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

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.[1]
- 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

[1] 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.[2] 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.[3] 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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[2] 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.

[3] 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).[4] 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 deliberatively 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."[5] 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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[4] 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.

[5] 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.

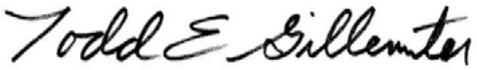
We ask that ICER consider evaluating the potential impact of any Framework changes, as well as observing for any real impacts going forward, along two key factors:

- 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; 916-233-3490) if there is any further information we can provide.

Sincerely,



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