



February 27, 2006

Michelle Atkinson
Executive Secretary
Medicare Coverage Advisory Committee
Coverage and Analysis Group, Office of Clinical Standards and Quality
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Mail Stop C1-09-06
Baltimore, MD 21244

**Re: Authoritative Drug Compendia That May Be Used in Determining
Medically Accepted Indications of Drugs and Biologicals Used in an Anti-
Cancer Chemotherapeutic Regimen under Medicare Part B**

Dear Ms. Atkinson:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the desired characteristics of published authoritative compendia. We understand that the Centers for Medicare & Medicaid Services (CMS) may use this information to determine or influence the medically accepted indications of drugs and biologicals employed in an anti-cancer chemotherapeutic regimen under Part B of the Medicare program. 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 health-care, agricultural, industrial and environmental biotechnology products.

We thank CMS for convening the March 30, 2006 Medicare Coverage Advisory Committee (MCAC) meeting to discuss the compendia that may be used to identify medically accepted indications of drugs and biologicals used in an anti-cancer chemotherapeutic regimen. As the representative of an industry dedicated to discovering new therapies and ensuring patient access to them, BIO understands that the practice of medicine constantly evolves through the incorporation of new clinical evidence into the standard of care. Specifically, in oncology, the standard of care can change over night as clinical researchers discover more effective, safer or alternative treatment regimens. Many of these new treatment options involve the use of drugs and biologicals for indications not initially approved by the Food and Drug Administration (FDA). New clinical uses of FDA-approved therapies offer patients and physicians new hope and greater choice in fighting illness and can be particularly important for patients with advanced stages of cancer.¹ It is imperative; therefore, that both CMS and Medicare contractors ensure 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 these deadly diseases.

BIO strongly supports the authority Congress has granted to Medicare carriers to cover newly recognized, medically accepted uses of drugs and biologicals in a timely manner. Congress recognized the critical role of new clinical uses of drugs and biologicals in fighting cancer when it mandated that Medicare cover indications of drugs used in anticancer regimens if they are listed in the American Hospital Formulary Service-Drug Information (AHFS-DI), the United States Pharmacopoeia-Drug Information (USP-DI) or its successor publications, or the American Medical Association Drug Evaluations (AMA-DE) or by clinical evidence in peer-reviewed literature.² BIO supports these standards for identifying medically accepted indications because they help to protect beneficiary access to the most appropriate treatment options, as supported by the latest clinical research.

As the MCAC notes in its public announcement regarding this meeting, the AMA-DE is no longer in publication and the USP-DI will cease publication under its current name in 2007 and will continue publication under a new name.³ In addition to the recent amendment enacted under the Deficit Reduction Act to

¹ 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>.

² Social Security Act (SSA) § 1861(t)(2), as amended by the Deficit Reduction Act, Pub. L. No. 109-171, § 6001(f) (Feb. 8, 2006).

³ See <http://www.cms.hhs.gov/mcd/viewmccac.asp?where=index&mid=33>.

recognize the USP-DI's successor publication, the statute allows the Secretary to revise the list of compendia "as is appropriate for identifying medically accepted indications for drugs"⁴ and to recognize a successor publication if the name of a statutorily designated publication is changed.⁵ Because the statute clearly indicates Congress's intent for Medicare to use at least three compendia, including the AHFS-DI and USP-DI (or its successor publication), we urge the MCAC at least to recommend adding the National Comprehensive Cancer Network® (NCCN) Drugs and Biologics Compendium™ and then to focus its efforts on identifying additional compendia that Medicare carriers could use to determine medically accepted indications.

The MCAC released a list of questions it will consider in reviewing and evaluating the evidence on the desirable characteristics of compendia. BIO believes the following criteria should be considered in selecting additional compendia for use in Medicare's coverage decisions.

1. Extensive breadth of listings

Cancer takes many forms, and different treatments are needed depending on the stage of the tumor and the patient's complications and comorbidities. BIO's members are committed to developing therapies to address the widely-varied needs of cancer patients. To protect patient access to these appropriate, advanced therapies, the compendium's listings must reflect the full breadth of treatment regimens, including supportive care, for each form and stage of the disease.

2. Quick throughput from application for inclusion to listing

As we noted above, the practice of medicine constantly evolves. Oncologists and cancer patient advocates have noted that delays in compendia updates have jeopardized patient access to the most innovative treatments available. Therefore, the compendium must be able to timely review and publish newly accepted treatment regimens to ensure Medicare beneficiaries' access to new treatment options. Specifically, BIO believes that compendia should be fully updated as soon as new clinical data are available and no later than quarterly. The updated listings must be then available to the public on a website or other convenient location.

3. Publicly transparent process for evaluating therapies

⁴ SSA § 1861(t)(2)(B).

⁵ SSA § 1873.

Because a compendium's decision to publish a listing can have a significant effect on beneficiary access to care, we recommend that the compendium use a transparent and consistent application and review process for new and revised listings. Given the volume of clinical research performed in the United States today, we expect that the compendium will need assistance in keeping track of newly accepted indications. In many cases, stakeholders may be able to bring treatment options to the compendium's attention. A publicly transparent and consistent process for evaluating therapies, with clear criteria for weighing evidence and making recommendations, will allow stakeholders to understand how and when to submit requests for new or revised listings. It also will help them prepare applications that include all of the information the compendium will need to recognize an indication as medically accepted.

For example, the evaluation process should include the following criteria to create greater transparency:

- Use of Pre-Specified Published Criteria for Weighing Evidence.
- Use of Pre-Specified Published Process for Making Recommendations.
- Publicly Transparent Process for Evaluating Therapies.
- Public Identification of the Members of the Advisory/Scientific Review Committees.

