delivery systems and recognize that the generation and appropriate appraisal of evidence is foundational to improving health outcomes <sup>2,3</sup>. However, we have significant continuing concerns about ICER’s current value assessment framework and believe it is critical that ICER revise its approach. We appreciate ICER’s willingness to consider changes to its current value framework.

With respect to the topics identified in the call for comment as highest priority for potential revision, we recommend the following:

- ICER should expand the range of patient-centered benefits evaluated in its evidence reviews and seek to quantify the impacts of these benefits in its cost-effectiveness analyses. Examples of such benefits include improvements in productivity, employability, and caregiver burden <sup>4,5</sup>. ICER should recognize the limitations of the QALY as a unitary measure of value (these limitations are described in more detail later), and instead diversify its approach to include other measures of value, for example through Multi-Criteria Decision Analysis (MCDA) <sup>6</sup>.
- ICER should base its methods for estimating the market uptake and budget impact of products on available real-world evidence, use assumptions that reflect typical practice for medication management in healthcare settings, and limit reliance upon list prices. Currently, inflated estimates of projected product use and cost



may significantly overstate budget impact in ICER's evidence reviews and result in misleading conclusions<sup>7</sup>.

- ICER should discontinue its current approach to the calculation of the “value-based price benchmark”. The linkage of cost-effectiveness and budget impact analysis underlying this measure has no scientific basis and inappropriately conflates value assessment with a measure of projected healthcare resource utilization<sup>2</sup>.

We strongly recommend that ICER revise its framework to ensure this separation in future.

Our specific recommendations pertain to ICER's conceptualization of its value framework and appropriate processes for operationalizing the framework in evidence reviews.

### **Issues regarding the conceptualization, scope, and methodological basis of ICER's value framework**

We urge ICER to develop and integrate a more holistic definition of value into its assessment framework and subject its revised value framework to thorough and transparent validation and testing. It is critical that ICER formally incorporate evidence meaningful to patients and society into its evidence reviews, broaden the scope of its assessments to include other potential benefits and a balanced representation of topics, and clearly state the limitations of its conclusions and recommendations.

*Perspective in ICER's evidence assessments should be diversified to consistently incorporate both societal and patient interests.* We recognize the importance of representing payer perspectives in evidence evaluations. However, it is also imperative to integrate societal and patient centered perspectives explicitly into ICER's value framework, enabling consideration of additional dimensions of value. The societal perspective permits a broader range of benefits to be included in appraisals and to better reflect the importance of supporting innovation. The formal inclusion of patient perspectives would further expand the scope of ICER's value assessments.

To address this, *ICER should quantify and expand the scope of benefits measured in its cost-effectiveness analyses.* Sanofi supports ICER's interest in capturing and formally incorporating additional patient-centered benefits in its cost-effectiveness analyses. The measurement of value should include a broad array of benefits of importance to patients and society<sup>8, 9, 10</sup>. Currently, ICER's consideration of such patient-centered outcomes is qualitative and does not permit effective integration of such factors in assessments. Methodology exists in many instances to quantify and incorporate such patient-centered dimensions and measure the benefits accrued. In other contexts, qualitative inclusion of such factors should be formalized as much as possible, to ensure meaningful consideration in assessments.

Sanofi recommends a comprehensive consideration of an intervention's value that includes the integration of unmet needs, populations, outcomes, contexts, and economic impacts. Assessment of outcomes should include, in addition to clinical effects, incremental impacts of the treatment on patient-reported outcomes and the ability to perform daily activities. Assessments of interventions should also include potential incremental effects of treatment on patients' experience of care, e.g., effects on the invasiveness or convenience of treatment, and benefits



with respect to adherence. It is also important to consider potential effects of the treatment on care pathways or other impacts on efficiency in the delivery of health services. Evaluation of economic impacts should also include effects on productivity of patients or caregivers, or impacts on non-health related expenditures. Considerations of context should explicitly recognize potential impacts on innovation. Finally, assessments should also consider evidence from a wide range of sources, including experimental, quasi-experimental, observational, and qualitative studies.

