BIO
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

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BY ELECTRONIC DELIVERY

Carolyn Clancy, M.D., Director
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
Eisenberg Building
540 Gaither Road
Gaithersburg, MD 20850

Re: Draft Report: Evidence Regarding Off-Label Indications for Targeted Therapies Used in Cancer Treatment

Dear Dr. Clancy:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the Agency for Healthcare Research and Quality's (AHRQ) "Report on the Evidence Regarding Off-Label Indications for Targeted Therapies used in Cancer Treatment" (the "Draft Report").[1] As an association whose members are dedicated to discovering new therapies using science and evidence-based medicine, BIO appreciates AHRQ's contributions in this area. We also urge AHRQ and other policymakers to avoid setting evidentiary standards that unduly interfere with the practice of medicine, however, or harm access to breakthrough treatments for patients that need them the most.

BIO's Membership and Evidence Development

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 members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products.

[1] Amy P. Abernethy et al., Report on the Evidence Regarding Off-Label Indications for Targeted Therapies Used in Cancer Treatment, August 26, 2009 (released by AHRQ on October 7, 2009), available at http://www.ahrq.gov/clinic/ta/targthrps/targthrps.pdf.

As the representative of an industry committed to discovering new therapies and ensuring patient access to them, BIO appreciates the analysis that AHRQ has provided regarding the use of targeted therapies for off-label indications. BIO's members are strongly committed to increasing the body of evidence available regarding diseases and their treatments. Our members invest millions of dollars each year on clinical studies, both before and after Food and Drug Administration (FDA) approval of their therapies, to produce high-quality clinical evidence to support FDA approval as well as medical decision-making. We also support the dissemination of this evidence to further clinical knowledge and enhance and improve the clinical decision making process.

The commitment of our member companies to developing evidence extends far beyond studies of a particular therapy. We support a rigorous evidence development process that encompasses all aspects of a disease from examining how it affects the body to studying the costs and benefits of therapies. Our members' research initiatives advance the understanding of disease pathology, diagnostic and therapeutic mechanisms of action, clinical effectiveness in naturalistic settings, health-related quality of life, and health economic impacts of therapies in addition to clinical safety and efficacy. The development and evaluation of therapies are part of this broader process and must be considered in context.

Our members' evidence development processes combined with Medicare's current coverage policies, especially the use of compendia, allows beneficiaries timely access to new therapies and encourages innovation. The Medicare statute and manuals give local contractors the flexibility and freedom to make timely coverage decisions, ensuring Medicare beneficiaries' access to the latest drugs and biologicals for medically accepted uses. These policies also encourage innovation and continued research by giving patients a choice of new therapies, recognizing new uses of therapies, and promoting a relatively stable and predictable reimbursement environment that is critical for many of our smaller member companies who depend on private sector investment. BIO requests that AHRQ specify in the Final Report that Medicare's current processes should continue so as to ensure patient access to care with needed oncology treatments.

The Role of Compendia in Protecting Access to Innovative Therapies

It is imperative that coverage policies keep up with the pace of innovation and clinical discovery to allow beneficiaries timely access to the most appropriate treatment options in their battles against deadly diseases. This is precisely why the Medicare statute requires contractors to cover "drugs and biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication," defined as a use approved by the FDA or a use of an FDA-approved drug supported by citations in certain compendia or by peer-reviewed

medical literature.[2] BIO supports these standards for identifying medically accepted indications because they help to protect beneficiary access to the most appropriate and promising treatment options.

