Biotechnology Industry Organization

July 30, 2013

BY ELECTRONIC DELIVERY

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RE: Patient-Centered Outcomes Research Institute's (PCORI's) Dissemination and Implementation Roundtable, Stakeholder Response

Dear Dr. Selby:

The Biotechnology Industry Organization (BIO) is pleased to submit feedback on several of the concepts proposed for discussion during PCORI's *Dissemination and Implementation Roundtable* ("the Roundtable") held on July 29, 2013 in Washington, D.C. and appreciates PCORI's efforts to garner diverse stakeholder input for this event.[1] BIO is the largest trade organization to serve and represent the biotechnology industry in the United States and around the globe. BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers, and related organizations in the United States. BIO members are involved in the research and development of novel interventions to prevent, treat, and cure diseases through the most advanced science.

BIO supports PCORI's goal of increasing the availability of accurate, scientific evidence to inform clinical decision-making, and we maintain an ongoing desire to see PCORI successfully carry out its statutory mandate, of which dissemination of clinical comparative effectiveness research (CER) is a vital component. The stated goal for the July 29th Roundtable is to serve as the foundation for developing a "request for proposal (RFP) for the commission [of a]…PCORI Blueprint for Dissemination and Implementation of Research."[2] To structure that input, PCORI proposes to the public the same series of questions that will be the focus of the Roundtable discussion, including current and ideal frameworks, mechanisms, and strategies for disseminating and implementing CER. BIO submits its perspective on these issues through the following comments that address PCORI's effort in the context of its statutory mandate and in terms of essential considerations for the appropriate communication of CER findings. These concepts are explored in detail below.

I. Realizing PCORI's Statutory Mandate: PCORI should focus on dissemination of findings of clinical comparative effectiveness information.

[1] PCORI. 2013. *Meetings & Events: Dissemination and Implementation Roundtable*. Washington, DC: PCORI. Available at: http://www.pcori.org/events/dissemination-and-implementation-roundtable/?type=.
[2] Ibid.

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PCORI should maintain a robust fidelity to the intent and provisions of its statutory mandate both to ensure it efficiently and successfully achieves what it was created to accomplish and because straying from its mandate risks creating unnecessary redundancies with the missions of other federal agencies. Thus, BIO urges PCORI to consider its current undertaking within the confines of its authorizing statue, the Affordable Care Act of 2010:

> The purpose of the Institute is to assist patients, clinicians, purchasers, and policy-makers in making informed health decisions by advancing the quality and relevance of evidence concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, and managed through research and evidence synthesis that considers variations in patient subpopulations, and the dissemination of research findings with respect to the relative health outcomes, clinical effectiveness, and appropriateness of the medical treatments, services, and items described in subsection (a)(2)(B)."[3]

PCORI's goal in establishing a dissemination Blueprint, "to guide the organization in disseminating research findings of funded research conducted in the national program areas," is clearly within the organization's statutory mission.[4] The statute specifically outlines the elements that at a minimum must be addressed in the dissemination of findings, which should be included in the development of a Blueprint for dissemination. These elements include that the findings: are conveyed in a comprehensible and useful manner to patients and providers; are fully conveyed and include considerations specific to certain subpopulations, risk factors, and comorbidities; include the limitations of the research and further research needs; and do not include practice guidelines or coverage, payment or policy recommendations.[5] The authorizing statute also requires that a peer review process evaluate "evidence from [any] primary research shall be reviewed to assess scientific integrity and adherence to methodological standards" as adopted by PCORI's methodology committee.[6] While PCORI stated during its Dissemination and Implementation Roundtable that it will address the need for peer-review at a later date, BIO urges PCORI to do so simultaneous to its current efforts. BIO believes that peer-review, along with these other elements, are minimum requirements for a robust Blueprint of accurate and appropriate dissemination of CER.