*ICER's "averaged" approach to value assessment is incompatible with the rapidly growing shifts in research and development and medicine toward targeted therapies and personalized care.* ICER's approach inherently limits its capability to recognize the significance of individual characteristics and heterogeneity of treatment response and inform personalized, shared decision making by physicians and patients. Methods based upon average effects poorly represent tailored treatment strategies and may deny patients access to important therapies from which they would benefit. Such approaches are also increasingly out of step with the emergence of targeted treatments based on patients' genotype or specific pathophysiology <sup>11</sup>. ICER should seek to adapt its value framework and methods to anticipate this emerging context.

*ICER should consistently expand the scope of its reviews beyond drugs and devices, which constitute only a minority of healthcare expenditures.* In its current iteration and focus, ICER's framework frequently disregards the majority of healthcare spending and ignores opportunities to reallocate "low value" interventions to fund innovative therapies. For example, the "Choosing Wisely" initiative seeks to identify low value interventions in health care and to reallocate resources to areas of higher value <sup>12</sup>. ICER could have a much larger favorable impact by expanding its focus to consistently include a broader range of interventions and evaluate potential redirection of resourcing across intervention categories.

*ICER should suspend evaluations of products that have not received FDA approval for a recognized treatment indication and recognize the uncertainties associated with measuring a drug's value at launch.* We are concerned that in recent reviews ICER appears to be increasingly focused on evaluating development products that have not yet received FDA approval or off label usage, e.g., in the current Multiple Sclerosis <sup>13</sup> and Rheumatoid Arthritis <sup>14</sup> treatments class reviews. Proceeding with value assessment in this context is problematic and a risk to patients, given that regulatory agencies have not finalized their evaluation of the evidence base and supported a treatment indication. Evidence on newly launched products is also limited in many ways and evolves as real world utilization proceeds. ICER's value assessments should reflect these uncertainties. We recommend that ICER focus on FDA approved products for which indications have been explicitly sanctioned and for which an adequate evidence base founded on well-controlled trials of efficacy and safety exists. In the context of emerging therapies, ICER should clearly state the uncertainties and limitations in its analyses at this early stage and establish explicit criteria for conducting updates of evidence assessments as real world utilization of products evolves. It is essential that long-term perspectives are better represented in ICER's value assessments.





*ICER's framework discourages innovation and does not advance value-based health care.* ICER potentially undercuts incentives to develop new medicines by setting fixed, siloed thresholds for spending on innovation and recommending limits on access to treatments that exceed the threshold. ICER's budget thresholds establish artificial and arbitrary limits on spending for innovative medicines. We recognize that affordability is a concept of critical importance to all participants in the healthcare system and support balanced discussions of this topic. However, ICER's approach is oversimplified and arbitrary, and we recommend that ICER suspend this component of its value framework until it identifies or develops valid approaches to this concept.

*ICER over-estimates new product uptake and should develop valid approaches to measuring this critical element of its value assessment.* ICER's current approach inflates budget estimates with potential severe consequences for patient and provider access to innovative medicines. ICER must develop more realistic utilization estimates that incorporate uptake predictions from clinical experts and manufacturers and recognize realistic medication management practices of payers.

*ICER should recognize the limitations of the QALY as a measure of value, and instead diversify its approaches to value assessment.* Cost per QALY approaches underestimate value and create perverse incentives in many cases<sup>15, 16, 17</sup>, including:

- 1) QALYs may undervalue survival benefits in populations presumed to have poor quality of life, e.g., Oncology and Congestive Heart Failure.
- 2) Cost per QALY approaches may provide undue incentives to develop treatments with marginal improvements relative to high cost products over drugs with large magnitude of benefit in patients with no treatment options
- 3) Cost per QALY approaches may undervalue and discourage development of orphan/rare disease products, as the size of the population is not a consideration.
- 4) Acute conditions may be undervalued.
- 5) Age differences are inadequately managed, i.e., interventions in youth are inherently valued above those targeted for later in life.

Taken together, these serious limitations should be acknowledged and alternative approaches included in ICER's value framework. ICER should also recognize that assessments using such measures should not be used for clinical decision making.