The Draft Report notes that the drug landscape in oncology is frequently changing. BIO understands that the practice of medicine constantly evolves through the incorporation of new clinical evidence into the standard of care, and that the ability of clinicians to make patient-centered decisions based on the scientific evidence is particularly important in oncology. The standard of care in oncology can change rapidly as clinical researchers discover more effective, safer, or more tolerable treatment regimens. These new treatment options often involve the use of drugs and biologicals for indications not yet approved by the FDA and offer patients and physicians renewed hope and greater choice in fighting illness. These advances can be particularly important for patients with advanced stages of cancer.[3] As scientific advances are publicized through peer-reviewed publications, drug and biological compendia often incorporate this information before manufacturers can file compelling data with FDA and receive updates to a product's FDA-approved labeling. Further, not all indications actually achieve FDA approval for a variety of reasons. In such cases, coverage based on compendia listings may be the only option for providing patient access. Thus, compendia are an important resource for physicians when determining the most appropriate treatment regimen for their patients who are Medicare beneficiaries and for payers in determining which uses to cover. Although all of the compendia are evidence-based, the content of the compendia may vary due to differences in publication schedules, priorities, review processes, local practices and methods of describing the evidence for each listing. Compendia protect beneficiary access to advanced cancer therapies by providing physicians and policymakers with a wider body of evidence to use in making treatment and coverage decisions.

Issues to Consider Concerning Comparative Effectiveness Research

The Draft Report notes the potential need to identify "a different model of evidence generation and evaluation" and specifically highlights comparative effectiveness research as one method to better inform evidence development. BIO 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. Comparative effectiveness information is a valuable tool that, together with a variety of other

[2] Social Security Act. 1861(t)(2).
[3] Off-Label Use of Anticancer Therapies: Physician Prescribing Trends and the Impact of Payer Coverage Policy, Sept. 2005, at 5, available at http://www.bio.org/speeches/pubs/CovanceReport.pdf

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 to deliver health care value by improving patient health outcomes.

Because the Draft Report was requested by the Coverage and Analysis Group at the Center for Medicare and Medicaid Services (CMS), it is important to clarify that comparative effectiveness research should not be used to make coverage and reimbursement decisions. As mentioned earlier, the Draft Report references the rapidly evolving nature of evidence development in oncology. The inappropriate use of comparative effectiveness research in coverage or reimbursement could have a stifling effect on this medical progress.

Further, BIO believes that the application of comparative effectiveness research should advance the goals of personalized medicine and encourage the development of targeted therapies rather than create one-size-fits-all policies. Advancements in the development of innovative and targeted 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. A reimbursement environment that allows the right drug or biological in the right form to reach the right patient in a timely manner is a critical corollary to these advances. Promoting innovation in personalized medicine requires clinicians to have the ability to make patient centered treatment choices without being required to conform to inflexible standards or practice guidelines. CMS and AHRQ must continue to be mindful of this delicate balance. In fact, NIH Director Dr. Francis Collins recently warned, "There is a potential collision" between personalized medicine and comparative effectiveness research.[4] He went on to say, "We need to be mindful of the goal of comparative effectiveness research and not lose all that we have gained in understanding how individuals differ and how that could be factored into better diagnostics and preventive strategies."[5] BIO believes comparative effectiveness research should move personalized medicine forward and not backwards.

Comparative Effectiveness Issues Specific to Targeted Medicines

The Draft Report notes that the quantity and quality of data varied widely across the indications included in the analysis, and that targeted therapies are used to treat diseases that are "frequently rare". While targeted therapies are not exclusively for rare diseases, due to the small size, heterogeneity, and other characteristics of certain patient populations, any therapies targeting rare or "orphan" diseases, as well as severe, rapidly progressive, or life-threatening diseases, are not conducive to comparative effectiveness studies. Government

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[4] Julie Steenhuysen, "Risks to Personalized Medicine Seen in U.S. Reform," Reuters, October 26, 2009, ~~available at~~ http://www.reuters.com/article/healthcareSector/idUSN2612455320091026.
[5] ~~Id.~~

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. With the FDA working to increase its ability to advance targeted therapies, accompanying research as well as coverage and reimbursement policies should not hinder such advancement through broad, non-targeted (non-personalized) reports, decisions, or policies.

Conclusion

BIO greatly appreciates the opportunity to comment on the important issues raised by the draft report regarding off-label indications for targeted therapies. We look forward to continuing to work with AHRQ to ensure patient access to critical drug and biological therapies.

Respectfully submitted,

/s/

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