BIO supports PCORI's efforts to disseminate CER findings to improve health care decision-making but believes that the mechanisms and standards of such communication directly impact its quality and usefulness to patients, providers, and other stakeholders. Not only should PCORI's dissemination efforts comply with the minimum requirements set forth in statue and described above, but PCORI's Blueprint for dissemination should ensure that CER communications are contextualized, balanced, and responsible. Individual CER findings will only be one part of what patients and providers utilize to assess treatment options, so it is crucial that these stakeholders are able to identify which findings are most relevant to an individual circumstance and how CER findings fit into the broader context of available treatment options. PCORI's dissemination Blueprint should include robust requirements for communicating:

- The scientific validity and quality of CER findings;
- Subpopulations to which CER findings are applicable;

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[3] Affordable Care Act of 2010 (ACA) § 6301(c).
[4] PCORI. 2013. Dissemination and Implementation Roundtable: Presentation Slides. Washington, DC: PCORI, p.19. Available at: http://www.pcori.org/assets/2013/07/PCORI-Dissemination-Implementation-Roundtable-072913.pdf.
[5] Ibid.
[6] Id. at § 6301(d)(7)(A).

- Limitations of CER findings; and
- CER findings in a timely manner and through a process that includes sufficient opportunities for stakeholder input.

PCORI's responsibility to accurately and appropriately disseminate information is heightened by the restrictions placed on other stakeholders' communications of CER findings.

A. PCORI's Blueprint for dissemination should include robust standards for CER communication.

PCORI's standards for disseminating CER should ensure that the scientific quality and validity of any findings is accurately communicated in a manner that is comprehensible and meaningful to patients, providers, and other stakeholders. The ability to translate this scientific information into an assessment of whether and how CER findings are credible and applicable is crucial to the ability of CER to positively impact clinical decision-making.

PCORI's Blueprint also should set robust standards to fulfill the statutory requirement to identify relevant subpopulations. All CER communications should clearly denote to which patient subpopulations and in what circumstances research findings may reliably be applied. This is particularly important because the understanding of effectiveness is impacted both by the characteristics of the intervention or treatment employed but also by the characteristics of the different subpopulations studied.

Similarly, though statute requires the limitations of CER be discussed in its dissemination activities, PCORI's standard should require that limitations—due to inherent study design, methodology, presence of confounding factors, bias—be identified in a way that includes an assessment of how those limitations affect the results of a study and its applicability to individual patients. This is especially important because CER may rely more heavily on observational studies rather than randomized control trials. The benefit of this is that the former research methodology is better able to study the differential aspects of treatments under real-world conditions, but its findings also are more susceptible to sources of bias and confounding. Accurately communicating such susceptibilities is a crucial aspect of transparent CER dissemination and facilitates patients' interpretations of how such research findings may be applied in their decision-making.

Finally, PCORI's Blueprint should ensure high-quality information is communicated reliably but also in a timely fashion to maintain pace with, and relevance to, an evolving standard of care. Any such framework of dissemination standards also should be subjected to a process similar to that of federal notice and comment rulemaking. This will allow for robust input from patients, providers, and other stakeholders that will not only aid PCORI in meeting its dissemination goals, but will set a high standard for CER dissemination generally.

B. PCORI's freedom to disseminate CER findings heightens its responsibility to do so accurately and appropriately.

PCORI's freedom from regulatory restrictions on its CER communications with stakeholders puts it in a unique and important position to make CER more accessible and comprehensible for use in clinical decision-making. For example, PCORI is empowered to disseminate CER findings that include off-label uses of approved therapies, while other stakeholders, i.e., biopharmaceutical manufacturers, must comply with regulatory restrictions on the

dissemination of information about their own products.[7] Such regulatory restrictions on the communication of CER findings could limit a manufacturer's ability to respond to potential inaccuracies in reported CER findings. This communications asymmetry confers a significant responsibility on PCORI to disseminate CER findings with sufficient context and in a fair and balanced manner. It also further emphasizes the need for opportunities for all stakeholders to provide input into the development of PCORI's Blueprint for CER dissemination.

C. PCORI's dissemination Blueprint should include mechanisms to incorporate evidence not formally generated by PCORI funding.