*ICER should adjust its comparative effectiveness methodology to avoid indiscriminate use of indirect treatment comparison.* The use of indirect treatment comparisons in the absence of direct head-to-head comparative evidence can lead to significantly flawed conclusions if populations or study designs differ fundamentally. In the presence





of significant heterogeneity in treatment populations and trial designs, indirect treatment comparisons cannot fully adjust for differences and will deliver suspect conclusions<sup>18, 19</sup>. This is especially of concern in the instance of unapproved or emerging products or off label usage, for which available comparative information is limited and for which the overall evidence base has not been systematically evaluated by regulatory organizations. ICER should limit firm comparative conclusions to contexts in which direct comparative data exist and heterogeneity between populations and protocols is limited.

*ICER should recognize the limitations of reliance upon list prices and implement alternative approaches to measuring the cost of interventions.* Base case assumptions in evidence evaluations must represent reality. As is well known, the list price does not translate to actual price paid because of discounts offered to purchasers. Sensitivity analyses should be consistently performed to reflect alternative price assumptions, taking into account input from external stakeholders. When such analyses result in material changes to the interpretation of findings, limitations of the conclusions should be acknowledged and reflected in the conclusions.

*ICER also applies other misleading approaches to the measurement and characterization of cost, and should adjust its procedures to reflect lifecycle considerations for products.* Most importantly, ICER's models should anticipate reductions in cost due to loss of exclusivity and generic entry.

### **Issues regarding process and governance in operationalizing ICER's evidence reviews**

Sanofi recognizes the improvements that ICER has made to its processes and appreciates the opportunity to provide comments at multiple stages of the development and execution of its evidence reviews. The recent establishment of an "open input" period prior to the development of the scope for evidence reviews and other outreach activities are positive. However, ICER should continue to implement more transparent processes and better integrate patient, provider, and manufacturer expertise in its deliberations. The development of evidence reviews should involve early and active dialogue with and opportunities for input from all relevant stakeholders. Additional effort is also required to ensure adequate time for response and the opportunity to evaluate reproducibility of the findings.

*ICER should incorporate greater patient and provider insight and expertise and independent perspectives into its evaluative panels and processes, including its Public Advisory Councils.* It is critical that independent patient and clinical expert perspectives, including the voices of objective academic representatives, are integrated into the committees who vote on the final evidence reports. Cost containment priorities should not predominate over a broader perspective on value, and a diverse representation and composition is key in establishing effective advisory councils. Additionally, we encourage ICER to expand opportunities for manufacturers to present our perspective during public discussions.

*ICER should utilize explicit criteria for prioritizing evidence assessment topics and updating reports.* ICER's process for identifying, prioritizing, and developing evidence review topics is still opaque in many respects, and



there appear to be no consistent criteria utilized to trigger updates of reports as evidence and utilization evolve. It is important that stakeholders have the opportunity to anticipate and have the opportunity to contribute ideas and expertise to ICER's agenda.

It is also critical to update and adapt conclusions in response to developing evidence and ICER has a responsibility to provide greater stewardship in this area. For example, the recent publication of ICER's model results from the review of the PCSK9i agents in the *Journal of the American Medical Association* continued to employ assumptions and inputs that are unrealistic and in conflict with evolving evidence on the utilization of these products. Uncritical use of such assumptions can result in misleading conclusions and support inappropriate restrictions on patients' access to important therapeutic innovation.

Finally, ICER should more clearly articulate the limits of its evidence reviews in informing coverage and reimbursement decisions and evaluation of treatment options between providers and patients. ICER provides tools and information to assist decision-making by others, i.e., patients and healthcare providers and other participants in the healthcare delivery system. It should not make determinative recommendations.

*ICER should allow sufficient time for public comments in response to its scope and evidence reports.* Currently, stakeholders are heavily taxed in managing responses on urgent timelines, often to inform multiple, concurrent reviews. Providing expert, constructive feedback requires a reasonable timeframe and opportunity to mobilize resources.

