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BIO's Statement Before the IOM's Committee on Comparative Effectiveness Research Priorities

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 1,200 biotechnology companies, academic institutions, state biotechnology centers, and related organizations in the United States. BIO is pleased to have the opportunity to submit comments for the consideration of the Institute of Medicine's (IOM's) Committee on Comparative Effectiveness Research (CER) Priorities.

As a representative of an industry committed to discovering new cures and ensuring patient access to them, BIO strongly supports efforts to increase the availability of accurate, scientific evidence to inform clinical decision-making. BIO believes that individual patients and their doctors should be armed with the best available information to help assess the relative clinical benefits and risks of various treatment alternatives. When appropriately applied, comparative effectiveness information is a valuable tool that, together with a variety of other types of medical evidence, can contribute to improving health care delivery. However, BIO is concerned that comparative effectiveness information may be used strictly as a means to contain costs, rather than deliver health care value by improving patient health outcomes.

The IOM has been asked by Congress, in the American Recovery and Reinvestment Act of 2009, to recommend priorities for spending on CER to the Secretary of Health and Human Services. BIO is pleased that the IOM's Committee on CER Priorities has solicited suggestions for the committee's consideration, as they gather input for this research endeavor, and we are pleased to submit these comments on this very important subject.

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However, before diving down into the granularity of which specific CER studies to undertake, it is imperative that this panel evaluate the lack of consistent methodologies in comparative effectiveness research. Doing so will enable CER to provide maximum benefits to patients.

Careful consideration should be given as to what methods should be selected. In addition, rigorous standards must be applied to the research method selected, such as randomized controlled trials (RCTs), retrospective studies, or data synthesis. These standards should consider both the benefits and challenges associated with different methodologies. For example, RCTs utilize a select population chosen to demonstrate reproducible and confirmatory evidence of the safety and efficacy of the product being studied. This allows practitioners to achieve confirmatory validation of the intervention or product's performance when used in a group of fairly homogeneous patients. In the real world the combination of multiple medical conditions or multiple treatments may require provider decisions to be made for not only similar patients,

but also for patients who are unlikely to be representative of the patients evaluated when generating the scientific evidence. On the other hand, retrospective studies come with their own set of limitations. First, the data that are used for retrospective studies are generally administrative data that were not designed for an effectiveness study. Thus, data elements that may be needed to adjust for differences in multiple medical conditions and overall health risks may be missing or incorrectly coded. Second, there may be bias for certain patients to be selected for treatment for which one cannot adjust with the previously collected data. CER's usefulness and practicality may be advanced by examining ways to reliably use observational data, how registries can be useful not just in identifying rare safety events but also in suggesting new treatment hypotheses. In their final form, comparative effectiveness research studies should include a concise description of the research question, transparency as to the inclusion or exclusion of evidence or clinical information, transparent analytical methods, discussion of limitations in the quality of the evidence and methods and overall conclusions. These studies should also include recommendations for refinement of methodology and recommendations for areas of future research.

Comparative effectiveness studies should capture all relevant aspects of diseases and their treatments using high standards of evidence. Comparative effectiveness analyses often ignore many important aspects of treatment interventions that affect patients or may not account for the spectra of disease severities. Increased worker productivity, reduced caregiver burden and savings to other parts of the health care system are also important benefits that may not be reflected in studies conducted with a narrow perspective.

Advancements in the development of innovative therapies are grounded in the ability of researchers to focus on the mechanisms of action that allow particular therapies to work in specific patient populations. Promoting innovation in personalized medicine requires clinicians to have the ability to make patient-centered treatment choices without conforming to inflexible standards or practice guidelines. In addition, many therapies targeting rare or "orphan" diseases, as well as severe, rapidly progressive, or life-threatening diseases, are not conducive to comparative effectiveness studies due to the vulnerabilities, small size, heterogeneity, and other characteristics of these patient populations. Government policies addressing comparative effectiveness need to acknowledge the limitations of current methodologies and ensure that they do not lead to conclusions and decisions that discourage or impede medical advancements and breakthroughs that can address unmet medical needs.

For these reasons, BIO believes it is important to recognize and acknowledge these methodological concerns prior to finalizing comparative effectiveness research priorities.

BIO urges the Committee to consider the following when establishing CER priorities:

- **Comparative effectiveness research should focus on the totality of the health care delivery system, and not just drugs and biologics.** Much of the interest in comparative effectiveness research to date has been narrowly focused on drugs, biologics, and medical devices. However, more value may be derived by focusing on areas that command a far greater portion of the healthcare dollar and for which there may be much greater uncertainty surrounding the outcomes of different treatment options. Comparative

effectiveness information that reflects the interactions among all of the various components of the health care system has the greatest potential to empower clinicians and patients to make more appropriate decisions when faced with "real world" clinical situations. In addition to comparing specific treatment interventions, research should also focus on how innovations in care delivery models, such as disease management programs and insurance design, may produce better health outcomes.

- **Comparative effectiveness research should be conducted through an open and transparent process involving all stakeholders, starting from the research planning stage.** BIO believes that broad stakeholder involvement is the best way to create a neutral advisory body, ensure thoughtful discussion and generate rigorous and also feasible recommendations. As the IOM has noted in the past, broad stakeholder participation creates a neutral discussion platform and BIO urges the IOM to include this same range of stakeholders for this Committee as well. Stakeholders should be afforded the opportunity to provide meaningful input into all steps along the study process, including the identification of priority areas to research, study design and research methods, and dissemination of results. Having all stakeholders at the table with full disclosure of potential conflicts of interest is a good way to manage potential biases and conflict of interest. Disclosure and broad representation are critical to ensure a balanced end product.

- **The goal of comparative effectiveness information is to inform clinical judgment and individual needs in medical decision-making.** The results of comparative effectiveness studies often illustrate the experience of the "average" patient on the "average" course of therapy. However, patients may respond differently to the same intervention in ways that cannot be anticipated—for example, the treatment may interact with medications they are taking, or known genetic characteristics may modify response to the treatment. In order to achieve the best possible outcomes, providers must have the flexibility to tailor the appropriate course of treatment for each patient based on individual patient preferences and clinical circumstances. Imposing rigid practice guidelines that fail to recognize such variations among patients can interfere with the ability of providers to deliver the most appropriate care for each patient and lead to suboptimal outcomes and increased health care costs.

In conclusion, by focusing on the totality of the healthcare systems, using a transparent process that draws upon the expertise of all stakeholders in order to inform the clinical decision judgment and individual needs in medical decision-making, comparative effectiveness research that captures all relevant aspects of diseases and their treatments using high standards of evidence will advance the goals of personalized medicine and provide maximum benefits to patients.