To fulfill its mandate to "to assist patients, clinicians, purchasers, and policy-makers in making informed health decisions," PCORI's dissemination Blueprint should include provisions to incorporate the full breadth of available evidence on a particular topic for a given patient population. PCORI is just one organization among many others—both public and private—that conducts CER, but its ability to bring together diverse stakeholders , communicate with diverse audiences, and communicate and disseminate CER findings freely is unique. Thus, PCORI should consider how it can best leverage all of the available evidence to provide healthcare decision-makers with a comprehensive portrait of the relevant CER landscape. To do this, the Blueprint should include mechanisms for patients, providers and other healthcare stakeholders that sponsor CER—e.g., registry data, real-world safety monitoring data, longitudinal patient-caregiver diaries—to contribute their information to PCORI's broader effort to inform healthcare decision-makers. Incorporating more than just PCORI-generated CER findings will improve the Blueprint's usefulness and credibility as well as serve as a standard for the field.

II. Additional Comments

For this Roundtable, PCORI is also seeking stakeholder discussion of "implementation" of CER findings. While the authorizing statute allows for PCORI to measure the uptake of its research findings in clinical practice, the organization's intention to include strategies "to speed implementation by actively facilitating how PCORI's research findings can be used"[8] could fall within the category of findings from which PCORI is explicitly prohibited from communicating, namely "practice guidelines, coverage recommendations, payment, or policy recommendations."[9] Given this risk, PCORI should limit the scope of its proposed Blueprint to potential frameworks and strategies for dissemination of findings only. Separately, it would be appropriate to develop a framework to accomplish the stated goal of "evaluat[ing] how the effect of the dissemination of such findings reduces practice variation and disparities in health care."[10]

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[7] See Perfetto, E., J. E. Jr. Bailey, K. R. Gans-Brangs, S. J. Romano, N. R. Rosenthal, and R. J. Willkie. 2012. Communication about results of comparative effectiveness studies: a pharmaceutical industry view. *Health Affairs* 31(10):2213-2219; and, Neumann, P. J. 2013. Communicating and Promoting Comparative-Effectiveness Research Findings. *New England Journal of Medicine* 369:209-211.

[8] PCORI. 2013. Dissemination and Implementation Roundtable: Presentation Slides. Washington, DC: PCORI, p.19. Available at: http://www.pcori.org/assets/2013/07/PCORI-Dissemination-Implementation-Roundtable-072913.pdf.

[9] ACA § 6301(d)(8)(A).

[10] PCORI. 2013. Dissemination and Implementation Roundtable: Presentation Slides. Washington, DC: PCORI, p.19. Available at: http://www.pcori.org/assets/2013/07/PCORI-Dissemination-Implementation-Roundtable-072913.pdf.

Finally, among the questions the Roundtable poses is one regarding "the best approach to develop a framework for implementing results of clinical effectiveness research."[11] BIO encourages PCORI to clarify that it meant to request information with respect to the clinical comparative effectiveness of medical treatments, services, and items as stated in statute above. Assessing the clinical effectiveness of individual therapies is the sole purview of the Food and Drug Administration, which retains the statutory mission and institutional expertise to accurately do so. Additionally, while PCORI's mandate includes the consideration of comparative clinical effectiveness, it is not limited to that topic, and therefore should not exclude other issues studied by patient-centered outcomes research, such as the relative appropriateness of treatments or relative health outcomes, from its focus.

III. Conclusion

BIO appreciates the opportunity to provide these comments. We look forward to continuing to collaborate with PCORI on this important issue of communicating CER in a balanced, comprehensible, and contextualized manner to assist patients and providers in making well-informed health care decisions. Please feel free to contact us with any further questions or for more information.

Sincerely,

/s/

Laurel L. Todd
Managing Director, Reimbursement and Health Policy

[11] PCORI. 2013. Dissemination and Implementation Roundtable: Submit Your Responses. Washington, DC: PCORI. Available at: http://www.pcori.org/funding-opportunities/dissemination-and-implementation-roundtable-share-your-thoughts/.