In conclusion, we appreciate ICER's willingness to consider modifications to its current value framework and to engage stakeholders and seek feedback on this topic. We look forward to continuing dialogue and further supporting ICER's efforts to establish a transparent, patient-centered approach to value assessment.

Yours Sincerely,

A handwritten signature in black ink that reads 'Bryan M. Johnstone'.

Bryan M. Johnstone, Ph.D.  
Vice President  
Head, Evidence Synthesis, PROs, and Communications  
Global Health Economics & Outcomes Research  
Sanofi



## *Citations*

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- <sup>3</sup>PhRMA. “Principles for Value Assessment.” Available at: <http://phrma.org/principles-guidelines/principles-for-value-assessment-frameworks>. Accessed September 11, 2016.
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Glenn Shirley ([gasgolfball@hotmail.com](mailto:gasgolfball@hotmail.com))

You are giving the insurance industry a reason to omit or downplay older drugs and robbing the public of taking advantage of generic available drugs. I will debate this statement with anybody. Disclose where you funding comes from and the percent from each. I have already experienced this problem; twice within a week. Prove there is a need for this type evaluation, you are taking RX out of the hands of the physician, is this your intent?

**Submitted electronically** via [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

September 11, 2016

Steven D. Pearson, MD, MSc, President  
The Institute for Clinical and Economic Review (ICER)  
One State Street, Suite 1050  
Boston, MA 02109

**RE: ICER Value Assessment Framework**

Dear Dr. Pearson,

St. Jude Medical appreciates the opportunity to comment on the proposed ICER Value Assessment Framework (2.0) to ensure greater transparency in reviewing the evidentiary guidelines for evaluating net health benefit. We share the same objective as ICER in terms of improving the healthcare system in advocating new technologies that add value for payers, providers and patients. Our comments focus on improving the current value assessment framework based on our recent experience with ICER's review of the CardioMEMS™ Heart Failure System. St. Jude Medical's comments will concentrate on ICER's value framework methodology when evaluating new interventions as it relates to medical devices with emphasis on the following: need for increased transparency, applicability of this framework on new medical device interventions, and market uptake assumptions.

***Need for Increased Transparency***

Patient, manufacturer, and other stakeholder engagement are critical to providing a comprehensive and balanced review of new technologies introduced into the healthcare market. We support this approach as it relates to public commentary and the opportunity for oral comment at the ICER public meetings during their review of new technologies. As part of this review process, ICER claims to provide a scoping document, in the spirit of transparency, and while the methods are outlined, the specific assumptions are not detailed. Assumptions are the crux of any modeling effort, so all assumptions must be spelled out for review by stakeholders. Without clear delineation of assumptions, it is difficult, if not impossible, to replicate and confirm modeling and approach. Alternatively, a direct line of communication should be established with the manufacturer who can provide early input on the references, data, and clinical input (from key opinion leaders who have worked on the specific technology) to clarify assumptions. Many manufacturers have teams that focus on healthcare economics and reimbursement which would be able to facilitate this early dialogue and requests for additional information.

Because ICER's reports are frequently used by public and private insurance plans, healthcare providers, and consumers, we strongly encourage ICER to work with industry stakeholders in the production of its final technology assessments. We strongly encourage that ICER allot appropriate time to discuss evidence with Industry and thoroughly vet any disagreements in the analysis, results, and conclusions.

### ***Applicability of framework assumptions on new medical device interventions***

Assumptions and concepts that are valid for evaluating pharmaceutical therapies do not necessarily apply to medical devices. ICER's preference for randomized clinical trials (RCTs) may be challenging due to blinding and ethical considerations for providing medical devices to one cohort but not the other. In lieu of RCTs, ICER should consider other forms of clinical evidence in factoring the affordability, effectiveness, safety and societal benefit of new device interventions. The National Institute for Health and Clinical Excellence (NICE) has updated its process and methods guides to consider the best available evidence to develop their recommendations.<sup>1</sup>