As part of its evaluation, the compendium should have an explicit review process, including a method for reviewers to ask questions and applicants to respond to them. Should the reviewers not find the evidence supporting a request to be adequate, they should clearly and concisely explain the reasons why, giving the applicant and other interested parties an opportunity to respond. Moreover, the compendia should establish expert panels comprised of practicing health care professionals and experts in the clinical topic under review. These members' identities, affiliations, and disclosures should be made public. By increasing the level of transparency for the compendia review process and welcoming an exchange of dialogue between compendia and stakeholders, the quality and comprehensiveness of the information published will be the best available.

Finally, the compendium should have a process in place to notify stakeholders of its decisions. Beneficiary access to therapy should not be limited or delayed because there was no notice given by a compendium, forcing the

stakeholders, including Medicare, to pore over the listings in order to find changes in them.

4. Detailed description of the evidence reviewed for every individual listing

The compendium should provide a detailed description of the evidence reviewed for every individual listing to help physicians and policymakers understand the basis for each listing. Compendia should employ the full range of valid data sources available to inform new listings, including both prospective and observational data, data collected by manufacturers and specialty societies, and data on patient-reported outcomes, such as quality of life, patient functionality and patient preferences that are important to patients and physicians. While current compendia publishers adhere to rigorous evidence standards before accepting new indications, consideration of emerging medical practice despite lack of published peer-reviewed literature on large randomized, controlled clinical trials, may be appropriate for consideration on a case-by-case basis. If a limited number of therapeutic alternatives exist for a particular disease, the compendia should strive to include current standards of care for treating such diseases in order to ensure patients have options for the best care available.

Each listing should provide sufficient detail to allow readers to determine whether the compendium considered all of the recent research regarding a treatment option and why it decided to designate a listing as, “recognized,” “not recognized,” or “acceptance not established.” In addition, we recommend that each compendium clearly explain its rating systems for the strength or quantity of evidence supporting an indication.

5. Medicare should continue to recognize at least three compendia

BIO recommends that Medicare continue to recognize at least three compendia. As noted above, the statute clearly reflects Congress’s intent for Medicare carriers to use at least three compendia, including the AHFS-DI and USP-DI or its successor publications. Because the AMA-DE no longer exists, we urge CMS to, at a minimum, replace this publication with the NCCN Drugs and Biologicals Compendium™ and focus on other publications. Recognition of additional compendia could 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. 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. To improve the chances of a treatment option being recognized by a compendium in a timely manner, we recommend that CMS continue to recognize multiple compendia for use in Medicare’s coverage decisions and allow each compendium the needed flexibility to add new indications.

6. The special case of therapies used to treat rare cancers

Therapies used to treat patients with rare cancers have a much greater challenge gaining recognition and listing in a compendium, instead relying on peer reviewed literature to publicize new indications. CMS accounts for this difficulty by instructing its carriers to “evaluate the quality of the evidence in published peer reviewed medical literature”⁶ for indications that are not described in the compendia. Providers treating patients suffering from rare cancers face a unique challenge. Research may identify promising treatment options; however, randomized controlled trials (RCTs) are unlikely to have been performed because of the small patient populations involved. If the compendia do not acknowledge this research, Medicare carriers might not cover the treatment option.

We ask the MCAC to take the unique issues facing treatments for rare cancers into account as it reviews the desired characteristics of compendia. First, the compendia should not limit their review only to large RCTs, but instead should examine data from other types of trials too. For example, data from Phase II trials can be very important and often is the only data available for indications involving rare cancers. Second, the compendia should describe the basis for their listings, so providers quickly can analyze the difference between a RCT and results based on a non-randomized trial involving a much smaller number of patients. We believe these characteristics will help ensure that patients battling rare cancers have access to appropriate new treatments as soon as possible.

7. Undesirable Characteristics

A. Specific Clinical Recommendations

The decision-making process should not infringe or impede physicians’ clinical judgment in choosing the most medically appropriate therapies for their patients. As such, the following characteristics should not be adopted by individual compendium:

⁶ Medicare Benefit Policy Manual (CMS Pub. 100-2), ch. 15, § 50.4.5.

- Explicit recommendations on the sequential use of a therapy or combination in relation to other therapies.
- Net benefit analysis based on potential harm and potential benefit.
- Explicit stratification of the risks of available therapies.
- Explicit listing of appropriate combination of therapies.

B. Conclusions Based on Unclear Evidence

The compendia should not explicitly list a medication as “not recommended” for an indication unless there is clear evidence supporting this conclusion. Compendia should remain silent on indications that are not currently supported by sufficient evidence since medical and scientific evidence is constantly evolving. Even though evidence does not support use of a therapy as safe and effective for a particular disease, the product still may be a promising therapeutic option once more data are collected.

8. Conclusion

We sincerely hope that the MCAC will give thoughtful consideration to our comments and will incorporate our suggestions. BIO’s members are at the forefront of cancer care, we are converting these deadly diseases from a death sentence to a chronic disease with the ultimate goal of curing all cancer. Please feel free to contact Jayson Slotnik at (202) 312-9273 if you have any questions regarding these comments. Thank you for your attention to this very important matter.

Respectfully submitted,

/s/

James C. Greenwood
President & CEO
Biotechnology Industry Organization

cc: Barry Straube, MD, Acting Chief Medical Officer, CMS
Steve Phurrough, MD, MPA, Director, Coverage and Analysis Group, CMS
Peter Bach, MD, MAPP, Senior Advisor, Office of the Administrator, CMS