St. Jude Medical has concerns that ICER's threshold for short-term budget impact could have broad reaching consequences for policy makers and other health technology bodies that rely heavily on this report for evaluation of coverage of new device interventions. More often than not, the health outcomes and cost effectiveness ratio established early in a medical device's life cycle improves over time. A relevant example is the left ventricular assist device (LVAD) where the cost effectiveness ratio has significantly improved as a result of improvements in survival ability and quality of life for both bridge-to-transplant and destination therapy patients. The need to look beyond the "alarm bell" triggers for new device interventions should be considered as new device therapies undergo a learning curve and greater utilization provides insights that enhance research and development for next generation devices. This also translates into clinical practice that often enhances patient selection criteria and patient management.<sup>2</sup> All of these important factors are dynamic and may not necessarily be considered in the original ICER review, particularly when there is no ability to update the data or provide additional consideration for measuring long-term value. As a result, we recommend that ICER modify their assumptions, modeling, and evaluations to be more in line with accepted conventions and guidelines for medical device reviews similar to the approach of NICE's Medical Technologies Evaluation Programme (MTEP).<sup>3</sup>

### ***ICER's market uptake assumptions***

ICER utilizes four categories (e.g., very high at 75% uptake, high at 50% uptake, intermediate at 25% uptake, and low at 10% uptake) of market adoption at 5 years for evaluating and recommending budget impact of new interventions.<sup>4</sup> The category that ICER applies is

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<sup>1</sup> NICE: Process and methods guides- Developing NICE guidelines: the manual. October 2014. <https://www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf>

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<sup>3</sup> <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-medical-technologies-evaluation-programme>

<sup>4</sup> <https://icer-review.org/announcements/improvements-value-framework/>

likely to influence the calculations for the potential budget impact of a new intervention. We have concerns about ICER's methodology and assumptions for market adoption as it relates to new device interventions. Novel medical devices are often disruptive technologies and, as a result, they are adopted slower than new pharmaceutical therapies. Additional challenges that slow medical device adoption include challenges in securing payer coverage, operator training and implantation, and lag in development of medical society guidelines in supporting appropriate utilization outside clinical trials.

To better inform market adoption assumptions, we suggest ICER use a variety of resources to validate its uptake assumptions such as publically available sales and analysts' data which better reflects real-world utilization. Transcatheter aortic valve replacement (TAVR) is one example of a revolutionary technology commercialized in the U.S. in 2012 that supported a low market uptake based on analysts' reports.<sup>5</sup> In the CardioMEMS review, if ICER utilized the "low uptake" model, based on available sales data rather than the "intermediate" criterion, the technology would have fallen well within the affordability equation for supporting cost-effectiveness. Again, we recommend utilizing outside resources to validate market adoption or that ICER models all criteria in their market adoption model and provides sensitivity analyses to show a range of scenarios for a more balanced perspective. These approaches provide a more realistic portrayal of adoption that mirrors commercialization for new device interventions in light of the unique challenges faced with their early adoption.

### ***Recommendations***

In summary, St. Jude Medical recommends the following to improve robustness and transparency of future ICER medical device reviews.

- Engage industry stakeholders early and throughout the review process by informing industry of ICER's assumptions and providing industry with an opportunity to share and discuss the latest available evidence, data, and key opinion leader feedback prior to publication of the final report.
- Fully understand the differences and guidance needed to appropriately review cost-effectiveness and budget impact of medical device interventions vs pharmaceuticals and modify the ICER approach to accommodate for those differences in future assessments.
- Provide the rationale and assumptions in modeling budget impact findings by reasonably leveraging best estimates of market uptake based on analysts' data and/or modeling all scenarios in ICER's market uptake model to show the differences in budget impact based on the various criteria.

We appreciate your consideration of these comments. It remains our desire to collaborate with third party organizations who share a common goal guided by patient care and the healthcare communities whom we serve. We look forward to continuing our advocacy in ways to best support a comprehensive review of new technologies that strive to achieve long-term cost-savings especially in disease states such as heart failure that are challenging to manage.

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<sup>5</sup> Credit Suisse. TAVI Comment. ASP Assumption for 2024 and 2025 Based on Model. Credit Suisse, New York; January 8, 2015.



Please let me know if you have questions. Feel free to contact me at (818) 493-3723 or [mcarlson@sjm.com](mailto:mcarlson@sjm.com) or you can also reach out to Robin Bostic, Vice President, Global Reimbursement and Healthcare Economics at [rbostic@sjm.com](mailto:rbostic@sjm.com).

Sincerely,

A handwritten signature in black ink that reads "Mark D. Carlson". The script is fluid and cursive, with the first name "Mark" and last name "Carlson" clearly legible.

Mark D. Carlson, MD, MA  
Chief Medical Officer and Vice President  
Global Clinical Affairs

September 1, 2016

Dear ICER:

I write in response to your call for suggestions for improvement to the ICER Value Assessment Framework.

I am the Chief Medical Officer for UnitedHealthcare, which is part of UnitedHealth Group. UnitedHealth Group is a diversified health and well-being company dedicated to helping people live healthier lives and making our nation's health care system works better for everyone through two distinct business platforms – UnitedHealthcare, our health benefits business, and Optum, our health services business. Our workforce of 225,000 people serves the health care needs of more than 125 million people worldwide, funding and arranging health care on behalf of individuals, employers, and government. Recognized as America's most innovative company in our industry by Fortune magazine for five years in a row, we bring innovative health care solutions to scale to help create a modern health care system that is more accessible, affordable, and personalized for all Americans.

UnitedHealthcare believes strongly in using the best data and the best science to improve the health of individuals and populations, achieve better outcomes and a better patient experience, and address the ongoing challenges of affordability. We strongly support ICER's mission and its range of reports, convening activities and analytic approaches, including ICER's Value Assessment Framework. In particular, the Value Framework's integration of clinical effectiveness, incremental cost for outcomes achieved, potential budget impact, and other consideration, combined with transparent and iterative processes, has been a major contributor to the field since ICER provides a real-world approach to integrating both clinical effectiveness and cost effectiveness in the short-term and longer-term horizon. Such cost effectiveness analyses have included both utilization and unit cost variables. The Value Framework has helped move discussions of "value" from the abstract and ethereal to the practical, here and now: what is the value of this treatment? At what price will that value be affordable to stakeholders and society overall? And finally, how will that value be measured?

Regarding areas for potential improvement to the Framework, my suggestions are as follows:

1. "Provisional Health System Value"-this label is intended to capture the tensions and trade-offs between long term and short term perspectives on value to the health system. I suggest an alternative label that is more descriptive, such as "Long Term Value Analysis" or "Short/Long Term Value Analysis"
2. Potential Budget Impact-the current framework focuses on uptake over 5 years. While budgetary impact is very complex and contains significant uncertainties, I suggest adding an analysis of whether effective mechanisms to manage budgetary impact have a low, medium, or high likelihood of success over this 5 year window. Such mechanisms could include: medical/utilization management; competitive product introductions promoting price competition; clinical protocol development/uptake by the medical community; among others.
3. Potential Budget Impact Threshold-the current framework uses net cost per individual intervention

that would increase national health care spending greater than GDP +1. This approach, while relatively simple, may miss the aggregate impact in a spending category, such as specialty drugs. In this area, many individual entities may be below the budget impact threshold, but the category in aggregate has significant budgetary impact. I suggest adding an analysis of “category budgetary” impact for this reason. A second issue in drug spending is ongoing price increases in many well established drugs, including generics. These price increases are “baked in” to the denominator in the current ICER approach, when in my view they should be normalized to GDP +1. Unlike other aspects of health spending (such as hospital or physician services) these are almost pure price increases and are not driven by increases in underlying input costs.

Thank you for the opportunity to comment on ICERs Value Assessment Framework. ICERs commitment to transparency, public input, and continuous improvement is laudatory, and I look forward to future versions of the Value Assessment Framework.

Sincerely,

A handwritten signature in black ink, appearing to read "Sam Ho, MD". The signature is fluid and cursive, with the first name "Sam" and last name "Ho" clearly visible, followed by "MD".

Sam Ho, MD  
Executive Vice President and Chief Medical Officer  
UnitedHealthcare